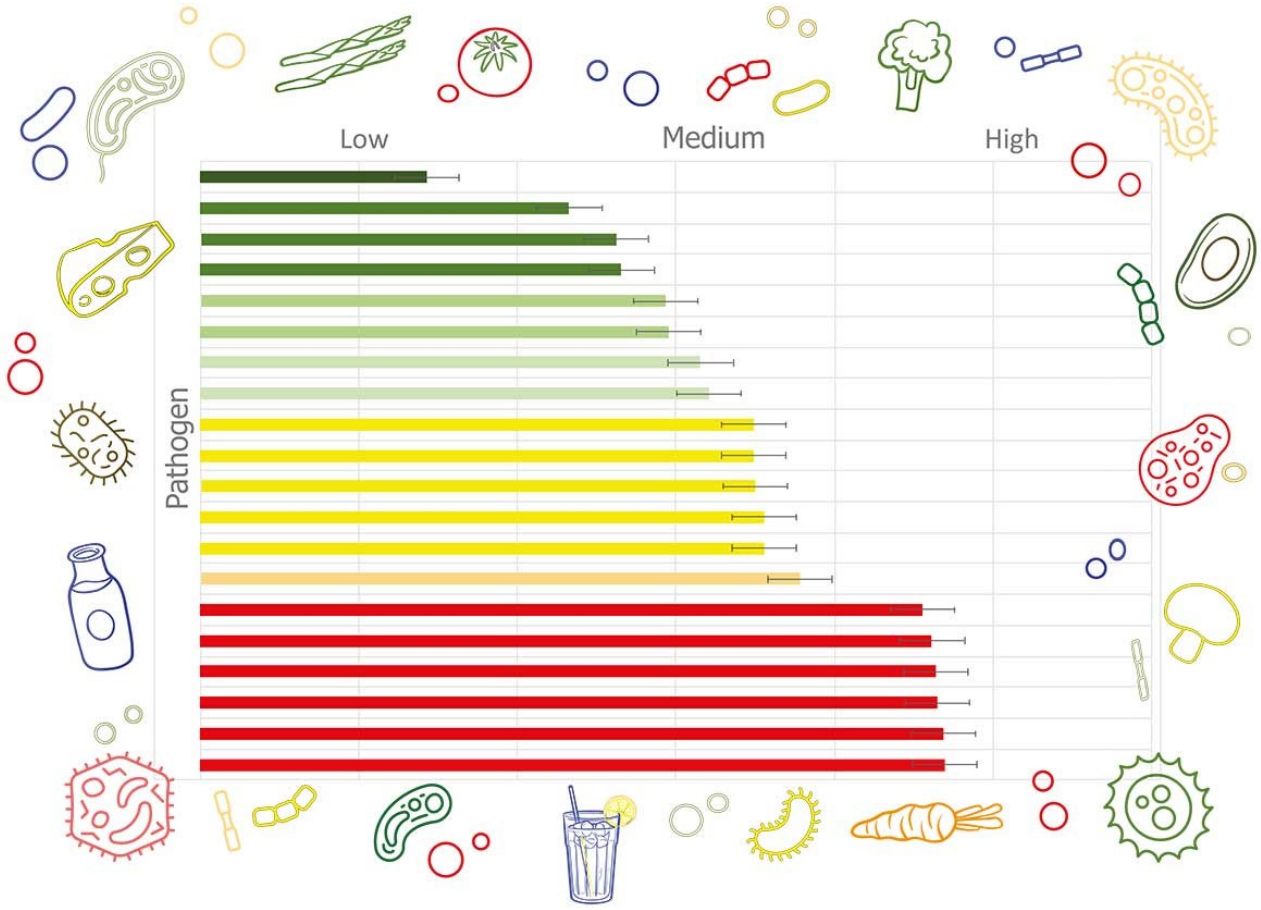
Vitenskapskomiteen for mat og miljø
Norwegian Scientific Committee for Food and Environment



VKM Report 2021: 10

Risk ranking and source attribution of food- and waterborne pathogens for surveillance purposes

Opinion of the Panel on Biological Hazards of the Norwegian Scientific Committee for Food and Environment

Final 09.06.2021
Report from the Norwegian Scientific Committee for Food and Environment (VKM) 2021: 10
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Norwegian Scientific Committee for Food and Environment (VKM)
Po 222 Skøyen
N – 0213 Oslo
Norway

Phone: +47 21 62 28 00
Email: vkm@vkm.no

vkm.no
vkm.no/english

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Final 09.06.2021

Risk ranking and source attribution of food- and waterborne pathogens for surveillance purposes

Authors of the opinion

VKM has appointed a project group consisting of 8 VKM members and one external expert to answer the request from the Norwegian Food Safety Authority. Members of the project group that contributed to the drafting of the opinion (in alphabetical order after chair of the project group):

Taran Skjerdal – Chair of the project group and member of the Panel on Biological Hazards in VKM. Affiliation: 1) VKM; 2) Norwegian Veterinary Institute

Marina Aspholm - Member of the project group. Affiliation: VKM, 2) Norwegian University of Life Sciences

Danica Grahek-Ogden – Member of the project group and project leader in the VKM secretariat. Affiliation: VKM.

Solveig Jore – Member of the project group. Affiliation: 1) VKM, 2) Norwegian Institute of Public Health

Georg Kapperud – Member of the project group. Affiliation: 1) VKM, 2) Norwegian Institute of Public Health, 3) Norwegian University of Life Sciences

Kjetil K. Melby – Member of the project group. Affiliation: 1) VKM, 2) University of Oslo; 3) Oslo University Hospital

Trond Møretrø – Member of the project group. Affiliation: 1) VKM, 2) Nofima

Mette Myrmel – Member of the project group. Affiliation: 1) Norwegian University of Life Sciences

Truls Nesbakken – Member of the project group. Affiliation: 1) VKM, 2) Norwegian University of Life Sciences

Lucy Robertson – Member of the project group. Affiliation: 1) VKM, 2) Norwegian University of Life Sciences

Norval Strachan – Member of the project group. Affiliation: 1) University of Aberdeen

The opinion has been assessed and approved by the Panel on Biological Hazards. Members of the Panel on Biological Hazards that contributed to the assessment and approval of the opinion (in alphabetical order before chair/vice-chair of the Panel/Committee):

Marina Aspholm - Member of the project group. Affiliation: VKM, 2) Norwegian University of Life Sciences

Solveig Jore – Member of the project group. Affiliation: 1) VKM, 2) Norwegian Institute of Public Health

Georg Kapperud – Member of the project group. Affiliation: 1) VKM, 2) Norwegian Institute of Public Health, 3) Norwegian University of Life Sciences

Kjetil K. Melby – Member of the project group. Affiliation: 1) VKM, 2) University of Oslo; 3) Oslo University Hospital

Trond Møretrø – Member of the project group. Affiliation: 1) VKM, 2) Nofima

Truls Nesbakken – Member of the project group. Affiliation: 1) VKM, 2) Norwegian University of Life Sciences

Lucy Robertson – Member of the project group. Affiliation: 1) VKM, 2) Norwegian University of Life Sciences

Taran Skjerdal – Chair/Vice-chair of the Panel on on Biological Hazards in VKM. Affiliation: 1) VKM; 2) Norwegian Veterinary Institute

Acknowledgment

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Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third-party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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1 Summary

Background

Providing risk managers with the information that they need for decision making is an important element in food-safety management. The present risk assessment was undertaken to establish a scientific basis that could be used to assist the Norwegian Food Safety Authority (NFSA) in implementing risk-based surveillance, monitoring, and control programmes for pathogens in food and water.

The assessment approach used here consisted of two steps:

(1) risk ranking of 20 selected pathogens based on the incidence and severity of their associated diseases following infection with the pathogens via food or water, and

(2) a source attribution process aimed at identifying the main pathogen-food combinations that may pose a risk to human health for each of the ranked pathogens.

We used an expert knowledge elicitation (EKE) procedure with a panel of nine experts, including all eight members of the Panel on Biological Hazards of the Norwegian Scientific Committee for Food and Environment (NSCFE) and one invited expert on food/water-borne viral infections.

Risk ranking

The 20 pathogens selected for risk ranking were defined in the terms of reference (ToR) received from NFSA. We performed a multicriteria-based ranking of the pathogens in terms of their public health impact from food/water-borne transmission in Norway.

The risk ranking utilized six criteria that estimated the incidence of food- and waterborne illness attributable to each pathogen, the severity of acute and chronic illness, the fraction of chronic illness, fatality rate, and the probability for future increased disease burden. For each pathogen, all criteria were scored by the expert panel members, and individual criterion scores were combined into an overall score for every pathogen. To achieve this, each criterion was weighted in terms of its relative importance, as judged by the expert panel. The overall scores so calculated were the basis for the ranking.

Source attribution

For each of the ranked pathogens, the subsequent source-attribution process aimed to identify the main food vehicles, reservoirs, and sources of infection for outbreak-related and sporadic cases of illness, the relative importance of food sources, and preventable risk factors in Norway. To achieve this, both microbiological and epidemiological data were scrutinized. These encompassed results from national surveillance and monitoring programmes, prevalence surveys, outbreak investigations, and research, including analytic

epidemiological studies. When Norwegian data were sparse or absent, international reports and research were used.

Results

The six highest-ranked pathogens were, in descending order: *Toxoplasma gondii*, *Campylobacter* spp., *Echinococcus multilocularis*, enterohaemorrhagic *E. coli* (EHEC), *Listeria monocytogenes*, and non-typhoid *Salmonella*. It should be emphasized, however, that confidence intervals revealed considerable overlaps between the scores.

The food vehicles associated with the pathogens varied widely. It is notable, however, that fresh produce was identified as being among the main food vehicles for 12 of the 20 pathogens, drinking water was associated with 8, and 5 were linked to raw milk or products thereof.

Reliability and validity

There are several limitations to the present assessment that should be considered when interpreting the results. An evaluation of the reliability and internal validity of the results is presented.

An expert-based, multicriteria ranking approach for scoring of data gaps was employed. In all, 13 criteria were scored by the panel members according to availability of the data utilized. This procedure identified considerable data gaps in crucial information needed in the preceding risk ranking and source attribution procedures.

Conclusion

Risk ranking of 20 selected food- and waterborne pathogens in terms of their public health impact was performed, and the main food vehicles associated with transmission of each pathogen were identified. The results presented may be subject to change over time as new data become available from surveillance and research on pathogens and the diseases they cause. Thus, the systematic and transparent process described in this report is probably most useful if it is repeated and updated regularly such that recent information can be taken into account.

Key words: VKM, risk assessment, Norwegian Scientific Committee for Food and Environment, pathogens, risk ranking

2 Sammendrag på norsk

Bakgrunn

Denne risikorangering ble utført for å utarbeide et vitenskapelig grunnlag som Mattilsynet kan bruke til å implementere risikobaserte overvåkings- og kontrollprogrammer for smittestoffer i mat og vann. Grunnlaget er nødvendig og viktig for å kunne ta beslutninger om håndtering av mattrygghet.

Metoden som ble brukt for rangering besto av to trinn:

(1) risikorangering av 20 smittestoffer, valgt med utgangspunkt i forekomst og alvorlighetsgrad av sykdommene som forårsakes av infeksjon med smittestoffene via mat eller vann.

(2) en prosess for å finne hvilke matvarer som er smittekilder for hver av de rangerte smittestoffene (kildetildeling), for å identifisere de viktigste kombinasjonene av smittestoff/mat som kan utgjøre en risiko for menneskers helse.

Vi brukte en såkalt «expert knowledge elicitation (EKE)- metode» med et panel på ni eksperter, inkludert alle medlemmene av panelet for hygiene og smittestoffer i VKM, og en ekstern ekspert på mat/vannbårne virale infeksjoner.

Risikorangering

De 20 utvalgte smittestoffene var definert i bestillingen fra Mattilsynet.

Risikorangeringen er basert på seks kriterier som vurderte forekomsten av mat- og vannbåren sykdom som kan tilskrives hvert smittestoff, alvorlighetsgraden av akutt og kronisk sykdom, andel av de smittede som blir kronisk syke, dødelighet og sannsynligheten for fremtidig økt sykdomsbyrde Hvert enkelt medlem av prosjektgruppa scoret alle kriteriene for hvert smittestoff, og kriteriepoengene fra hvert enkelt medlem ble satt sammen til en samlet poengsum for hvert smittestoff. Hvert kriterium ble vurdert av prosjektgruppen og dets relative betydning vektet opp mot de andre kriteriene. De endelige beregningene som inkluderte scoringer og vekting, var grunnlaget for rangeringen.

Kildetildeling

Kildetildelingen hadde som mål å identifisere:

- de viktigste matvarer hvor de stoffene er regelmessig påvist
- reservoarene for smittestoffene
- infeksjonskildene for utbrudd og sporadiske sykdomstilfeller
- den relative betydningen av mat som smittekilde
- risikofaktorer som kan forebygges

For å identifisere kildene undersøkte vi både mikrobiologiske og epidemiologiske data. Undersøkelsene omfattet resultater fra nasjonale overvåkings- og kontrollprogrammer, forekomstundersøkelser, utbruddsundersøkelser og forskning, inkludert analytiske epidemiologiske studier. Når norske data var sparsomme eller fraværende, brukte vi internasjonale rapporter og forskning.

Resultater

De seks høyest rangerte smittestoffene var i fallende rekkefølge: *Toxoplasma gondii, Campylobacter* spp*., Echinococcus multilocularis,* enterohaemorrhagic *E. coli (*EHEC*), Listeria monocytogenes* og ikke-tyfoid *Salmonella*. Det må understrekes at konfidensintervaller avslørte betydelige overlapp mellom scoringer

Det var stor variasjon med hensyn til hvilke matvarer som var kilde til det enkelte smittestoff. Det er imidlertid nødvendig å bemerke at ferske vegetabiler ble identifisert som en av de viktigste matvarekildene for 12 av de 20 smittestoffene, drikkevann var assosiert med åtte, og fem var knyttet til råmelk eller produkter av råmelk.

Pålitelighet og validitet

Rangeringen har usikkerheter som bør vurderes når man tolker resultatene. Rapporten inneholder en evaluering av resultatenes pålitelighet og validitet..

Prosjektgruppen har evaluert resultatenes pålitelighet og validitet og har scoret datamangler ved å benytte ekspertbasert multikriterierangering. I alt ble 13 kriterier scoret i henhold til tilgjengeligheten av dataene som ble brukt. Evalueringen identifiserte at det manglet betydelige mengder data i informasjon som er nødvendig for risikorangering og kildetildeling.

Konklusjon

VKM har rangert 20 utvalgte mat- og vannbårne smittestoffer med hensyn til risiko for negativ påvirkning av folkehelsen, og identifisert de viktigste matvarene som er kilder til overføring av hvert enkelt smittestoff. Resultatene kan endres over tid etter hvert som nye data fra overvåking og forskning på smittestoffer og sykdommene de forårsaker blir tilgjengelige. Den systematiske og transparente prosessen som er beskrevet i denne rapporten blir trolig mest nyttig hvis den gjentas og oppdateres regelmessig med ny informasjon.

3 Background and terms of reference as provided by the Norwegian Food Safety Authority/ Norwegian Environment Agency

The Norwegian Food Safety Authority annually carries out various monitoring and surveillance programmes for infectious agents in food on the Norwegian market. Food and drink should not contain infectious agents hazardous to health. A good overview of the occurrence of infectious agents in food is important and is achieved through monitoring. To be able to prioritize which infectious agents and foods should be monitored in the future, the Norwegian Food Safety Authority needs a knowledge-based ranking of infectious agents in food and drink that may pose a potential risk to public health.

This ranking should be based on defined and justified criteria for assessment of the health risk associated with various agent-food combinations. The overview will give The Norwegian Food Safety Authority knowledge-based monitoring and surveillance of infectious agents in food and drink.

Terms of Reference

As a basis for the Norwegian Food Safety Authority's monitoring of human pathogens in food, we want VKM to prepare a ranking of infectious agents and food combinations which may pose a risk to public health. Food here refers to different types of food and drink sold on the Norwegian market (both raw materials, processed, and ready-to-eat food, produced in Norway and abroad). The level of detail should be assessed by VKM, food groups and the use of several levels may be relevant.

In order to determine which criteria are to be used as a basis for the ranking, VKM should take into consideration that the report will be used as a basis for the Norwegian Food Safety Authority's future monitoring and surveillance. Aspects that may be relevant to consider are, e.g., the number of registered cases of illness per year (acquired both in Norway and abroad), the severity of disease, the incidence and size of outbreaks in Norway and abroad, findings from monitoring programmes, data from RASFF (Rapid Alert System for Food and Feed), EFSA, VKM and others knowledge institutions, exposure in the population (incl. vulnerable groups), infectious agents' traits related to growth and survival, the origin of the food, production process etc. The choice of criteria must be justified in the report.

It is desirable that VKM also includes additional information that is relevant for sampling and analysis of the various infectious substances/foods; e.g. seasonal variation in occurrence. Below is a list of some of the most common foodborne infectious agents that cause disease

in humans. The Norwegian Food Safety Authority wishes these infectious agents to be included in VKM's assessment. Others infectious agents can also be included if VKM deems it appropriate.

For some infectious substances, there is currently extensive regulatory control, such as for trichinosis, tuberculosis caused by *Mycobacterium bovis*, brucellosis and transmissible spongiform encephalopathy. These infectious agents, as well as antibiotic resistance, are not included in the list.

Human pathogens that should be included in the ranking, in alphabetical order, are:

- *Anisakis simplex*
- *Bacillus cereus*
- *Campylobacter* spp.
- *Clostridium botulinum*
- *Clostridium perfringens*
- *Cryptosporidium* spp.
- *Echinococcus multilocularis*
- *Escherichia coli*
- *Giardia duodenalis*
- Hepatitis A virus
- Hepatitis E virus
- *Listeria monocytogenes*
- *Norovirus*
- *Salmonella* spp.
- *Shigella* spp.
- *Staphylococcus aureus*
- *Toxoplasma gondii*
- *Vibrio* spp.
- *Yersinia enterocolitica*

4 Literature and data

4.1 Literature search

PubMed

For each pathogen, literature searches were undertaken using the Advanced Search Builder provided by PubMed (www.ncbi.nlm.nih.gov/pubmed). There was no restriction on language or publication year. The search strings applied are specified in the individual sub-chapters in chapter 13.

Websites

In addition, searches were performed on the websites of the Norwegian Food Safety Authority, Norwegian Veterinary Institute, Institute of Marine Research, Norwegian Institute of Public Health , Norwegian Scientific Committee on Food and the Environment, European Food Safety Authority, European Centre for Disease Prevention and Control, and World Health Organization to identify relevant reports from ongoing surveillance and monitoring programmes, including annual reports, status descriptions and surveys, inspection projects, outbreak investigations, microbial risk assessments, and scientific opinions, as well as general descriptions of the various agents and diseases.

Relevance screening

The titles of all hits were scanned, and for those that were of potential relevance, the abstracts were also inspected. Citations were excluded if they did not relate to the terms of reference. The reference lists in selected publications and reports were scrutinized to identify additional articles, international reviews, or reports, overlooked by the primary searches.

4.2 Data

NFSA provided data on prevalence of agents in different foodstuffs from surveillance and monitoring programmes as well as the data form RASFF from year 2000. Additional data were obtained from literature searches described above.

5 Method for risk ranking

The 20 pathogens selected for risk ranking were defined in the terms of reference (ToR) received from NFSA. We performed a multicriteria-based ranking (multicriteria decision analysis; MCDA) of the pathogens according to their public health impact, using an expert knowledge elicitation (EKE) procedure with a panel of nine experts. All experts in the panel have a PhD in their field of expertise, six of them are university professors, two are senior researchers and one is a researcher. The experience in their respective fields (after PhD) ranges from 14 to 39 years.

The decision about using a quantitative method was based on the availability of the evidence, which was deemed to be sufficient. MCDA suited our needs as:

- it enables incorporation of expert opinion and empirical data from a variety of sources
- it is a flexible methodology that can be adapted to suit the context of the risk-ranking exercise
- the number of criteria used can be varied according to need
- weighting can be assigned to criteria
- it can be readily implemented in widely used software, such as Microsoft Excel
- new information can be incorporated as it emerges in order to update the ranking, without needing to rerun the entire ranking exercise

There is no standard methodology for conducting multicriteria assessments; such rankings are often designed for specific risk-management purposes. However, the majority of these rankings follow a similar approach: a number of selected hazards are scored according to a set of criteria, including, but not always limited to, public health. The criteria scores are then multiplied by individual weights to calculate an overall score for each hazard.

In the present report, a modified expert-based, multicriteria ranking tool developed and applied by a Joint FAO/WHO Expert Meeting (FAO & WHO, 2014) was employed.

5.1 Identification and definition of criteria for ranking

The 20 selected pathogens were ranked according to their public health impact in Norway using six criteria related to the incidence and severity of illness (C1 - C6), which were subsequently weighted to calculate an overall risk score for every pathogen. For each of the six criteria, five scoring levels were defined (Table 5-1).

Table 5-1. Criteria and scoring levels with their definitions.

Criteria		**Scoring levels**				
		0	**1**	**2**	**3**	**4**
C1	Number of foodborne illness	<10	10 – 100	100 – 1 000	1 000 – 10 000	>10 000
C2	Acute morbidity severity	0	Very mild	Mild	Moderate	Severe
C3	Chronic morbidity severity	0	Very mild	Mild	Moderate	Severe
C4	Fraction of chronic illness	0 %	<25%	25-50%	50-75%	>75%
C5	Case fatality ratio	0 %	<0.1%	0.1-1%	1-10%	>10%
C6	Probability for increased human burden of disease	0 %	0–25% (low)	25–75% (medium)	75–100% (high)	100% (still increasing)

Compared with the FAO/WHO report on risk ranking of foodborne parasites (2014), the following modifications were implemented:

- exclusion of criteria relevant for trade as those were beyond the remit defined by the ToR
- exclusion of the criterion for geographical distribution, as this is of marginal relevance in a national ranking
- modification of the intervals for scoring number of illness to be appropriate for the size of the population of Norway

Scoring levels used for acute and chronic morbidity severity are in accordance with those used in the FAO/WHO report (2014).

A short description of the criteria and data sources employed to score the pathogens are presented below. Detailed information is provided in Chapter 14, Appendix III - Supplementary information on criteria for risk ranking and exposure assessment.

Other sources of information, like the incidence of outbreaks in Norway and abroad, findings from monitoring programmes, data from RASFF (Rapid Alert System for Food and Feed), EFSA, VKM and others knowledge institutions, exposure in the population (incl. vulnerable groups), infectious agents traits related to growth and survival, the origin of the food and production process were used in source attribution. Detailed information is presented in chapter 13, Appendix II – Source attribution.

5.1.1 Number of illnesses (C1)

For each pathogen, the total number of ill persons reported to have been infected in Norway was estimated using information from the following sources:

- Norwegian Surveillance System for Communicable Diseases (MSIS, see 14.2.1)
- Web-based Outbreak Alert System (Vesuv, see 14.2.2)
- Norwegian Syndromic Surveillance System (NorSySS, see 14.2.3)
- National and international scientific articles and reports

Data from the surveillance system (MSIS) were adjusted to correct for underestimation due to under-reporting and under-ascertainment. This was achieved by using information from the sources 2-4 listed above, as described in Appendix III.

5.1.1.1 Number of illnesses attributable to food- and waterborne transmission

Many food- and waterborne illnesses can be transmitted in several different ways:

- By direct contact with infectious animals or persons, or with the infectious agents in their faeces, urine, vomit or secretions
- Indirectly via vehicles (food and beverages of animal or vegetable origin, other animal products, objects, and water)
- Indirectly via vectors (insects and ticks, e.g., tularaemia).

The proportion of illnesses attributable to food- and waterborne transmission varies between diseases, and there are major differences between countries. For the majority of the diseases in this report, scientific data about the relative importance of different sources of infection in Norway are insufficient to justify reaching firm conclusions. Estimates of the number of illnesses attributable to food and water were therefore largely a best guess (see Chapter 14).

5.1.2 Morbidity severity and lethality (C2 – C5)

The severity of acute and chronic morbidity, the fraction of chronic illness, and case-fatality rates were evaluated and scored using information from national and international publications.

Detailed information on each disease was obtained from the web-based Guidelines for Communicable Disease Control (Smittevernveilederen) published by the Norwegian Institute of Public Health (NIPH) *https://www.fhi.no/nettpub/smittevernveilederen/* and elsewhere as appropriate

For each disease, the Guidelines include information on clinical manifestations (symptoms, duration of acute illness, sequelae, possible chronic consequences, and death rate), sources and mode of infection, agent reservoir, and infection control measures. The Guidelines are adapted to Norwegian conditions and present an overview of incidence and trends for the diseases based on MSIS data.

5.1.2.1 C234 – a combined criterion for morbidity severity

The criteria for morbidity severity (C2, C3 and C4) are interdependent; for instance, there is an obvious relation between C3 and C4 (Chronic morbidity severity and Fraction of chronic illness). This was taken into account by combining these three criteria into a single, adjusted criterion for morbidity severity: C234 = [C2 x (4-C4) + C3 x C4]/4. The rationale for this equation is explained below:

Each of the criteria C2, C3 and C4 is scored on a scale from 0 to 4 (Table 5-1). In the equation for C234, fraction of chronic illness and fraction of acute illness in the patient population are regarded as inverse variables, the sum of which is always 4: If the fraction of chronic illness (C4) is high, the fraction of patients who only develop acute illness is correspondingly low, (4 - C4), and *vice versa*. For instance, if all cases are chronic (C4 = 4), then the fraction of patients with acute illness, only, equals (4 - C4) = 0. Conversely, if no cases are chronic, C4 = 0, and the fraction of patients with only acute illness equals (4 - C4) = 4. Since C4 is scored between 0 and 4, the sum of C4 and (4 - C4) will in any case be equal to 4.

In the equation, the scores for acute illness severity (C2) and chronic illness severity (C3) are assigned dissimilar importance according to how common the fractions of acute and chronic illness are in the patient population. This is achieved by multiplying C2 and C3 by their corresponding fractions, (4 - C4) and C4, respectively, which are then added to obtain an overall morbidity severity score: [C2 x (4 - C4) + C3 x C4]. However, note that the score for C234 obtained by this calculation varies on a scale with 16 being the highest achievable value, as opposed to the other criteria, C1, C5 and C6, which are scored from 0 to 4. To ensure that all criteria have the same scaling, the overall score for morbidity severity is divided by 4. Thus, C234 = [C2 x (4 - C4) + C3 x C4] / 4. This results in C1, C234, C5 and C6 having the same relative importance in the total score. This is necessary to ensure that

the relative importance attributed to C234 is not four times greater than the scores for each of the criteria C1, C5, and C6.

5.1.3 Probability for increased human burden of disease (C6)

This criterion was used to assess different factors likely to impact the future levels of food- and waterborne illness acquired in Norway due to infection with each of the pathogens under consideration. The factors considered included:

- Technological changes: implementation of new procedures for production, processing, storage and distribution of foods
- Changes in consumer preferences and habits: trends in eating habits, preferences, avoidance behaviour, and knowledge about food safety, including compliance with adequate kitchen-hygiene practices
- Changes in trade policy: increased import of foods from countries where the level of contamination is higher than in Norway, including import of new products
- Regulatory changes: implementation of directives, regulations, decisions, and other acts as a result of international trade agreements, which may influence food-production standards or trade
- Demographic changes: escalating numbers of elderly people and persons with reduced immunity, who are more susceptible to infection, and for whom an infection may have serious consequences
- Epidemiological changes in the pathogens: introduction of variants with increased virulence or increased potential for survival, growth, and dissemination in the food chain
- Climate change: Warmer and wetter climate influencing contamination, growth, and survival of pathogens at various stages throughout the food-production chain, in the environment, and in drinking water supplies

5.2 Expert knowledge elicitation (EKE)

EKE is a scientific consensus methodology that synthesises the opinions of experts on a subject, for which there is uncertainty due to insufficient data, data are inconclusive or lacking, or is concerned with the study of rare events. EKE allows for an "educated guess" for the topic under consideration. In the present assessment, EKE was chosen to score and rank the pathogens due to uncertainty and lack of data, as described in 5.1. This approach was also utilized to score data gaps (see 8.2).

In performing EKE, some factors need to be taken into consideration. The persons participating should be experts in the area under assessment. In the present study, the risk ranking was carried out by a panel consisting of nine experts, including all eight members of the Panel on Biological Hazards of the Norwegian Scientific Committee for Food and Environment (NSCFE) and one invited expert on viral infections (MM). Thus, the panel

encompassed experts in all three pathogen groups under consideration (i.e., bacteria, viruses, and parasites), although no one member was an expert on all three pathogen groups.

The objective of obtaining the experts' informed judgment, based on all relevant evidence, was met by conducting systematic literature reviews, also including data available from national and international sources. Discrepancies in interpretations or judgements among panel members were addressed by adopting strategies designed to help experts harmonise the use of criteria and scales for scoring. This included repeating the process of scoring and group discussions twice to allow the panel members to provide, and listen to, comments from those with greater expertise, review their scores accordingly, and co-ordinate the results.

5.3 Expert scoring of each pathogen based on the criteria

Prior to risk ranking, each member of the expert panel was requested to compile available information on the incidence and medical consequences for 1-3 selected pathogens; pathogens were allocated to the experts according to their competence and experience. The results are presented as separate, pathogen-specific chapters in Appendix I - Hazard identification and characterisation.

This information was shared with all panel members and used to direct the panel members towards information relevant to the scoring criteria. Each expert then scored all pathogens independently according to the six criteria listed in Table 5-1. For each criterion, the agents were scored on a scale ranging from 0 to 4 (defined in Table 5-1). Expert scores were sent to the NSCFE secretariat by mail and were compiled in a separate table for each pathogen. After the first round of scoring, a meeting was organised to facilitate discussion of criteria scores for each pathogen.

Discussions around large discrepancies in initial scores allowed the panel members to identify differences in interpreting criteria. Once the expert panel reached consensus and greater clarity and agreement on criteria definitions were obtained, experts conducted a review of their scores.

Following a second round of independent scoring, the panel again discussed the revised results and agreed on final criteria scores. For each criterion and pathogen, the mean value of the scores from the nine panel members was calculated (Table 5-2). Figures illustrating scoring of number of illness (C1) against C234, C5 and C6 are shown in Figure 5-1, Figure 5-2, and Figure 5-3. Although the weighting was not taken into account, the figures may serve to illustrate the influence of weighting on the ranking. For instance, if C1 is considered the most important criterion (W1 = 1), the highest ranked pathogens are norovirus followed by *Campylobacter*. Likewise, when morbidity severity is considered to be of maximum importance (W234 = 1), this results in following ranking (in descending order): *Toxoplasma*, *E. multilocularis*, EHEC, *C. botulinum, Listeria* etc. (see Figure 5-1).

Table 5-2. Final scores, represented by mean values over scores from the nine panel members, for pathogens against six public health criteria (C1-C6).

Pathogen	C1 Number of foodborne illness cases	C2 Acute morbidity severity	C3 Chronic morbidity severity	C4 Fraction of chronic illness	C234 (see 5.1.2.1)	C5 Case fatality ratio	C6 Probability for increased HBD [1]
Anisakidae	0.33	1.56	0.78	0.33	1.49	0.00	1.00
B. cereus	1.89	1.56	0.67	0.56	1.43	0.00	0.89
Campylobacter **spp.**	3.22	2.56	2.67	1.00	2.58	1.00	2.11
Cl. botulinum	0.33	3.78	2.89	2.33	3.26	0.89	0.67
Cl. perfringens	1.56	2.00	0.44	0.22	1.91	0.56	0.56
Cryptosporidium **spp.**	1.89	2.33	2.11	1.67	2.24	0.78	2.22
E. coli **(EHEC)**	1.78	3.11	3.56	1.44	3.27	2.00	1.78
E. multilocularis	0.22	0.11	3.56	3.78	3.36	3.44	2.67
G. duodenalis	1.78	2.00	2.00	1.11	2.00	0.11	2.00
Hepatitis A virus	1.11	2.78	1.22	0.78	2.48	1.67	1.56
Hepatitis E virus	0.78	2.67	3.00	1.22	2.77	1.89	1.44
L. monocytogenes	1.00	3.11	3.11	1.78	3.11	3.11	1.89
Norovirus	3.44	1.78	0.89	0.78	1.60	0.56	1.33
Other pathogenic *E. coli*	1.89	2.33	2.11	1.00	2.28	1.00	1.44
Salmonella	2.67	2.89	2.56	1.22	2.79	1.33	1.78
Shigella **spp.**	1.67	2.22	1.89	1.11	2.13	1.00	1.22
S. aureus	1.67	1.89	1.33	0.78	1.78	0.56	0.78
T. gondii	1.56	3.11	3.67	2.67	3.48	2.00	2.00
Vibrio **spp.**	0.78	2.22	2.11	1.22	2.19	1.22	2.67
Y. enterocolitica	1.78	2.33	2.67	2.00	2.50	1.00	1.11

[2] HBD, human burden of disease.

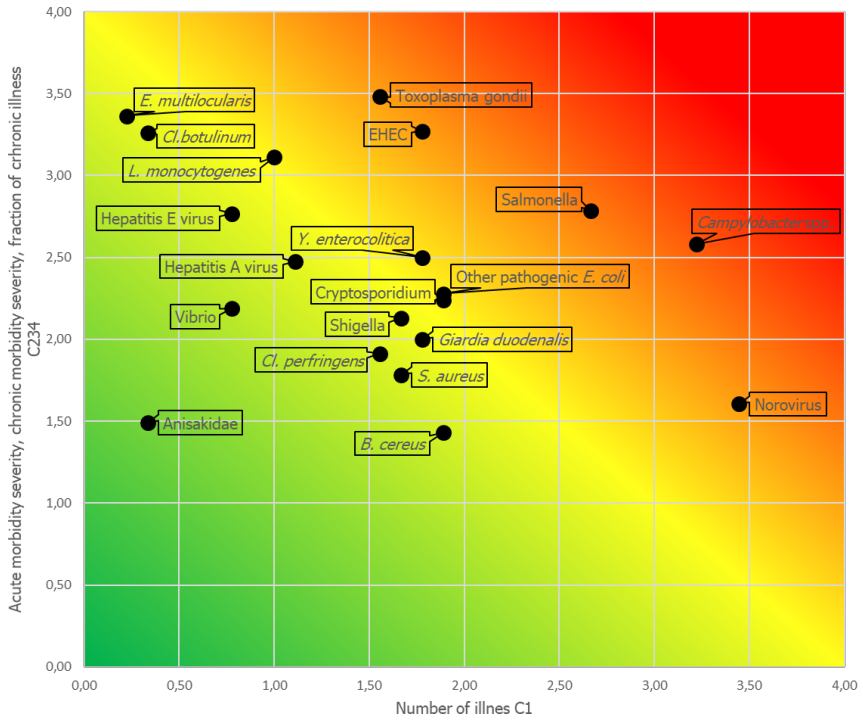

Figure 5-1. Pathogen scores of two public-health criteria: no. of foodborne illnesses, C1 and morbidity severity, C234. The axis scales represent the mean scores assigned by the panel members, as shown in Table 5-2.

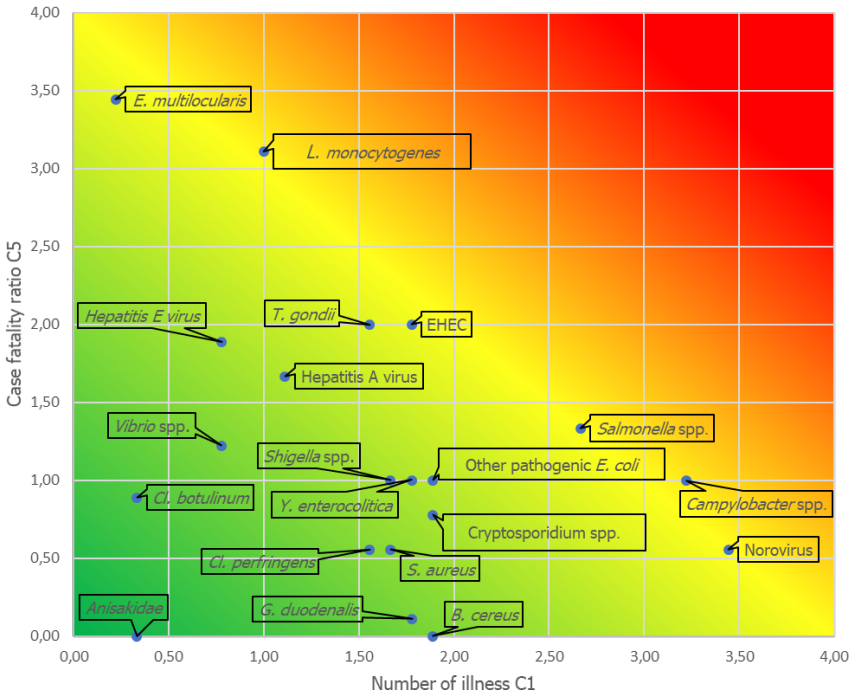

Figure 5-2. Pathogen scores of two public-health criteria: No. of foodborne illnesses, C1 and case fatality ratio, C5. The axis scales represent the mean scores assigned by the panel members, as shown in Table 5-2.

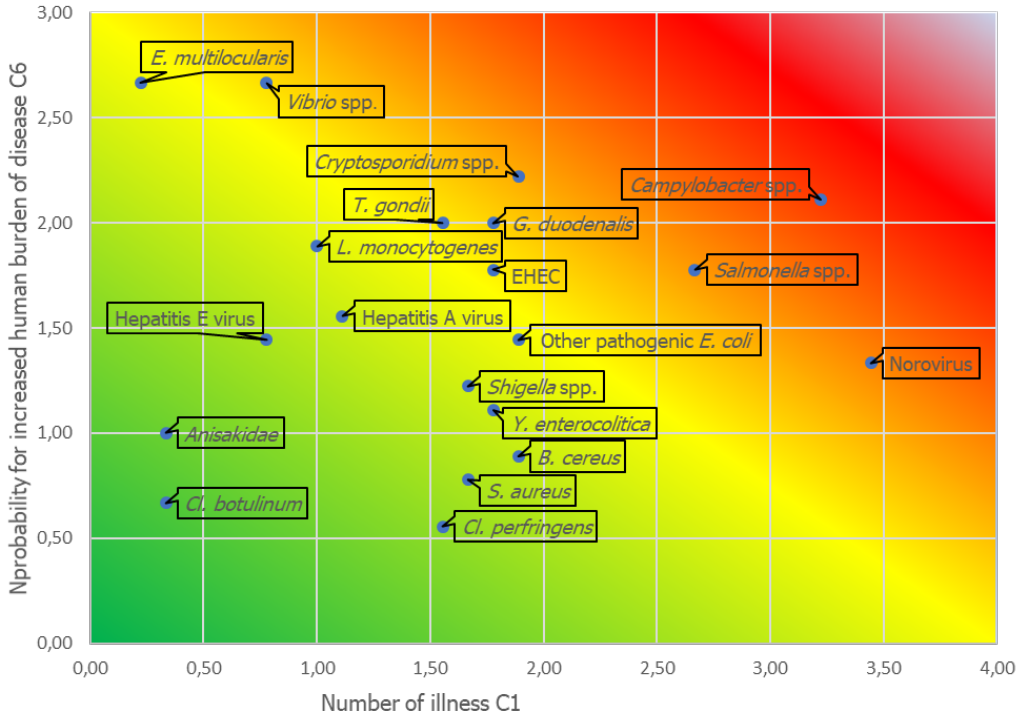

Figure 5-3. Pathogen scores of two public health criteria: No. of foodborne illnesses, C1 and probability for increased human burden of disease, C6. The axis scales represent the mean scores assigned by the panel members, as shown in Table 5-2.

5.4 Weighting of each criterion

In the present multicriteria assessment, individual criterion scores were combined into an overall score for each pathogen. To achieve this, each criterion was weighted as a fraction of the total score, with all weights summing to 100%. Thus, criteria weights reflect the relative importance of the individual criterion in the overall score. In this approach, each criterion is basically assigned its own weight. However, since the criteria for morbidity severity (C2, C3 and C4) are interdependent, they were combined into a single, adjusted criterion for morbidity severity, C234, as explained in section 5.1.2.1.

Accordingly, C234 required a single weight for morbidity severity, shown in Table 2-4 as W234. Thus, although six criteria were used to compute the overall score for each pathogen, there are only four criteria weights.

In the present risk ranking, each member of the expert panel weighted the criteria independently and mean values were calculated (Table 5-3).

Table 5-3. Weighting of the criteria as agreed by the nine members of the expert panel, A-I.

	A	B	C	D	E	F	G	H	I	Mean
W1. Number of foodborne illness cases	0.30	0.33	0.31	0.33	0.30	0.25	0.33	0.31	0.33	0.31
W234. Morbidity severity	0.25	0.33	0.35	0.33	0.30	0.40	0.33	0.33	0.33	0.33
W5. Case fatality ratio	0.25	0.23	0.25	0.23	0.25	0.25	0.23	0.24	0.23	0.24
W6. Probability for increased HBD[1]	0.20	0,11	0.09	0.11	0.15	0.10	0.11	0.12	0.11	0.12
Total	1	1	1	1	1	1	1	1	1	1

[1] HBD, human burden of disease.

5.5 Calculation of overall pathogen scores and subsequent ranking

The overall risk ranking score for each pathogen was calculated by the following equation:

Overall score = (C1 x W1) + [C2 x (4-C4) + C3 x C4]/4 x W234 + (C5 x W5) + (C6 x W6)

where C represents the pathogen-specific criteria scores (Table 2-2) and W represents the weighting for each criterion that is the same for all pathogens (Table 2-3).

As previously explained, C2, C3 and C4 were combined to generate an adjusted score for morbidity severity (see 5.1.2.1), otherwise the calculation is straightforward: individual pathogen criterion scores were multiplied by the relevant fractional weights, and then summed.

The equation is adapted from a corresponding algorithm used in the multicriteria-based risk ranking of foodborne parasites conducted by FAO/WHO (FAO & WHO, 2014) and subsequently adopted by other similar ranking exercises (Bouwknegt, Devleesschauwer, Graham, Robertson, & van der Giessen, 2018; L. Robertson, Sehgal, & Goyal, 2015) .

A spreadsheet model was developed to calculate overall scores for each pathogen and the resulting scores formed the basis for risk ranking of the pathogens included in this report (Table 3-1).

5.6 Calculation of standard deviation and confidence interval

5.6.1 Calculating standard deviation

The final score (FS) is obtained from the following equation:

$$FS = [(C1 \times W1) + [C2 \times (4-C4) + C3 \times C4]/4 \times W234 + (C5 \times W5) + (C6 \times W6) \quad (1)$$

The above equation can be simplified by setting

C234 = [C2 x (4-C4) + C3 x C4]/4 (2)

So that the equation (1) becomes:

FS = (C1 x W1) + (C234 x W234) + (C5 x W5) + (C6 x W6) (1a)

To obtain the error (i.e. standard deviation) in the Final Score it is possible to use the method of propagation of errors to estimate it from the error in each of the variables (Ku, 1966). In general terms, given that *y* is a function of variables v_1, v_2, $\ldots v_n$, then the variance of *y* can be obtained from:

$$\sigma^2(y) = \sum_{i=1}^{n} \left(\frac{\partial y}{\partial v_i}\right)^2 \sigma^2(v_i) \quad (3)$$

Where $\sigma^2(y)$ is the variance of *y*, $\sigma^2(v_i)$ is the variance of the i'th of n variables and $\left(\frac{\partial y}{\partial v_i}\right)$ is the partial derivative of *y* with respect to the i'th variable.

The propagation of errors was conducted in two stages. The first stage involved estimating the standard deviation in C234 in equation (2) and the second stage estimated the standard deviation in the final score from equation (1a).

Estimating the standard deviation in variable C234 (i.e. σ_{C234}):

C234 is a function of 3 variables: C2; C3 and C4. The standard deviation of each of these variables σ_{C2} , σ_{C3} and σ_{C4} was calculated from the scores of the experts. Applying equation (3) to equation (2) an equation for the variance of the variable C234 is obtained.

$$\sigma_{\mathrm{C234}}{}^2 = \left(1 - \frac{\mathrm{C4}}{4}\right)^2 \sigma_{\mathrm{C2}}{}^2 + \left(\frac{\mathrm{C4}}{4}\right)^2 \sigma_{\mathrm{C3}}{}^2 + \left(\frac{\mathrm{C3}}{4} - \frac{\mathrm{C2}}{4}\right)^2 \sigma_{\mathrm{C4}}{}^2 \quad (4)$$

This was then calculated for each of the pathogens under study.

Estimating the standard deviation in the Final Score C234 (i.e. σ_{FS}):

The Final Score (FS) is a function of 8 variables: C1; W1; C234; W234; C5; W5; C6 and W6. The standard deviation of each of these variables (except C234 which was calculated above) was determined directly from the scores of the experts. Applying equation (3) to equation (1a) enables the following expression for the variance of FS to be obtained.

$$\sigma_{\mathrm{FS}}{}^2 = (\mathrm{W1})^2\sigma_{\mathrm{C1}}{}^2 + (\mathrm{C1})^2\sigma_{\mathrm{w1}}{}^2 + (\mathrm{W234})^2\sigma_{\mathrm{C234}}{}^2 + (\mathrm{C234})^2\sigma_{\mathrm{W234}}{}^2 + (\mathrm{W5})^2\sigma_{\mathrm{C5}}{}^2 + (\mathrm{C5})^2\sigma_{\mathrm{W5}}{}^2 + (\mathrm{W6})^2\sigma_{\mathrm{C6}}{}^2 + (\mathrm{C6})^2\sigma_{\mathrm{w6}}{}^2 \quad (5)$$

The standard deviation of the Final Score (i.e. σ_{FS}) can be found by simply taking the square root of the above equation. This was performed for all the pathogens in the study.

5.6.2 Calculating the 95% confidence interval

Since n (the number of experts) is low (i.e., 9) assuming a normal distribution will provide an underestimate (Brase & Brase, 2015). Hence, a t-distribution is used, and the confidence interval covers $\pm\ t_{\mathrm{n}-1;\,\alpha/2}\frac{s}{\sqrt{n}}$, where $t_{\mathrm{n}-1;\,\alpha/2}$ is the critical t value and α is 0.05 and s is the standard deviation.

6 Risk ranking

The results of the risk ranking are presented in Table 6-1, in which the 20 pathogens are listed in descending order according to their overall score. The table also shows scores and weights for all criteria that formed the basis for calculation of overall scores and the ensuing ranking.

Hence, the six highest-ranked pathogens were, in descending order: *T. gondii*, followed by *Campylobacter* spp., *E. multilocularis,* enterohaemorrhagic *E. coli* (EHEC), *L. monocytogenes*, and non-typhoid *Salmonella*.

However, the confidence intervals reveal considerable overlaps between the scores as shown in Figure 6-1.

Table 6-1. Pathogens risk-ranked against public health criteria, based on the overall score for each pathogen.

Pathogen	C1 Number of foodborne illness cases	Weight C1	C234 (see 5.1.2.1)	Weight C234	C5 Case fatality ratio	Weight C5	C6 Probability for increased HBD	Weight C6	Overall risk score	95% CI
T. gondii	1.56	0.31	3.48	0.33	2.00	0.24	2.00	0.12	**2.35**	0.26 (2.09-2.61)
Campylobacter **spp.**	3.22	0.31	2.58	0.33	1.00	0.24	2.11	0.12	**2.34**	0.20 (2.14-2.54)
E. multilocularis	0.22	0.31	3.36	0.33	3.44	0.24	2.67	0.12	**2.32**	0.26 (2.06-2.58)
EHEC	1.78	0.31	3.27	0.33	2.00	0.24	1.78	0.12	**2.32**	0.24 (2.08-2.56)
L. monocytogenes	1.00	0.31	3.11	0.33	3.11	0.24	1.89	0.12	**2.31**	0.22 (2.09-2.53)
Salmonella	2.67	0.31	2.79	0.33	1.33	0.24	1.78	0.12	**2.28**	0.22 (2.02-2.50)
Norovirus	3.44	0.31	1.60	0.33	0.56	0.24	1.33	0.12	**1.89**	0.24 (1.65-2.13)
Hepatitis E virus	0.78	0.31	2.77	0.33	1.89	0.24	1.44	0.12	**1.78**	0.23 (1.55-2.01)
Cryptosporidium **spp.**	1.89	0.31	2.24	0.33	0.78	0.24	2.22	0.12	**1.78**	0.25 (1.53-2.03)
Other pathogenic *E. coli*	1.89	0.31	2.28	0.33	1.00	0.24	1.44	0.12	**1.75**	0.21 (1.54-1.96)
Y. enterocolitica	1.78	0.31	2.50	0.33	1.00	0.24	1.11	0.12	**1.75**	0.17 (1.58-1.92)
Hepatitis A virus	1.11	0.31	2.48	0.33	1.67	0.24	1.56	0.12	**1.75**	0.20 (1.55-1.95)
Shigella **spp.**	1.67	0.31	2.13	0.33	1.00	0.24	1.22	0.12	**1.60**	0.17 (1.43-1.77)
Vibrio **spp.**	0.78	0.31	2.19	0.33	1.22	0.24	2.67	0.12	**1.58**	0.24 (1.34-1.82)
G. duodenalis	1.78	0.31	2.00	0.33	0.11	0.24	2.00	0.12	**1.48**	0.18 (1.30-1.66)
Cl. botulinum	0.33	0.31	3.26	0.33	0.89	0.24	0.67	0.12	**1.47**	0.29 (1.18-1.76)
S. aureus	1.67	0.31	1.78	0.33	0.56	0.24	0.78	0.12	**1.33**	0.25 (1.08-1.58)
Cl. perfringens	1.56	0.31	1.91	0.33	0.56	0.24	0.56	0.12	**1.31**	0.28 (1.03-1.59)
B. cereus	1.89	0.31	1.43	0.33	0.00	0.24	0.89	0.12	**1.16**	0.23 (0.93-1.39)
Anisakidae	0.33	0.31	1.49	0.33	0.00	0.24	1.00	0.12	**0.71**	0.25 (0.46-0.96)

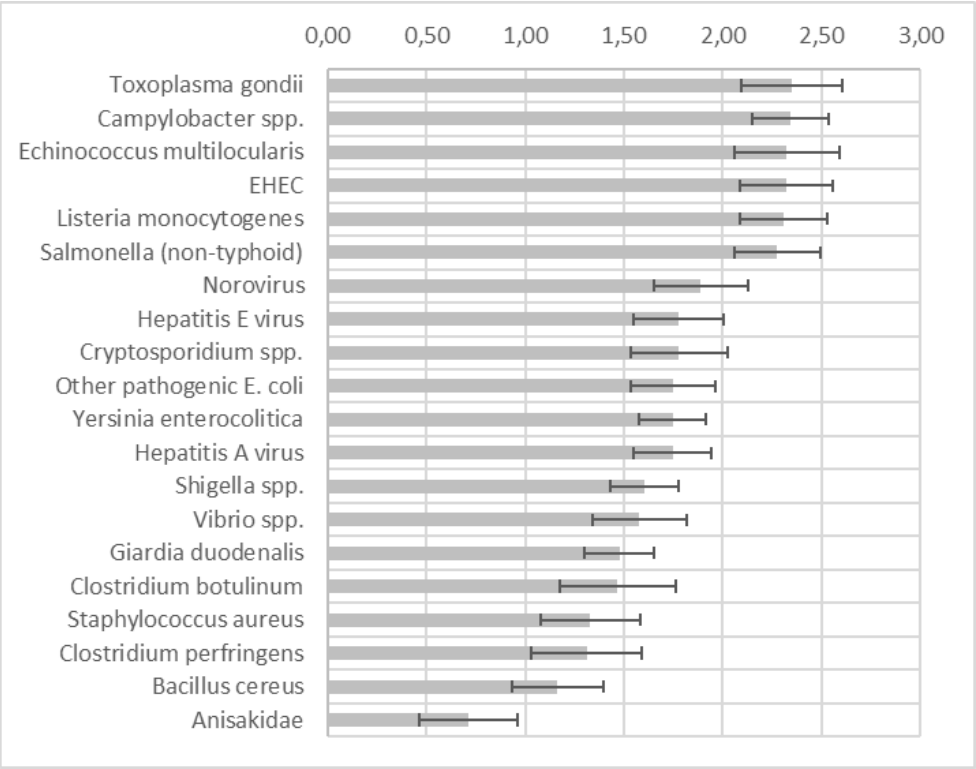

Figure 6-1. Risk ranking of 20 food- and waterborne pathogens by their overall risk score (grey bars). Horizontal lines indicate 95% confidence intervals. Data from Table 6-1.

As previously explained, ranking presented in Table 6-1 is based on unequal weighting of the criteria (see 5.4). The ranking obtained should equal weights be assigned to each of the criteria is shown in Figure 15-1 in Appendix IV.

7 Source attribution

7.1 Identification of key foods of concern in Norway for each pathogen

For each pathogen, initial identification of key foods of concern in Norway was obtained from the following sources:

- Surveillance and monitoring programmes under the auspices of the Norwegian Food Safety Authority (NFSA)
- National surveys (prevalence studies)
- Baseline surveys conducted by European Food Safety Authority (EFSA), in which Norway was included
- Rapid Alert System for Food and Feed (RASFF)

- Outbreak investigations in Norway in which the source of infection was identified (Vesuv)
- Analytic epidemiological investigations aimed at identifying sources of infection and risk factors for sporadic cases of disease
- Previous risk assessments and opinions from Norwegian Scientific Committee on Food and Environment (NSCFE)
- Information on food consumption patterns in the Norwegian population, and food imports

When Norwegian data were sparse or absent, information was obtained from:

- Risk assessments and opinions published by EFSA
- Data from other countries with a similar epidemiological situation
- Data from reference laboratories and outbreak investigations in other countries for which sources and risk factors are relevant for Norway

Each member of the expert panel was commissioned to assemble data required in source attribution for the same 1- 3 pathogens as those subjected to their earlier data assimilation in the risk-ranking process (chapter 12). For every pathogen, a detailed description of the data used to identify the main food vehicles and their relative importance is presented as a separate chapter, with concluding paragraphs, in chapter 13. The resulting qualitative source attributions are summarized in Table 7-1.

Table 7-1. Pathogens, main food vehicles, reservoirs, food attribution and risk factors.

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Parasites:				
Toxoplasma gondii **(Section 12.5)**	Meat from sheep, pigs and cattle Fresh produce [1] Meat from cervids	Felidae, notably cats, lynx (definitive hosts), Other mammals and birds (intermediate hosts)	Analytic epidemiology suggests undercooked meat and unwashed, fresh produce are the major food vehicles Cat contact probably less important than food (the transmission stage is not infectious immediately after shedding in cat faeces)	• Eating undercooked red meat (pork, mutton/lamb, beef, venison) • Eating unwashed raw vegetables, herbs, fruits or berries • Direct or indirect contact with faeces from cats, for instance when cleaning the cat litter tray or while gardening (note that fresh cat faeces will not be infectious for T. gondii, even if the cat is infected) • Inadequate cleaning of kitchen utensils after being used with raw meat • Foreign travel (proportion unknown)
Echinococcus multilocularis **(Section 12.2)**	Fresh produce, notably forest berries and leafy vegetables eaten raw	Canidae, particularly foxes, dogs, wolves. Cats of minor importance (definitive hosts) Small rodents (intermediate hosts) Enzootic status in mainland Norway: not yet detected	Food- and waterborne transmission are acknowledged potential routes of infection. Contact with dogs and drinking contaminated water are known risks. The contribution of contaminated food is less clear. However, most studies are from endemic areas and the situation in countries such as Norway is less clear	• Unsanitary contact with infected dogs • Direct or indirect contact with faeces from infected dogs and other definite hosts • Drinking untreated water • Eating unwashed raw vegetables, herbs, fruits or berries contaminated with parasite eggs • Travel to endemic areas, incl. Svalbard

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
***Cryptosporidium* spp.** **(Section 12.3)**	Drinking water Fresh produce [1] Fruit juice Unpasteurized milk	Cattle, sheep, goats	Mainly food- and waterborne, proportions unknown. Water may be most important vehicle Water- and foodborne outbreaks documented, animal contact – raw goat's milk incriminated	• Drinking untreated water • Direct or indirect contact with faeces from human or animal shedders. • Eating foods and fruit juice contaminated by faeces from human or animal shedders [1] • Consumption of unpasteurized milk • Foreign travel (30-40 % of cases in Norway)
Giardia duodenalis **(Section 12.4)**	Drinking water Fresh produce [1]	Humans	Direct transmission from infected shedders is very important. Waterborne transmission can also be important, and foodborne transmission, especially directly before serving, has also been documented. Water probably most important vehicle A substantial waterborne outbreak has been documented in Norway	• Drinking untreated water • Direct or indirect contact with faeces from human shedders • Eating foods contaminated by faeces from human shedders, exceptionally from animals [1] • Foreign travel (ca. 50 % of cases) The infection is usually not zoonotic
Anisakidae **(Section 12.1)**	Marine fish Cephalopods	Marine fish and squids (paratenic hosts), marine mammals (definitive hosts), krill (intermediate hosts)	Exclusively foodborne (fish, squid)	• Eating raw, pickled, smoked, undercooked, lightly salted, or improperly frozen wild marine fish or squid harbouring the larvae
Bacteria:				

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
***Campylobacter* spp.** **(Section 12.15)**	Drinking water Poultry Red meat Fresh produce [1] Unpasteurized milk	Wild birds Poultry Sheep, cattle, pigs Dogs, cats	Analytic epidemiology suggests drinking water and poultry are main vehicles Water may be most important source Water- and foodborne outbreaks documented – poultry and water most frequently involved – raw milk	• Drinking untreated water • Food safety violation (e.g., cross-contamination) when cooking raw poultry meat • Food-safety violation during barbecues • Consumption of undercooked poultry products • Unsanitary contact with pets and livestock (dogs, cats, poultry, pigs, cattle, sheep) • Consumption of unpasteurized milk and products thereof • Eating other foods contaminated from animal or human shedders [1] • Foreign travel (40-50% of cases)
Zoonotic *Salmonella* (non-typhoid) **(Section 13.16)**	Various foods of animal or vegetable origin Fresh produce [1] Drinking water	Wild birds Hedgehogs Imported pet reptiles Livestock (not enzootic)	Analytic epidemiology suggests imported food and wild birds are most important vehicles Food-, water- and animal-borne (hedgehogs) outbreaks documented - numerous food categories involved, mainly imported	• Unsanitary contact with reservoir animals • Consumption of imported food, including meat and fresh produce [1] • Food-safety violation when cooking imported food • Drinking untreated water • Foreign travels (> 70% of cases)
Non-zoonotic *Salmonella* (Typhi hand Paratyphi) **(Section 13.16)**	Various foods of animal or vegetable origin	Humans (not endemic)	Human shedders infected abroad are most important vehicles	• Direct or indirect contact with faeces from human shedders • Consumption of food or water contaminated from human shedders [1] Travel to endemic areas (> 90% of cases)

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Zoonotic, enteric *E. coli* **(EHEC and aEPEC)** **(Section 12.14)**	Meat from sheep and cattle Fresh produce [1] Unpasteurized milk Drinking water	Cattle, sheep, goats	Mainly food- and waterborne Documented outbreaks incriminate cured sausage, raw milk and products thereof, animal contact, organic lettuce	• Consumption of undercooked beef or lamb/mutton products • Food-safety violation when cooking raw beef or lamb/mutton • Eating other foods contaminated from animal or human shedders [1] • Consumption of unpasteurized milk and products thereof • Drinking untreated water • Unsanitary contact with cattle, sheep or human shedders • Foreign travel (ca. 30% of cases)
Shigella* spp.** **(Section 13.17)** **Non-zoonotic, enteric *E. coli: **ETEC, EIEC, tEPEC, EAEC** **(Section 13.14)**	Fresh produce [1] Various foods of animal or vegetable origin	Humans (not endemic)	Human shedders infected abroad and imported food most important vehicles Documented outbreaks involve imported fresh produce, kebab	• Direct or indirect contact with faeces from human shedders, • Consumption of food or water contaminated from human shedders [1] • Drinking untreated water Travel to endemic areas (Shigella > 90% of cases)
***Vibrio* spp.** **(Section 12.18)**	Seafood, notably shellfish - oysters, clams, and crabs	Seawater, sediments, marine plankton, shellfish and fish	Undercooked shellfish most important food vehicle	• Consumption of undercooked seafood, most notably imported shellfish • Bathing in contaminated water

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Yersinia enterocolitica **(Section 13.19)**	Pork Fresh produce [1] Drinking water	Pigs	Analytic epidemiology suggests mainly foodborne, water probably less important than food Documented outbreaks incriminate pork products and imported fresh produce	• Consumption of raw, rare or undercooked pork products • Food safety violation when cooking raw pork (e.g., cross-contamination) • Drinking untreated water • Eating other foods contaminated from porcine or human shedders [1] • Unsanitary contact with pigs • Foreign travels (20-40% of cases)
Listeria monocytogenes **(Section 13.13)**	Ready-to-eat meat and fish products with long shelf-lives: Fermented fish (rakfisk) Smoked and cured fish Cold cuts Soft cheeses Products made of unpasteurized milk	Ubiquitous in environment	Exclusively foodborne Foodborne outbreaks documented - fish, dairy and meat products involved	• Maturation of foods at temperatures that allows growth • Inappropriate storage conditions, thawing conditions, etc., at all stages in the farm-to-fork chain. • Undercooking of contaminated food • Prolonged storage of food leftovers, including opened packages. • Eating contaminated foods after "use by" date. *Listeria* tends not to affect that odour and appearance of food, and high concentrations are therefore not detected. • Incorrect use of "best before" and "use by" date labelling. • Combinations of different ingredients resulting in conditions that promote higher *Listeria* growth than would be expected with the individual ingredients

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Clostridium botulinum **(Section 13.10)**	Fermented fish (rakfisk) Cured meats Honey (infant botulism)	Ubiquitous in environment	Mainly foodborne intoxication – food safety violation Documented outbreaks involve homemade rakfisk and cured meats	Food safety violation when preparing: • Homemade fermented fish (rakfisk) • Homemade cured meats • Home-canned food Infant botulism: Consumption of imported honey, occasionally other products
Bacillus cereus *Clostridium per-fringens* **(Section 13.9 and 13.11)**	Various foods of animal or vegetable origin	Ubiquitous in environment	Exclusively foodborne intoxication/infection - food safety violation decisive Foodborne outbreaks documented – several food categories involved	Violation of elementary food-safety principles: • Holding hot food warm at insufficiently high temperatures (< 60°C) • Insufficient or too-slow cooling of food • Prolonged storage of food at room temperature • Inadequate heating of previously cooked foods
Staphylococcus aureus **(Section 13.12)**	Various foods of animal or vegetable origin Products made of unpasteurized milk	Humans Livestock Pets	Foodborne intoxication - food safety violation decisive Foodborne outbreaks documented – several food categories involved incl. raw milk products	Violation of elementary food-safety principles: • Holding hot food warm at insufficiently high temperatures (< 60°C) • Insufficient or too slow cooling of food • Prolonged storage of food at room temperature • Inadequate heating of previously cooked foods For *S. aureus* also: • Eating food contaminated from human or animal carriers
Viruses:				

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Norovirus **(Section 13.8)**	Any food contaminated by a shedder Oysters, mussels Fresh produce [1] Drinking water	Humans	Food, water and objects contaminated by faeces or vomit from human shedders are vehicles Water- and foodborne outbreaks documented – numerous food categories involved, notably oysters and imported fresh produce	• Direct infection by faeces or vomit from human shedders • Contact with objects contaminated from human shedders (e.g., cutlery, utensils, tableware, toys, doorknobs, faucets) • Eating foods not intended for heating contaminated by faeces or vomit from shedder • Eating undercooked shellfish, notably raw oysters • Drinking untreated water
Hepatitis A virus **(Section 13.6)**	Any food contaminated by a shedder Oysters, mussels Fresh produce [1] Drinking water	Humans	Food, water and objects contaminated by faeces from human shedders are vehicles Documented foodborne outbreaks involving imported frozen berries	• Direct infection by faeces from human shedders • Eating food not intended for heating contaminated by faeces from shedders [1] • Contact with objects contaminated from human shedders • Eating undercooked shellfish, notably raw oysters • Drinking untreated water • Foreign travel (ca. 30 % of cases)

Pathogen	Main food vehicles	Reservoir	Food attribution [2]	Main risk factors [3]
Hepatitis E virus **(Section 12.7)**	Pork liver and, to a lesser extent, pork meat	*Low-income countries*: Humans (genotypes 1 and 2) *High-income countries:* Pigs, wild boars, deer (genotypes 3 and 4)	High-income countries: Probably transmission from reservoir animals through various foods (presumably primarily pork), exact route of transmission uncertain	Low-income countries (genotypes 1, 2): • Consumption of food or water not intended for heating contaminated by faeces from human shedders High-income countries (genotypes 3, 4): • Consumption of raw, rare or undercooked pork products • Unsanitary contact with pigs • Foreign travel (proportion unknown)

[1] Including unwashed raw vegetables, herbs, sprouts, unpeeled fruits, leafy greens and berries.

[2] Ready-to-eat foods are relevant for all pathogens and are not mentioned specifically.

[3] Belonging to a vulnerable group is a risk factor for almost all pathogens and are not mentioned specifically.

8 Data gaps

8.1 Identification and definition of criteria for scoring of data gaps

An expert-based, ranking tool for scoring of data gaps was developed. In all, 13 criteria were scored by the panel members according to the availability and quality of the data utilized in the preceding risk ranking (chapter 12) and source attribution (chapter 13) (see Table 8-2):

- All six public health criteria, C1 through C6, which formed the basis for risk ranking of pathogens (Appendix I)
- Seven criteria pertaining to exposure (reservoirs, sources of infection, and risk factors), which formed the basis for source attribution (chapter 13)

The scale for scoring was agreed to be 1-4 (Table 8-1), ranging from no data to considerable data available, thus preventing selection of a median value for convenience. If a criterion was not relevant (e.g., no reservoir in animals) no score was assigned, and further information should be sought in the background information provided in the exposure-assessment chapters in Appendix II.

Table 8-1. The scale for scoring of data gaps.

Score	**1**	**2**	**3**	**4**
Definition	Considerable data available	Some data available	Little data available	No data available

8.2 Expert scoring of data gaps based on the criteria

In order to score data gaps, the expert panel was divided into four smaller groups of 2-3 experts, each group being responsible for scoring a selected subset of pathogens. The group members were provided with the lists of pathogens and available background material (Appendices I and II) and requested to score the data gaps independently. The scores were sent by mail to the NSCFE secretariat where the scores from all group members were compiled in a separate table for each pathogen. After the first round of scoring, a group meeting was organised to facilitate discussion of the scores.

Discussions around large discrepancies in first scores allowed the group to identify differences in interpreting criteria or scoring scale. Once the group of experts reached consensus and greater clarity and agreement on criteria definitions, experts conducted a review of their scores, which were subsequently sent to the secretariat and mean values of were calculated for each criterion.

Following the second round of scoring, a meeting for all panel members was organised at which the results were discussed, and final data-gaps scores were agreed. In order to

calculate an overall data-gap score for each pathogen, the scores for all 13 criteria were added, and the final score was averaged (Table 8-1), thus facilitating interpretation (Table 8-2).

Table 8-2. Scoring of each pathogen for data gaps related to the 13 criteria employed in risk ranking and source attribution.

Pathogen	Number of food-borne illness	Acute morbidity severity	Chronic morbidity severity	Fraction of chronic illness	Case fatality ratio	Probability for increased HBD	Surveillance data (animals and food)	Occurrence in reservoir animals (zoonotic potential)	Occurrence in food or water	Sources of infection in outbreaks	Sources of infection for sporadic cases	Relative importance of different food sources	Risk factor identification	Overall score	Average
Anisakidae	3.5	1	3	2	2.5	3	3	1	2.5	3.5	3	2.5	2	32.5	2.50
E. multilocularis	3	1	1	1	2	2.5	3	2	3	4	3.5	3	3	32	2.46
Cryptosporidium	3	1	1.5	2	2	2	2	2	2	2	3	2	2	26.5	2.04
G. duodenalis	3	1	1	2	1	2	3	2	2	2	3	2	2	26	2.00
T. gondii	2	1	1.5	2	2	2.5	3.5	1	3	4	2	2	2	28.5	2.19
***E. coli* EHEC**	1	1	1	1	1	2	2	1.33	1.33	2	2.67	2	2	20.33	1.56
***Campylobacter* spp.**	1	1	1	1	1	2	2	1	1.33	2	2.67	2	2	20	1.54
Salmonella	1	1	1	1	1	2	2	1	1	1.67	2.33	2	2	19	1.46
***Shigella* spp.**	3	2	3	3	3	2.67	3	3	2.33	3	3	2.33	3	36.33	2.79
***Vibrio* spp.**	2.3	2.33	3	3	3	3	3	2.33	2	3	3	2.33	3	35.32	2.72
Y. enterocolitica	1	1	1	1	1	2.33	2.33	2	2	2.33	2.67	2	2	22.66	1.74
B. cereus	3	1	1.67	2.33	1	3	2.67	NR	2.67	2	3	3	1	26.34	2.20
Cl. botulinum	1	1	1.33	1	1	3	2.67	NR	2.33	1	1.67	2	1	19	1.58
Cl. perfringens	3	1	1.67	2	1.33	3	3.33	NR	2.67	2.67	3	3	2	28.67	2.39
S. aureus	3	1	1.67	2.33	2	3	3	2	2.33	2.33	3	2.67	2.67	30	2.31
L. monocytogenes	1,33	1	1.67	2	1.33	2.67	1.33	2.33	1.67	1.33	3	2	2	23.66	1.82
Hepatitis A virus	2	2	2	2	2	3	3	NR	3	2	4	2	2	29	2.42
Hepatitis E virus	4	3	2	3	3	4	4	4	4	4	4	3	3	45	3.46
Norovirus	2	1	2.5	2.5	3	3	2	NR	2	1.5	4	1	1	25.5	2.12

NR - the criterion is not relevant for the pathogen concerned (e.g., no animal reservoir of zoonotic relevance). Further information regarding the pathogen in question is available in the background chapters in Appendix II.

9 Discussion – reliability and validity of the results

There are several limitations to the present assessment that must be considered when interpreting the results.

9.1 Reliability of expert knowledge elicitation (EKE)

Although there are advantages of using EKE, the method has several sources of uncertainty and bias that challenge its reliability. However, structured protocols can improve the quality of the judgements and reduce sources of bias.

The reliability of EKE will always be sensitive to which experts participate and the extent of expertise incorporated into the estimates. This is particularly so when, as in this case, various different items are being evaluated, as no individual is likely to be an expert in all the fields under consideration, and it is difficult to assess the influence of their expertise on their evaluation. This can be avoided by having a much large panel in which only those individuals that have expertise on the particular pathogen (in this case) undertake the assessment. This was not possible for us, and, in our case, the expert panel consisted of nine researchers, including all eight members of the Panel on Biological Hazards of NSCFE and one invited expert on foodborne viral infections (MM). Although the individual participants were experts in several of the pathogens, none were experts on all. Thus, the panel encompassed experts in all three pathogen groups under consideration (i.e., bacteria, viruses, and parasites). Nevertheless, all participants evaluated all pathogens and we are aware that experts in particular pathogens may give undue prominence to their own speciality.

In most cases, the need for expert judgement arises when empirical data are sparse or unavailable. There are considerable data gaps in essential information required to complete the risk ranking and source attribution in this report (Table 4-1). Hence, EKE using a multicriteria approach was considered a feasible procedure that was possible to carry out within the time frame and resources allocated to the project.

Although structured protocols can improve the reliability of expert opinions in EKE, their use does not guarantee accurate estimates, and there is no way of evaluating judgements for their accuracy or calibration.

Discrepancies and ambiguity in interpreting criteria, scoring scale, terminology, or definitions concerning the questions to be answered are also issues that can reduce reliability and bias the results. In the present assessment, this was mitigated by conducting several rounds of elicitation followed by plenary discussions to clarify ambiguities and enable panel members to review their evaluation. On the other hand, this procedure that searches for consensus and co-ordination can, in turn, contribute to challenging the reliability of the results by

exaggerating the opinion of those panel members who express their judgment with the greatest conviction.

9.2 Reliability of the risk ranking

The multicriteria-based risk ranking employed six criteria related to public health (C1 - C6), which were weighted to calculate an overall risk score for each pathogen.

Only one of these criteria (C1) is liable to significant alteration over time, either in terms of increased or decreased number of illnesses. The next four criteria (C2 - C5) concern the severity of the diseases, and it is unlikely they will vary significantly, unless more virulent variants of the pathogens should be introduced. The last criterion (C6) estimates the probability of increased disease burden of the pathogens. Other factors that affect the burden of disease, such as socio-economic and psychosocial consequences, were not included in the assessment.

Below is a discussion of the reliability of the criteria scores and their weighting, and how this affects the internal validity of the present results and the efficacy of prospective re-evaluation of the ranking.

C1 – number of foodborne illnesses

For most pathogens, an attempt was made to estimate the total number of persons infected in Norway via food/water-borne transmission using data from the Norwegian Surveillance System for Communicable Diseases (MSIS) as the main source of information (see Appendix III). Data from surveillance were adjusted to correct for underestimation due to under-reporting and under-ascertainment.

However, there is considerable uncertainty about the number of patients who are not detected by surveillance because they do not seek healthcare. Likewise, the proportion of patients who do visit a doctor, but are not appropriately tested to reach a specific aetiological diagnosis, is unknown. Among the 20 pathogens included in this assessment, seven are the causative agents of diseases that are not notifiable to the surveillance system at all (e.g., norovirus and *Toxoplasma*). Hence, the most important basis for estimating the incidence is lacking. For most diseases, only rough estimates for the total number of illnesses acquired in Norway were possible.

Many food- and waterborne illnesses can be transmitted in several different ways. The proportion of illnesses attributable to food- and waterborne transmission varies. For most diseases in this report, available scientific data are insufficient to justify reaching firm conclusions about the relative importance of different sources of infection. Estimates of the number of illnesses attributable to food and water were therefore largely a rough best guess. Nevertheless, we believe that this is sufficient to score the diseases on the semi-quantitative scale used in this report. (These problems are described in detail in chapter 14, Appendix III, and lack of available information is indicated as data gaps in Table 8-2.)

Scoring of C1 was achieved using five scoring categories. It is worth noting that the intervals within each category are unequal (e.g. 100-1000 vs. 1000-10000); this can influence the scoring and consequently the ranking. This scale implies that even large differences in the number of illnesses will not necessarily be reflected in the scoring level. For instance, a significant increase from 100 to 1000 cases will not change the score; it will still be equal to 2. Correspondingly, an increase from 1000 to 9000 cases will nonetheless be scored as 3.

This makes the C1 score a fairly insensitive tool to differentiate the pathogens according to illness number; even significant alterations in incidence will not necessarily be reflected in the score and consequently will not be reflected in the ranking. As C1 is the only criterion that is likely to change significantly in the future, the inability of the C1 score to capture even major changes has implications for the efficacy of a prospective re-calculation of the ranking when updated information are available.

C2 – C5. Morbidity severity and lethality

The criteria C2 – C5 reflect the degree to which acute and chronic manifestations of illness reduces health-related quality of life. They depend on both the severity and duration of illness, with death being the worst possible outcome. Although considerable information is available on clinical manifestations, there are significant data gaps for several diseases (see Chapter 4 and the hazard characterization in Appendix I).

Furthermore, determining the relative impact of diseases, in terms of clinical importance, by assigning disability scores on a scale ranging from very mild to severe, is not a straightforward, easy task.

The expert panel consisted of nine researchers representing diverse professions and qualifications, many of whom were not trained in assessing clinical issues. The plenary meeting revealed substantial discrepancies in interpretation of the scoring scales. Nevertheless, the joint meeting facilitated discussion of the scales, clarified definitions and medical terminology, and allowed panel members to review and revise their scores and to coordinate the results.

Nevertheless, the scoring of these criteria is vulnerable to misjudgements. One example is that of *Yersinia enterocolitica*, which scored significantly lower than non-typhoid *Salmonella*, and at the same level as *Campylobacter*, with respect to criterion C234 that describes morbidity severity (see Table 6.1 and Figure 6-2). This was ultimately accepted without correction, despite the comparatively high frequency of sequelae associated with yersiniosis in a population where HLA-B27 is frequent (e.g., reactive arthritis). Likewise, the acute manifestations of yersiniosis are often more severe and more prolonged than in salmonellosis and campylobacteriosis (e.g., the pseudo-appendicitis syndrome). Correspondingly, it might be argued that *Shigella* could have received a higher score, although *S. sonnei* is the prevailing species acquired in Norway.

C6 - Probability of increased human burden of disease

The last criterion (C6) aims at predicting the future disease burden of the pathogens, and the scoring is basically a qualified guess.

C6 is influenced by a number of factors including: trade agreements and political decisions affecting import of food, feed, and live animals; globalization of the food market; changes in legislation and regulations concerning food safety; new methods for production, processing, storage and preparation of food; changes in consumer preferences, consumption patterns, eating habits, and food-handling practices; knowledge of, and compliance with, the principles of food safety; demographic changes, notably increasing numbers of elderly and immunocompromised persons and migration; introduction of more virulent and infectious variants of the pathogens; climate changes that may affect the prevalence, survival, growth, and dissemination of pathogens. Whereas many of these factors can lead to an increased incidence of food- and waterborne illnesses, and thus the disease burden they represent would rise, some of the factors listed above may act in the opposite direction and reduce the incidence of infection, and thus the burden of disease. It is not obvious that conditions will inevitably get worse; it could be argued that the situation is more likely to improve.

Moreover, food safety benefits from considerable attention among authorities and consumers. Billions are invested to make safe food even safer. Any substantial increase in the incidence of foodborne illnesses would be expected to be counteracted by control and preventive measures to diminish the problem. Outbreaks of a particular disease are likely to result in focus on instigation of measures to reduce the likelihood of recurrence.

Calculating the net effect is, with our present knowledge, a heroic and impossible endeavour due to uncertainties related to factors that affect future disease burden and the ability and willingness to implement control measures. C6 was, not unexpectedly, the criterion that caused the greatest disagreement within the expert panel.

Weighting

While scoring of the criteria was, in principle, based on available empirical data, the weighting reflects the panel members' subjective assessment of the importance of each criterion in terms of its public health impact. No formal attempt was made to quantify and compare the burden of disease attributable to each particular criterion. The weighting was therefore more intuitive than evidence based.

Although it is unlikely that small changes in weighting will significantly alter the ranking, it is obvious that large differences will influence the results as shown in Figure 15-1. For instance, if C1 (number of foodborne illnesses) is considered the most important criterion (W1 = 1), the highest ranked pathogens will become norovirus and *Campylobacter* (see Figure 5-1). Likewise, when morbidity severity is granted maximal importance (W234 = 1), the following ranking order ensues: *Toxoplasma*, *E. multilocularis*, EHEC, *C. botulinum*, *Listeria* etc.

9.3 Reliability of the source attribution

For each of the ranked pathogens, the source attribution process aimed at identifying pathogen-food combinations that may pose a risk to public health.

To achieve this, we used available information from surveillance and monitoring programmes, surveys, outbreak investigations and research, including analytic epidemiology, as detailed in chapter 7 and chapter 14, Appendix III. The results obtained were compiled in chapter 7 and Table 7-1.

Considerable amounts of work have been invested to determine the prevalence, growth, and survival of pathogens at various stages in the food chain. However, such investigations are not sufficient to draw definitive conclusions regarding the significance of the food product compared with other possible sources (relative importance), or what proportion of illnesses can be ascribed a particular food source (absolute importance) (see the discussion in chapter 9).

Information about sources of infection in outbreaks may provide an indication of which foods are most important, but only a small fraction of outbreaks is detected and notified. Even among those outbreaks investigated and reported, the implicated food source is often not identified for a significant proportion of the exposed group. Hence, data from outbreak investigations are not necessarily representative. As for the far more numerous sporadic cases, the source of infection remains, with few exceptions, unknown.

To address these issues, a series of analytic-epidemiological studies have been conducted to identify the most important risk factors and sources of infection for sporadic cases of disease and estimate the relative significance of these sources in terms of their contribution to overall disease burden (Appendix III). Only four of the pathogens investigated in this report (*Yersinia*, *Campylobacter*, *Salmonella,* and *Toxoplasma*) have been examined in such a way in Norway, and most studies were carried out several decades ago.

Nevertheless, despite insufficient evidence on the relative importance of different sources of infection, we believe that it is possible to suggest the most likely main food vehicles for each pathogen with a reasonable degree of certainty. This is because relatively comprehensive information is available on the prevalence of the pathogens in specific foods and food-producing animals and data has been accrued from outbreak investigations.

10 Conclusion

Food- and waterborne diseases are a global issue, and food safety is a major priority. These diseases cause considerable medical, socioeconomic, and psychosocial burdens on society and on the individual patients afflicted. Providing risk managers with the information they need for decision making is an important element of food-safety management.

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The present assessment was undertaken to provide a scientific basis enabling the Norwegian Food Safety Authority to implement risk-based surveillance, monitoring and control programmes for pathogens in foods.

To respond to this need, we performed a multicriteria-based risk ranking of 20 selected pathogens in terms of their public health impact, using an EKE procedure with a panel of nine experts.

The risk ranking utilized six criteria to describe incidence, clinical consequences, and the probability for increased disease burden of the pathogens, and each criterion was weighted to calculate an overall risk score for each of the pathogens. Other factors that affect disease burden, such as socio-economic and psychosocial consequences, were not included in the assessment. The six highest-ranked pathogens were, in descending order: *T. gondii*, *Campylobacter* spp., *E. multilocularis*, enterohaemorrhagic *E. coli* (EHEC), *L. monocytogenes*, and non-typhoid *Salmonella*. Confidence intervals, however, revealed substantial overlaps between scores.

For each of the ranked pathogens, a subsequent source-attribution process aimed at identifying the main food vehicles, reservoirs, sources of infection for outbreak-related and sporadic cases of illness, the relative importance of food sources, and preventable risk factors.

Despite insufficient evidence on the relative importance of different sources of infection, we concluded that it was possible to identify the most probable main food vehicles for each pathogen with a reasonable degree of certainty.

The food sources varied widely. It is notable, however, that fresh produce was identified as a main food vehicle for 12 of the 20 pathogens, drinking water was associated with 8, and 5 were linked to raw milk or products thereof.

There are several limitations to the present assessment that should be considered when interpreting the results. We identified considerable data gaps in crucial information that is needed for risk ranking and source attribution. An evaluation of the reliability and internal validity of the results is also presented.

It is important to emphasize that the present ranking and source attribution may be subject to change in the future as new data become available from surveillance and research on foodborne pathogens and the diseases they cause. Thus, the systematic and transparent process described in this report is probably most useful if it is repeated regularly to take more recent, updated information into account.

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12 Appendix I - Hazard identification and characterisation

12.1 Anisakidae

12.1.1 Organism

Several species of roundworms within the ascaridoid nematode family Anisakidae can cause the zoonotic disease anisakiasis in humans. The two species most often associated with anisakiasis are *Anisakis simplex* and *Pseudoterranova decipiens*, in Norwegian collectively referred to as "kveis" (FAO & WHO, 2014; NIPH, 2020b).

The complex life cycle of anisakid nematodes involves a marine intermediate host (euphasid crustacean, krill), a paratenic host (marine fish or squid) and a definitive host (marine mammal) in which the adult stage develops (FAO & WHO, 2014). The larval stage is found in the viscera or muscle of a wide range of marine fish and squids, which maintain larvae that are infective to humans and marine mammals.

Anisakiasis is acquired when people ingest raw, undercooked, or lightly salted fish or squids harbouring the larvae. Humans are accidental hosts in which the parasites rarely develop further.

Anisakidae larvae are prevalent in marine fish in Norwegian waters, including common food fishes (section 13.1).

12.1.2 Illness and consequences

12.1.2.1 Acute morbidity

Anisakiasis involves acute abdominal symptoms, usually within hours after ingestion of larvae (NIPH 2020, WHO & FAO 2014). When humans eat infected fish, the parasites migrate to the gastrointestinal mucosa, where they die, causing slight enteritis, but also very painful ulcers. This nonspecific abdominal distress can be mistaken for other conditions such as peptic ulcers, food poisoning, and appendicitis. If the larvae pass into the submucosa and muscularis of the intestines, a severe eosinophilic granulomatous response may also occur 1 to 2 weeks following infection, causing symptoms mimicking Crohn's disease, and rarely intestinal perforation can occur.

12.1.2.2 Chronic morbidity

There is little information on chronic morbidity. Most infections are self-limiting as larvae are unable to survive for long periods in the human host, but the associated tissue damage can cause longer lasting symptoms.

Antigens that remain in the fish muscle after the parasites are killed (e.g. after freezing or thorough cooking) can cause allergic reactions in some individuals (Audicana & Kennedy, 2008; Rahmati et al., 2020). Occupational allergy, including asthma, conjunctivitis and contact dermatitis, has also been observed in fish-processing workers.

Rahmati et al. (2020) conducted a systematic review to compare the global distribution of *Anisakis*-infected fish, with emphasize on allergic anisakiasis. The hot spot areas for allergic anisakiasis were North and northeast of Atlantic Ocean, southwest of USA, west of Mexico, south of Chile, east of Argentina, Norway, UK and west of Iceland. According to the authors, the highest rate of allergic anisakiasis was in Portugal and Norway with the prevalence rate of 18.45 - 22.50%.

However, Lin et al. (2014) observed a very low seroprevalence of anti-*Anisakis* IgE in a Norwegian population compared with other high fish-consuming countries (0.0% - 0.2%). Their study indicates that the prevalence may be overestimated by certain analytic methods due to a considerable degree of cross-sensitization to shrimp and house dust mites.

12.1.2.3 Case-fatality ratio

There is little information available on illness fraction or case fatality rates, probably because most cases are acute and treated when necessary.

12.1.2.4 Occurrence

Number of illnesses attributable to foodborne transmission

In 1975-90, anisakiasis was notifiable to the Norwegian Surveillance System for Communicable diseases (MSIS). No cases were recorded in that period (NIPH, 2020b).

Nevertheless, serious disease has been described a few times in Norway (NIPH, 2020b). In other countries such as The Netherlands and Japan, where raw fish is used more frequently in some dishes, the disease is not uncommon.

Outbreaks

Very few outbreaks of anisakiasis have been described in humans (Cabrera, 2010), and there are no registered outbreaks in Norway.

12.1.2.5 Likelihood of increased human burden

According to a WHO report, there has been an increase in recorded incidence of anisakiasis throughout the world in the last two decades, probably due to better diagnostic tools, increased demand for seafood, and a growing demand for raw or lightly cooked food, although none of these factors has been rigorously evaluated (WHO & FAO 2014).

A meta-analysis covering the years from 1978 to 2015, detected a significant 283-fold increase in *Anisakis* spp. abundance in marine fish and invertebrates, and no change in the abundance of *Pseudoterranova* spp. (Fiorenza et al., 2020). The positive temporal trend observed was strongly driven by data from the north-eastern Atlantic. The reason for the increase, including long-term ecological or environmental changes influencing the populations of host species, is debated. This increase in *Anisakis* spp. prevalence may have implications for human health, marine mammal health, and fisheries profitability. The likelihood of increased human burden in Norway will largely depend on any changes in the consumption of raw or undercooked marine fish.

12.1.2.6 Scorecard

Table 12-1. Final scores for *Anisakidae* based on EKE of nine experts.

Anisakidae	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	1	0	0	0	0	0	2	0	0	0.33
Acute morbidity severity	2	2	2	1	2	0	2	1	2	1.56
Chronic morbidity severity	2	0	0	0	1	1	0	2	1	0.78
Fraction of chronic illness	0	0	0	0	0	1	0	1	1	0.33
Case fatality ratio	0	0	0	0	0	0	0	0	0	0.00
Probability for increased HBD	1	1	1	1	1	1	1	0	2	1.00
Total	6	3	3	2	4	3	5	4	6	4.00

12.2 Echinococcus multilocularis

12.2.1 Organism

Echinococcus multilocularis is a cestode (tapeworm), widely distributed in temperate and cold regions of the northern hemisphere. As with all tapeworms, it has an indirect lifecycle, with the tapeworm stage in the intestine of the definitive host and the larval (metacestode) stage in small mammals. The predator-prey cycle between wild canids and rodents means that the lifecycle is difficult to interrupt and has enabled the wide distribution of this parasite. The definitive hosts are canids; these are usually red foxes (*Vulpes vulpes*) in temperate regions, but Arctic foxes (*Vulpes latrans*) in Arctic and sub-Arctic regions. Wolves and other wild canids can also contribute to the lifecycle. Although domestic dogs are susceptible to

infection, the prevalence of infection of dogs in Europe tends to be low; the importance of dogs for public health is due to the close relationship between dogs and their owners. Domestic cats are poor definitive hosts and of very minor importance in the lifecycle but cannot be entirely excluded from being contributors towards human infections. The intermediate hosts are often voles (in Europe *Microtus arvalis*); in countries where this rodent is not found (such as Norway and Sweden), other rodents can also act as intermediate hosts. In Sweden, water vole (*Arvicola amphibius*) and the field vole (*Microtus agrestis*) have been found to be infected, and in Norway (Svalbard) the sibling vole (*Microtus levis*) can act as intermediate host. Humans are infected as dead-end aberrant intermediate hosts following ingestion of the tapeworm eggs excreted in the faeces of infected canid definitive hosts. Ingestion of these eggs can be from contamination of hands from touching soil or the fur of infected dogs that already are contaminated, or, if the excreted eggs should contaminate food that is consumed raw (such as salad vegetables or berries), via the foodborne route. Due to the sylvatic nature of the lifecycle, berries from woodlands or other areas where foxes roam are considered as potential risks should high levels of infection occur in the resident fox population. The eggs of *E. multilocularis* are extremely robust; for example, they can withstand heating to + 65°C for 120 min and freezing at -18°C for several months (EFSA, Koutsoumanis, et al., 2018). They are more resistant to elevated temperatures when suspended in water, and therefore are likely to survive long on water droplets on food. In temperate environments, the eggs may survive for months or years.

Figure 12-1. Lifecycle of *Echinococcus multilocularis* (EFSA, Koutsoumanis, et al., 2018).

12.2.2 Illness and consequences

12.2.2.1 Acute morbidity

There is no acute morbidity associated with infection with *E. multilocularis.*

12.2.2.2 Chronic morbidity severity and fraction of chronic illness

The disease caused by ingestion of viable eggs of *E. multilocularis* is called alveolar echinococcosis (AE) and is caused by the infiltrative growth and development of the metacestode. Rather than forming a fluid-filled cyst, as do other species of *Echinococcus* in the intermediate host (both appropriate and dead-end), the metacestodes of *E. multilocularis* develop as small, thin-walled vesicles, densely packed with protoscolices. These can infiltrate the surrounding host tissue continuously throughout life. The predilection site for metacestodes is almost always the liver, and, both pathologically and macroscopically, the metacestodes resemble slow-growing malignant tumours; indeed, at later stages of the disease metastases may occur in distant organs. Due to symptoms being caused by growth and spreading of the metacestodes, the period of time between infection and diagnosis ranges from months to years; diagnosis, when made, is usually at an advanced stage of the disease. This means that source-attribution studies are very difficult and; linking disease to specific food exposures is almost impossible. In addition, outbreaks of alveolar echinococcosis are unlikely to be identified. Thus, the severity of chronic morbidity is extreme, and of those infected, a high proportion exhibit chronic morbidity as usually the disease is not identified until then.

12.2.2.3 Case-fatality ratio

Survival statistics vary according to country; for example, whereas in Switzerland (where the occurrence of the parasite is well known and the infrastructure and medical awareness is good), patient survival after first diagnosis is reduced by only a few years compared with that of the general population, in Lithuania over 30% of patients survive less than a year after first diagnosis. Reduced survival is due to diagnosis often being at an advanced stage of disease. The global disease burden in DALYs has been estimated at 687,723 (37 per patient) – reflecting disease severity and limited treatment options, but also that the majority of cases are diagnosed in western China where medical infrastructure may be limited.

12.2.2.4 Occurrence

Number of illnesses attributable to foodborne transmission including outbreaks

In Europe, AE is not notifiable in all countries and in many European countries reporting of echinococcosis cases are lumped together, despite their very different pathologies and epidemiologies. Data reported to ECDC from Norway indicates that not all infections in humans are identified at the infectious species; for example, of the 8 cases of echinococcosis

reported from Norway in 2016 and 2017, 4 were speciated (*E. granulosus*) and 4 were not (ECDC, 2017).

This means that between country comparisons are difficult. However, it is worth noting that there is convincing evidence for emergence for this parasitosis in some regions of Europe, with convincing data from Austria, Lithuania, Poland, and Switzerland. In some countries this may reflect urbanization of the lifecycle, and increased contamination of the environment in populated areas. The disease severity as well as the expansion of the parasite (along with the fox host) in Europe is presumably the reason why a European risk ranking of foodborne parasites based on EKE (Bouwknegt et al., 2018) placegd *E. multilocularis* as being of highest importance, both throughout Europe and in both Northern and Eastern Europe (and in second place in SW and SE Europe).

Between 1995 and 2019 there have been 57 cases of echinococcosis registered in MSIS. It is noteworthy that 20 of these (35%) have been registered in the last 3 years (6 in 2017 and 7 in both 2018 and 2019). Whether this increasing trend indicates better diagnostic tools or more cases is unknown. It is also worth noting that 8 cases of echinococcosis were reported to ECDC for 2016 and 2017, but 13 were recorded in MSIS, indicating a mismatch between data gathered at the national and European levels. Of the cases registered in MSIS, for 41 infecting species data were provided (1 case of *E. multilocularis* and the other 40 *E. granulosus*). Of the 57 cases, 42 (74%) were hospitalised. It is interesting that 55 cases were described as being acquired abroad and only 2 as unknown. Without knowing further about the individual cases it is impossible to interpret further. However, it should be remembered that many years, even decades, can pass before diagnosis, so it is very difficult to determine where an infection occurred unless the individual has not travelled in their past.

Outbreaks: No outbreaks have been registered in VESUV; this is unsurprising. Given that the pathological nature of echinococcosis is a slowly developing, albeit severe, disease, it is not usually associated with outbreaks.

12.2.2.5 Probability of increased human burden of disease

E. multilocularis is not endemic in mainland Norway, but is in Sweden and Denmark, and also is established on Svalbard. It is therefore assumed that it is only a matter of time before it establishes in mainland Norway (VKM et al., 2012), given that foxes are no respecters of national borders. This is likely to result in the potential for increased likelihood of human infection within Norway.

12.2.2.6 Scorecard

Table 12-2. Final scores for *Echinococcus multilocularis*, based on EKE of nine experts.

E. multilocularis	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	0	0	0	0	1	0	1	0	0	0.22
Acute morbidity severity	0	1	0	0	0	0	0	0	0	0.11
Chronic morbidity severity	4	4	4	4	3	3	3	3	4	3.56
Fraction of chronic illness	4	4	4	4	3	4	4	3	4	3.78
Case fatality ratio	3	3	3	3	4	3	4	4	4	3.44
Probability for increased HBD	1	2	4	3	3	2	4	2	3	2.67
Total	12	14	15	14	14	12	16	12	15	13.78

12.3 Cryptosporidium spp.

12.3.1 Organism

Cryptosporidium spp. are protozoan endoparasites, usually intestinal. Currently around 40 species of *Cryptosporidium* have been described, some of which are host-species specific, but around 20 species have been associated with human infection. Nevertheless, most human infections with *Cryptosporidium* in Europe are due to two species (*C. hominis*, which is largely human-specific, and *C. parvum*, which is zoonotic). Due to the different epidemiologies of the different Cryptosporidium species, determining the infecting species is important in human infections as this may assist in identifying the source of infection. Although the infecting species of *Cryptosporidium* has not been determined for all human cases of cryptosporidiosis in Norway despite informing EFSA that this is done; (EFSA, Koutsoumanis, et al., 2018), the data that we do have indicate that *C. parvum* is responsible for most endemic infections in Norway. In Sweden all human cases are speciated and major outbreaks (thousands of cases) associated with *C. hominis* have been identified, as well as infections with more unusual species such as *C. viatorum, C. meleagridis, C. felis*, and chipmunk genotype.

The lifecycle of *Cryptosporidium* is completed within a single host, and starts with the ingestion of a sporulated oocyst (ca. 5 µm diameter); from each oocyst, four sporozoites are released in the intestine and here they invade epithelial cells where both asexual and sexual replication occur, resulting in the production of large numbers of oocysts, which are released fully sporulated and infective, in the host faeces.

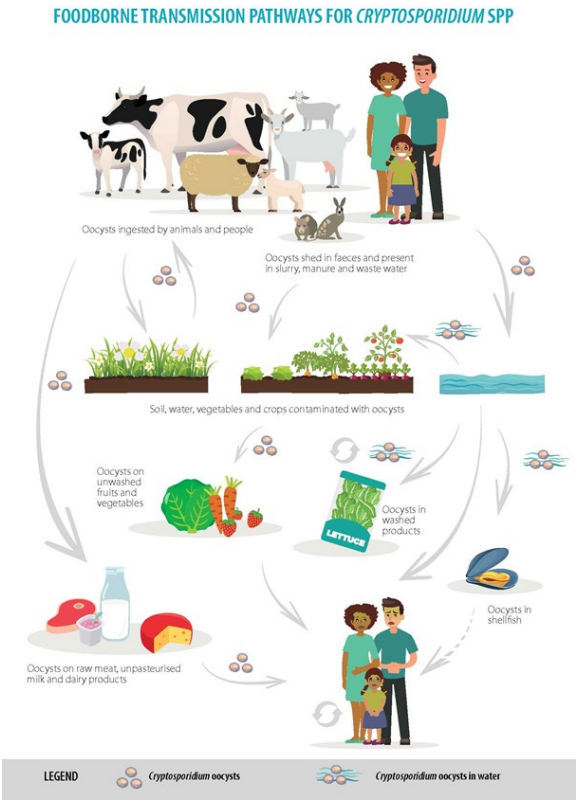

Figure 12-2. Life cycle of *Cryptosporidium* (EFSA, Koutsoumanis, et al., 2018).

The invasive sporozoites of *Cryptosporidium* are protected by the thick oocyst wall, and they can survive for prolonged periods (several months) in the environment, particularly under moist, cool conditions. Extremes of temperature, UV, and ammonia are known to reduce survival, and treatments of food such as pasteurization, low-temperature freezing, freeze-thawing, and desiccation are known to reduce oocyst survival.

12.3.2 Illness and consequences

12.3.2.1 Acute morbidity

Cryptosporidiosis is predominantly a gastrointestinal disease, with diarrhoea, abdominal pain, nausea or vomiting being the main symptoms. Other common symptoms include mild fever, anorexia, malaise, fatigue and weight loss. Diarrhoea is frequently of sudden onset and usually watery and voluminous, with three to six stools passed each day. In otherwise healthy people, the symptoms usually last for 2-3 weeks, tailing off gradually and resolving spontaneously. However, they can last longer and about 30% of cases experience relapses. People with impaired immune systems (e.g., people with some congenital or infectious immunodeficiencies and some transplant recipients) are at risk of developing more severe and protracted symptoms. Very few drugs are available for treating cryptosporidiosis. Of these, only one, nitazoxanide, is licensed in the United States, but not in Europe.

12.3.2.2 Chronic morbidity severity and fraction of chronic illness

Although the majority of patients in Europe seem to recover well from cryptosporidiosis, studies from Netherlands (Iglói et al., 2018), Sweden (Rehn et al., 2015), UK (Carter et al., 2019; Hunter et al., 2004; Stiff, Davies, Mason, Hutchings, & Chalmers, 2017), and Poland (Pielok et al., 2019) indicate that sequelae occur relatively frequently. These may be intestinal (e.g. chronic diarrhoea, IBS) or non-intestinal (e.g., arthropathies, stiffness in the lumbosacralis region, eye pains, and headaches). These post-infection sequelae are usually not included in calculation of DALYs, but were considered in the European prioritisation ranking of foodborne parasites (Bouwknegt et al., 2018), and contributed to *Cryptosporidium* being ranked 2nd in both Northern Europe and Western Europe, and 5th on a Europe-wide basis. It is difficult to put numbers on the proportion of individuals that suffer from post-infectious sequelae following acute cryptosporidiosis, due to limitations such as recall bias. However, data from Sweden collected two years after the Östersund waterborne outbreak indicate that over 40% of cases may report long-term chronic effects (Lilja, Widerström, & Lindh, 2018).

12.3.2.3 Case-fatality ratio

Although cryptosporidiosis is not a cause of death in industrialized countries at present (but was so in AIDS patients before retroviral treatment had advanced significantly around 30 years ago), it is associated with mortality in countries where paediatric diarrhoeal disease has a considerable impact on child survival.

12.3.2.4 Occurrence

Number of illnesses attributable to foodborne transmission, including outbreaks

There are 1530 *Cryptosporidium* cases registered in MSIS 1995-2019 Table 11-2 of which just 18 (1%) have been speciated (despite EFSA being informed that all cases are speciated in Norway; (EFSA, Koutsoumanis, et al., 2018)). These were all *C. parvum*. Of these approximatley 50% were acquired in Norway and the other 50% either abroad or unknown. A relatively high proportion of cases (19%) required hospitalisation.

However, the proportion of these cases that are known to be associated with foodborne transmission is unknown. Unless an outbreak occurs, the extent of waterborne transmission is also difficult to determine. Transmission can also be direct (person-to-person or animal-to-person) or via recreational water use (in many countries, swimming-pool associated outbreaks are relatively common) or other environmental matrices.

Outbreaks

Four outbreaks caused by *Cryptosporidium* were registered in VESUV 2005-2019 with just 25 cases associated with these outbreaks. Given that just one documented outbreak of cryptosporidiosis that occurred in 2012 reported 40 cases (Lange et al., 2014) there seems to be a mismatch between what is known and what is reported in VESUV. *Cryptosporidium* is

widely known as a waterborne parasite, with major outbreaks reported, including in Scandinavia, and associated with both drinking water and recreational water. However, several foodborne outbreaks have also been recorded, and these have been associated with a range of food products (an overview of outbreaks in (EFSA, Koutsoumanis, et al., 2018). Although fresh produce has been the food associated with most foodborne outbreaks, fresh juices, unpasteurized milk and other dairy products are also relevant. In Norway, the only foodborne outbreak recorded occurred in 2018 and was associated with self-pressed apple juice (Robertson, Temesgen, Tysnes, & Eikås, 2019). During 2019, 5 outbreaks of foodborne cryptosporidiosis were reported in Sweden of which 3 were associated with kale salad and one was associated with spinach in a commercial freshly-pressed fruit and vegetable drink (Whitworth, 2020).

12.3.2.5 Probability of increased human burden of disease

Climate change is likely to increase the likelihood of water contamination, and hence infection. Globalisation, as well as consumer tendencies towards eating more fresh, uncooked food, are also likely to increase the likelihood of infection. The increased proportion of immunosuppressed (including elderly) people in society is also likely to increase the likelihood of more severe infections. In addition, globalisation is likely to increase the likelihood of import of new and different gentoypes and species of *Cryptosporidium* into Norway. Currently, the majority of human infections in Norway are with the zoonotic species, *C. parvum*, but other species and genotypes are not far away (the large waterborne outbreaks in Sweden were with *C. hominis*, of a subtype that has been described as "hypervirulent" (e.g., (Li et al., 2018)). While an appropriate chemotherapeutic treatment remains elusive, the burden of disease seems likely to increase.

12.3.2.6 Scorecard

Table 12-3. Final scores for *Cryptosporidium*, based on EKE of nine experts.

Cryptosporidium **spp.**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**Mean**
Number of foodborne illnesses	2	2	3	2	2	1	2	1	2	1.89
Acute morbidity severity	2	2	3	2	2	2	3	2	3	2.33
Chronic morbidity severity	2	1	2	2	2	2	2	3	3	2.11
Fraction of chronic illness	1	1	2	1	2	2	2	2	2	1.67
Case fatality ratio	1	1	0	0	0	1	2	1	1	0.78
Probability for increased HBD	2	2	3	2	2	1	4	2	2	2.22
Total	10	9	13	9	10	9	15	11	13	11

12.4 Giardia duodenalis

12.4.1 Organism

Giardia duodenalis (syn. *G. intestinalis*, syn. *G. lamblia*) is a intestinal, protozoan endoparasite. The taxonomy is complex and controversial, but it is currently usually considered as a species-complex with 7 different Assemblages (which have also been proposed as different species). Of these Assemblages, those known as A and B are considered to be most likely to be infectious humans. Although both these Assemblages seem to be able to infect some animals, most evidence suggests only minor zoonotic transmission under most circumstances. The taxonomy is complicated by some Assemblages having been sub-divided into sub-Assemblages that have different host specificities; for example, Assemblage A consists of sub-groups AI, AII, AIII – of which AI occurs mostly in animals, but has been detected in humans, AII has been mostly found in humans, but has been detected in animals, and AIII has rarely been detected in humans (Sprong, Cacciò, van der Giessen, network, & partners, 2009).

The lifecycle of *G. duodenalis* is completed within a single host and starts with the ingestion of a cyst from which two trophozoites are released in the intestine. The flagellated trophozoites are extracellular, remaining in the intestinal lumen or attaching to the intestinal epithelium where they replicate by binary fission. Further back in the intestine, the trophozoites encyst to form the robust transmission stage, the cyst, that is passed in the faeces and is immediately infectious upon excretion.

In the external environment, the trophozoites of *G. duodenalis* are protected by the cyst wall, and they can survive for prolonged periods (several months) in the environment, particularly under moist, cool conditions. Cyst survival is compromised by various environmental pressures, and *Giardia* cysts are generally considered less robust than *Cryptosporidium* oocysts.

12.4.2 Illness and consequences

12.4.2.1 Acute morbidity

Giardiasis (giardiasis) is predominantly a gastrointestinal disease, with diarrhoea, abdominal pain, and nausea or vomiting being the main symptoms. Other common symptoms include mild fever, anorexia, malaise, fatigue and weight loss. Diarrhoea is usually fatty and foul smelling, and may be acute and violent, or, more commonly, intermittent. The latter manifestation may limit the likelihood of infected people seeking medical assistance as they believe that they have recovered, before relapsing. The infection usually responds well to treatment (usually with a nitroimidazole compounds such as metronidazole, tinidazole, ornidazole, or secnidazole), although in a communitywide outbreak situation, some cases usually need an alternative treatment (as occurred during the waterborne outbreak in Bergen in 2004; (Mørch, Hanevik, Robertson, Strand, & Langeland, 2008).

12.4.2.2 Chronic morbidity severity and fraction of chronic illness

Although the majority of patients in Europe seem to recover well from giardiasis following treatment, without treatment chronic giardiasis can be expected in a substantial proportion of patients and is associated with chronic or intermittent diarrhoea and intestinal malabsorption, resulting in steatorrhea, lactase deficiency, and deficiency of vitamin A, vitamin B12 and folate (Robertson, Hanevik, Escobedo, Mørch, & Langeland, 2010). However, even after successful clearance of the parasite, long-term, post-infection sequelae may occur (and have been repeatedly reported following the outbreak in Norway, and are associated with a lower quality of life metric; (Litleskare et al., 2019). These symptoms are usually post-infection IBS and/or chronic fatigue. Unless diagnosed and treated, a substantial proportion of those infected seem likely to develop chronic illness.

12.4.2.3 Case fatality ratio

Giardiasis is not associated with mortality in industrialized countries.

12.4.2.4 Occurrence

Number of illnesses attributable to foodborne transmission including outbreaks

There are 9392 cases of giardiasis registered in MSIS 1995-2019, of which around 7% required hospitalisation. The number of cases seems to be rising, having increased annually since 2015, although this may reflect improvements in diagnostics or at any other stage in the diagnostic chain. The majority of cases are assumed to have been acquired abroad.

However, the proportion of these cases associated with foodborne transmission is unknown. Transmission via contamination of drinking water supplies is probably the most likely mode of foodborne transmission (cysts survive well in a damp environment, but are susceptible to desiccation). Transmission can also be direct (person-to-person) or via recreational water, and based on published reports globally foodborne transmission (not including drinking water) seems to be a less prominent transmission route.

Outbreaks

As with *Cryptosporidium, Giardia* is widely known as a waterborne parasite, associated with major outbreaks, including in Norway, associated with drinking water. Aside from outbreaks associated with drinking water, relatively few foodborne outbreaks have been reported, and in these instances, it often seems that the food handler has contaminated the food immediately prior to consumption. Only 2 outbreaks caused by *Giardia* were registered in VESUV 2005-2019.

12.4.2.5 Probability of increased human burden of disease

It is unclear whether if the human burden of *Giardia* infection in Norway is likely to increase. However, climate change factors and globalisation may suggest a trend in that direction,

particularly regarding an increased likelihood of transmission via contaminated drinking water. Improved sewage infrastructure may diminish the risk of water contamination.

12.4.2.6 Scorecard

Table 12-4. Final scores for *Giardia duodenalis*, based on EKE of nine experts.

Giardia duodenalis	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illness	2	2	2	2	2	2	2	1	1	1.78
Acute morbidity severity	2	2	2	2	2	2	2	2	2	2.00
Chronic morbidity severity	3	1	2	2	2	3	2	2	1	2.00
Fraction of chronic illness	1	1	2	1	1	1	1	1	1	1.11
Case fatality ratio	0	0	0	0	0	0	1	0	0	0.11
Probability for increased HBD	1	2	2	2	2	1	4	2	2	2.00
Total	9	8	10	9	9	9	12	8	7	9

12.5 Toxoplasma gondii

12.5.1 Organism

Toxoplasma gondii is an obligate intracellular parasite that causes the infectious disease toxoplasmosis. *T. gondii* is one of the most common parasites, being found in most species of warm-blooded animals, including humans, worldwide (FAO & WHO, 2014; NIPH, 2020c; Torgerson & Mastroiacovo, 2013).

Domestic cats and other animals in the cat family (Felidae) are the definitive hosts for *T. gondii*. During the acute phase of their infection, cats shed parasite eggs (oocysts) in faeces. When excreted, the oocysts are not infective until sporulation is completed, a process which usually takes around three days. Oocysts are transmitted through the faecal-oral route to intermediate hosts, which include humans, most mammals and birds. Cats also infect each other in this way. Infection with oocysts can occur directly, for instance by cleaning the cat litter tray, or indirectly through vehicles contaminated by cat faeces like food, water, objects and the environment (FAO & WHO, 2014).

In the intermediate hosts, *T. gondii* first develop into a rapidly dividing stage known as tachyzoites, before developing tissue cysts containing numerous parasite cells, most commonly in skeletal muscle, myocardium, brain, and eyes. The cysts usually persist throughout the life of the host. The parasite is transferred to new intermediate hosts, or to definitive hosts from their prey, by consuming raw, rare, or undercooked meat containing the tissue cysts.

Thus, humans and other intermediate hosts acquire toxoplasmosis in two main ways: by ingestion of meat from animals harbouring tissue cysts or by ingestion of oocysts from cat faeces via direct contact or indirectly through vehicles. If a female host is pregnant when first infected, the parasite may move through the placenta to the foetus (intrauterine or congenital transmission). Another transmission route is by tachyzoites in unpasteurized milk.

The parasite can cause disease in humans and other intermediate hosts. Cats are frequently infected when they are young. Although they develop only mild symptoms, cats shed large quantities of oocysts for a few weeks. In Norway, *T. gondii* is widespread in many warm-blooded animals, especially cats and sheep, but also in cattle, pigs and wild deer (see 13.5). *T. gondii* is one of the most common causes of abortion and stillbirth in sheep. All domestic animals are susceptible to infection, and virtually all edible portions of an animal can harbour viable *T. gondii* cysts.

Freezing of meat at temperatures below - 12°C for approximately one week, or adequate cooking, inactivates tissue cysts of *T. gondii*. However, the oocysts survive well in the environment and can retain their infectivity for months, even under the snow in winter (EFSA, Koutsoumanis, et al., 2018; NIPH, 2020c). The infective dose is low.

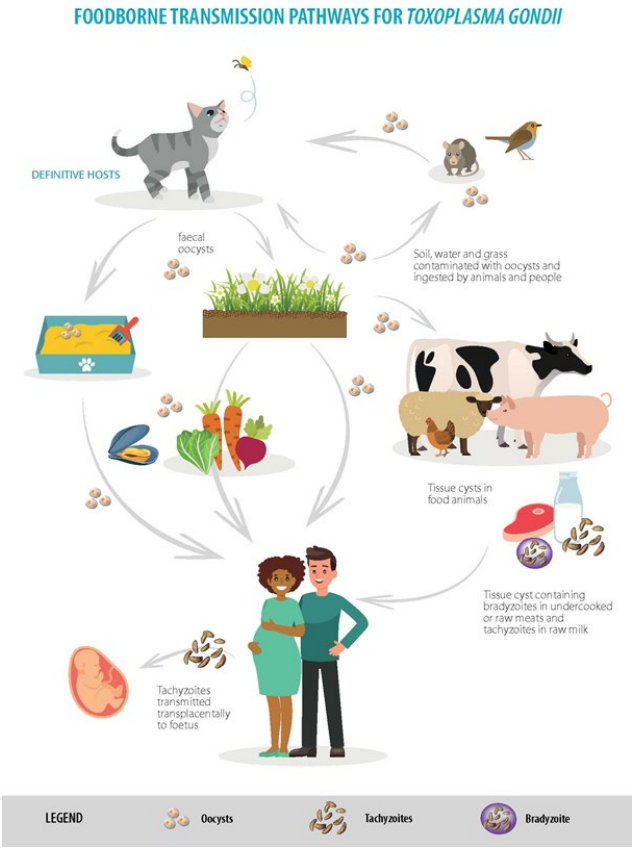

Figure 12-3. Life cycle of *Toxoplasma gondii*.

12.5.2 Illness and consequences

12.5.2.1 Acute and chronic morbidity

If a woman becomes infected with *T. gondii* for the first time immediately before or during pregnancy, the parasite can be transferred to the foetus. Pregnant women infected earlier in life have lifelong antibodies against the parasite that protect the unborn child. Transmission of the parasite, especially in the first part of pregnancy, can cause spontaneous abortion, stillbirth, ventricular dilatation, and intracranial calcification. In neonates, the infection may present as hydrocephalus, seizures, retinochoroiditis, spasticity, deafness, hepatosplenomegaly, jaundice or rash. Children who are asymptomatic at birth, may suffer from mental retardation later in life or from retinochoroidal lesions causing visual impairment or blindness. In children with congenital toxoplasmosis, the infection can be reactivated up to approximately 20 years of age and cause eye infections. Women infected during gestation usually experience no or only mild, nonspecific, symptoms themselves (FAO & WHO, 2014; NIPH, 2020c; Torgerson & Mastroiacovo, 2013).

Persons with immune deficiency can also develop serious illness, either by activation of a latent infection or by primary infection. In such individuals, the parasite can cause diseases like encephalitis, myocarditis and pneumonia, which may be life threatening in the absence of treatment.

Infection with *T. gondii* in immunocompetent people is largely asymptomatic or produces mild, flu-like symptoms (NIPH, 2020c). A number of studies have suggested that the parasite can provoke neuropsychiatric disorders even in individuals who do not have congenital toxoplasmosis (Coccaro et al., 2016; Hurley & Taber, 2012). Such disorders include increased risk behaviour, aggression, self-destruction, suicide, Alzheimer's disease, and schizophrenia. However, a review of current data concluded that if *T. gondii* influences human behaviour or disease, the effect is likely to be subtle and/or may be highly dependent on the genetic background of the individual or the context of the infection (e.g., *T. gondii* strain type, route of infection, and how long the individual has been infected) (Johnson & Koshy, 2020).

A study from the Unites States shows that atypical genotypes of *T. gondii* common in both North and South America have been associated with severe ocular and systemic disease and unusual presentations of toxoplasmosis in immunocompetent patients (Pomares et al., 2018).

12.5.2.2 Chronic morbidity severity and fraction of chronic illness

Congenital toxoplasmosis is mainly a lifelong, chronic, condition (Torgerson & Mastroiacovo, 2013). Nevertheless, deaths may occur, and the infection carries a significant risk of mortality among neonates infected *in utero*. In addition, *Toxoplasma* infection is responsible for an unknown number of undiagnosed abortions and stillbirths (see above).

Toxoplasmosis may be fatal in immunocompromised persons after activation of a latent infection or by primary infection. Toxoplasmic encephalitis is one of the most common infections resulting in death among AIDS patients (FAO & WHO, 2014).

12.5.2.3 Case-fatality ratio

No data are available from Norway. Calculation of case-fatality ratios is significantly hampered due to the absence of a routine screening programme for pregnant women, and because specific diagnostic tests are infrequently performed even in patients for whom toxoplasmosis is a possible cause of death.

12.5.2.4 Occurrence

In Norway, the seroprevalence of *T. gondii* infection among women of childbearing age is low in comparison with that in many other European countries and has been stable at 9-10% for the last 40 years (Findal et al., 2015; Jenum, Kapperud, et al., 1998). Consequently, the remaining 90 percent are susceptible to infection during gestation. The prevalence varies geographically and increases with age. In a nationwide survey of 36,000 pregnant women, the incidence of primary infection during pregnancy was 0.2%; the incidence was highest in Oslo (0.5%) and very low in Northern Norway (<0.1%) (Jenum, Stray-Pedersen, et al., 1998). In 30% of the cases, the parasite was transmitted to the foetus. The transmission rate increased significantly throughout pregnancy.

Unlike diarrhoeal diseases, congenital toxoplasmosis is a chronic disorder that persists throughout the life of the host. Hence, the cumulative number of cases in the population increases every year with successive addition of new cases from each new birth cohort, amounting to a considerable prevalence. Congenital toxoplasmosis is thus a disease with major health impact and large socio-economic consequences.

Toxoplasmosis is not a notifiable disease in Norway and no routine screening of pregnant women has been implemented.

Proportion of illnesses attributable to food- and waterborne transmission

In 1992-1994, a nationwide case-control study was conducted to identify risk factors for *T. gondii* infection among pregnant women in Norway (Kapperud et al., 1996). The principles for case-control studies are explained in Appendix III. The following factors were independently associated with an increased risk of primary infection during pregnancy (estimates of attributable fractions are given in parentheses; figures indicate the relative importance of the factors):

- Eating raw or undercooked minced meat products (29%)
- Eating raw vegetables or fruits that have not been washed (28%)
- Eating raw or undercooked mutton or lamb (22%)
- Eating raw or undercooked pork (18%)
- Cleaning the cat litter box (16%)

- Washing the kitchen knives infrequently after preparation of raw meat, prior to handling another food item (11%)

Thus, the majority (>60%) of infections with *T. gondii* in pregnancy are caused by consumption of foods containing tissue cysts or contaminated with oocysts (see section 13.5). Congenital toxoplasmosis can be regarded as indirectly foodborne when resulting from a primary foodborne infection in the mother.

Outbreaks

Very few outbreaks of toxoplasmosis have been described in humans, and there are no registered outbreaks in Norway. This reflects, at least partly, that most cases of infection do not result in acute symptoms that prompt the infected to seek medical attention.

12.5.2.5 Likelihood of increased human burden

T. gondii is more prevalent in mild and humid regions and is less common in northern Europe and in northern Norway than further south (EFSA, Koutsoumanis, et al., 2018; NIPH, 2020c). Thus, the risk of infection is higher in southern European countries than in Norway. A milder and wetter climate may favour the survival of oocysts in the environment and could lead to an increased incidence of toxoplasmosis in Norway. However, if such climate change leads to temperatures fluctuating around zero degrees, with repeated episodes of freezing and thawing, the survival of oocysts is presumably reduced.

Introduction of new, more virulent genotypes of *T. gondii* may increase the burden of disease. Such genotypes, which are common in North and South America, particularly Brazil, have been associated with severe ocular and systemic disease and unusual presentations of toxoplasmosis in immunocompetent patients (Pomares et al., 2018).

12.5.2.6 Scorecards

Table 12-5. Final scores for *Toxoplasma gondii*, based on EKE of nine experts.

Toxoplasma gondii	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	2	2	1	1	1	2	1	1.56
Acute morbidity severity	3	3	3	3	3	3	4	3	3	3.11
Chronic morbidity severity	4	4	3	4	4	4	4	3	3	3.67
Fraction of chronic illness	2	3	3	3	3	2	2	4	2	2.67
Case-fatality ratio	2	3	1	3	2	1	2	2	2	2.00
Probability for increased HBD	3	1	2	2	2	1	4	1	2	2.00
Total	16	16	14	17	15	12	17	15	13	15

12.6 Hepatitis A virus

12.6.1 Organism

Hepatitis A virus (HAV) is a positive-sense, single-stranded RNA virus that belongs to the family *Picornaviridae,* genus *Hepatovirus.* Three genotypes infect humans, but only one serotype has been described. There is no insect vector or animal reservoir for HAV.

Hepatitis A virions shed in the faeces of infected individuals are small, 27 nm diameter, with icosahedral protein capsids (Lemon, Ott, Van Damme, & Shouval, 2017). The virus is naked, does not have a lipid envelope, and this makes the virus particle more stable in the environment.

Viruses cannot multiply outside a host, but HAV can survive in the environment and in several food products, and can persist under standard storage conditions beyond the usual storage periods (reviewed by (Sánchez, 2015)). The infective dose is probably low.

The most important factors affecting the environmental stability of viruses are temperature, pH, relative humidity, moisture content, sunlight exposure, and type of food. Freezing is ineffective at inactivating HAV in foods. HAV is relatively resistant to temperatures below 70°C, but heating foods to 85°C for 1 min is effective in inactivating HAV (Favero & Bond, 1998; Sánchez, 2015).

Acidification of food is not a suitable procedure to control HAV in foods, as HAV remained infectious at treatments of pH 1 and 38 °C for 90 min (Céline Gallot et al., 2011).

An outbreak caused by HAV, associated with the consumption of dried tomatoes indicates that if food is contaminated before drying, a significant fraction of HAV will remain infectious.

The half-life for HAV on hands was found to be approximately 6 h, but increased to 51-187 h on a non-porous surface at room temperature, showing better survival at low relative humidity (Sattar, Tetro, Bidawid, & Farber, 2000).

Infected persons may excrete from 10^6 to 10^{11} viruses per gram of faeces (Sánchez, 2015). Hepatitis A virus can contaminate food via contaminated irrigation water, shellfish production areas, wash water, surfaces, and hands.

12.6.2 Illness and consequences

12.6.2.1 Acute morbidity

Acute HAV infection is typically self-limiting and characterized by nausea, vomiting, abdominal pain, malaise, anorexia, myalgia, fatigue, and fever (Iorio & John, 2021). Patients may develop pruritus and more than 70% develop jaundice. Symptoms may last for two months and 10-15 % of symptomatic cases have disease for up to 6 months. The severity of

symptoms varies with age and comorbidities, particularly underlying chronic liver disease. Less than 30 % of infected children under the age of 6 years develop symptoms and these are nonspecific and more influenza-like (MMWR, 1999).

Acute hepatic failure is observed in less than 1 % of cases (Shin & Jeong, 2018).

Extra-hepatic manifestations occur rarely, but may include pancreatitis, rash, acute kidney injury with interstitial nephritis or glomerular nephritis, pneumonitis, pericarditis, haemolysis, and acute cholecystitis. Neurological complications have also been reported, such as mononeuritis, Guillain-Barré, encephalitis, and central myelitis (Iorio & John, 2021).

Most patients recover naturally from acute hepatitis A and develop lifelong protective immunity. However, about 10% of patients progress to atypical clinical courses such as prolonged hepatitis (up to six months), relapsing hepatitis, cholestatic hepatitis, and autoimmune hepatitis.

12.6.2.2 Chronic morbidity severity and fraction of chronic illness

Chronic infection has not been reported (Lemon et al., 2017).

12.6.2.3 Case fatality ratio

Very rarely, HAV infection causes fulminant hepatitis and liver failure (overall case fatality ratio is 0.1 to 0.3% in EU/EEA). Patients with underlying chronic liver disease and people older than 50 years have higher case fatality ratios (1.8%) (Gossner, Severi, Danielsson, Hutin, & Coulombier, 2015).

12.6.2.4 Occurrence

Outbreaks

Registered foodborne outbreaks in Norway (https://www.fhi.no/sv/utbrudd/oversikt-over-storre-utbrudd/utbrudd-av-hepatitt-a-i-norge/):

2000: Nine cases on an oil platform in the North Sea. Contaminated food was probably the source.

2013: In the Nordic countries, 117 cases were caused by frozen straw berries imported from Morocco or Egypt.

2014: A total of 33 cases were associated with mixed frozen berries in a cake imported from Germany. A HAV strain detected in the cake was identical to the patient strain.

12.6.2.5 Likelihood of increased human burden

Immunity to HAV is low in the Scandinavian population, so susceptibility to infection is high. However, there are good vaccines against hepatitis A and people travelling to countries endemic for HAV are encouraged to get vaccinated. This is especially important for food handlers. In endemic countries, people are usually infected during childhood, show no symptoms, and develop lifelong immunity. Improved hygienic conditions in these countries may shift HAV infections to infecting people more severely when they get older. This could be an ongoing development, until hygienic conditions reach a sufficiently high level that HAV infections are only sporadic.

As HAV may be imported into Scandinavian countries with contaminated foods like berries and leafy greens, a situation with more HAV infections may arise if these products are imported from countries moving from a level of high endemicity to a lower level. As consumption of these foods is increasing in Scandinavia, follow-up on the production of imports from such countries will be important and vaccination of food handlers (at all stages from farm-to-fork) should be evaluated.

12.6.2.6 Scorecard

Table 12-6. Final scores for Hepatitis A virus, based on EKE of nine experts.

HAV	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	1	1	1	1	1	1	1	1	1.11
Acute morbidity severity	2	3	2	3	3	3	3	3	3	2.78
Chronic morbidity severity	0	2	0	0	3	2	3	0	1	1.22
Fraction of chronic illness	1	1	0	0	1	1	1	1	1	0.78
Case fatality ratio	1	2	2	1	2	2	2	1	2	1.67
Probability for increased HBD	2	1	1	2	2	2	1	1	2	1.56
Total	8	10	6	7	12	11	11	7	10	9.11

12.7 Hepatitis E virus

12.7.1 Organism

Hepatitis E virus (HEV) is a positive-sense, single-stranded RNA virus that belongs to the family *Hepeviridae* genus *Orthohepevirus* (Seth & Sherman, 2020). Hepatitis E virions are 27-30 nm diameter, with icosahedral protein capsids and no lipid envelope (naked). Depending on classification, 7-10 genotypes have been found and HEV1-4 infect humans (Seth & Sherman, 2020). Genotypes 3 and 4 have a reservoir in pigs and deer and are recognized as zoonotic viruses (Khuroo, Khuroo, & Khuroo, 2016).

Only one serotype has been described. A vaccine has been licenced in China, but is not available in other countries (Seth & Sherman, 2020).

HEV1 is endemic in Asia, Africa and Latin-America, while HEV2 dominates in African countries and Mexico. HEV1 and 2 cause massive epidemics in regions that have poor socio-economic conditions due to drinking water sources being polluted with sewage.

HEV3 has a world-wide distribution and HEV4 is mostly found in Asia and Central Europe.

In industrialized countries, HEV3 and 4 are spread through foodborne zoonotic transmission. Domestic pig and wild boar represent a HEV source through faeces, meat and liver (Khuroo et al., 2016). Eating parboiled flesh or liver or raw/undercooked sausages could be responsible for outbreaks of hepatitis E.

HEV is less stable than HAV regarding thermal inactivation, however HEV-infected pig liver homogenates maintain infectivity if incubated at 56° for 1 h. Boiling or frying for 5 min completely inactivates the virus (Feagins, Opriessnig, Guenette, Halbur, & Meng, 2008).

Concerning HEV survival in water, the virus does not have higher resistance to inactivating factors (heat, UV, chlorine, physical removal), than viral indicators (MS2 phage) or HAV (Fenaux et al., 2019).

12.7.2 Illness and consequences

12.7.2.1 Acute morbidity

In most patients, HEV causes a self-limiting illness which lasts a few weeks. Following an incubation period of 2 to 6 weeks, symptoms of hepatitis develop, with fever and nausea followed by abdominal pain, vomiting, anorexia, malaise, and hepatomegaly. Jaundice occurs in about 40% of patients (Kamar, Marion, Abravanel, Izopet, & Dalton, 2016). Most infections with HEV3 and 4 are asymptomatic and (67-98 %) clinical cases are usually men more than 55 years of age (Lhomme, Marion, Abravanel, Izopet, & Kamar, 2020).

In developing countries, excess mortality is seen in pregnant females (20-25 % in the final trimester) and individuals with underlying chronic liver disease. A higher virulence of HEV1 might be the reason, as this is the only genotype known to cause complications in pregnancy (Sayed, Vercouter, Abdelwahab, Vercauteren, & Meuleman, 2015).

In developed countries patients who have underlying chronic liver disease have a poor prognosis, and individuals who are immunosuppressed often develop chronic infection (Lhomme et al., 2020).

12.7.2.2 Chronic morbidity

Chronic infection with genotypes 1 and 2 has not been documented, but this could be due to limited studies in developing countries (Kamar et al., 2016).

In developed countries chronic infection with HEV3 (the virus replicates for more than 3 months) is seen with rapidly progressive cirrhosis (10 % of chronic infections) in organ transplant recipients, patients requiring chemotherapy, and individuals with HIV (Lhomme et al., 2020).

Hepatitis E has been associated with neurological, renal, and haematological extrahepatic manifestations. The most notable neurological manifestations include Guillain-Barré syndrome and meningoencephalitis. Renal manifestations include glomerulonephritis, and cryoglobulinemia. There have been cases of autoimmune haemolytic anaemia, aplastic, anaemia, thrombocytopenia, and pancreatitis (Kamar et al., 2016)

12.7.2.3 Case fatality ratio

The case-fatality ratio varies with genotype. In countries where HEV1 is endemic the ratio can be as high as 25 % in pregnant women, while in developing countries, HEV3 and 4 give a case-fatality ratio in the general population between 0.1% and 3% (Mushahwar, 2008).

12.7.2.4 Occurrence

Hepatitis E was notifiable to MSIS from 1991 to 2002. During this period, 24 cases were registered, all of which were people infected abroad. Norwegian Institute of Public Health collected data on HEV diagnoses from Norwegian laboratories in the period 2002-2018. In the last five years 13 cases were detected (https://www.fhi.no/nettpub/smittevernveilederen/sykdommer-a-a/hepatitt-e---veileder-for-helsepers/). Currently hepatitis E data is not collected in Norway and information on the occurrence of HEV infection is limited. However, antibodies against HEV have been found in 14 % of Norwegian blood donors and in more than 75 % of pigs tested. According to some medical personnel, hepatitis E is a neglected disease in Norway and the lack of information probably means that cases of hepatitis E are wrongly diagnosed as toxic hepatitis (Brantsæter, 2016).

Hepatitis E is not notifiable at the EU level, but some countries have surveillance systems and report cases to ECDC (Figure 9-4). In the period 2005 – 2015 there was an increase in locally acquired confirmed cases and 78 % of cases registered in France, Germany and UK (EFSA et al., 2017).

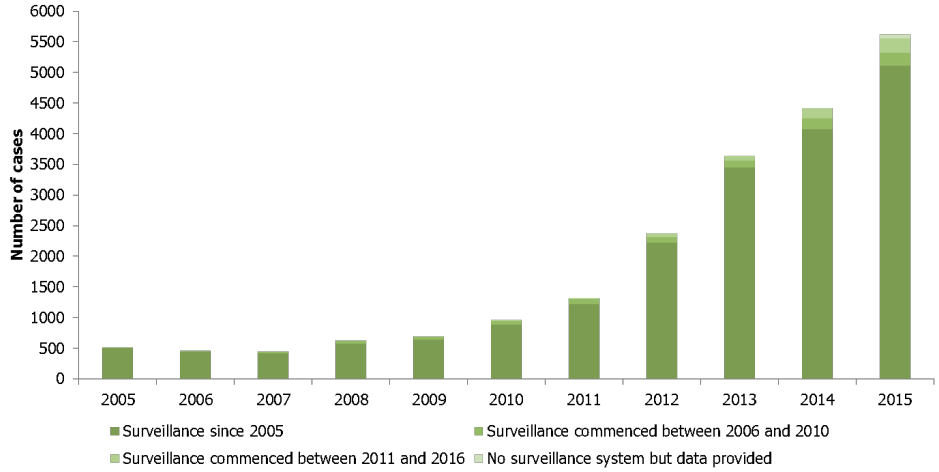

Figure 12-4. Reported cases of hepatitis E infection in Europe in 2005-2011. Data available for: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, United Kingdom

Outbreaks

In developing countries large outbreaks of hepatitis E caused by HEV1 and 2 in contaminated drinking water occur.

For HEV3 and 4, most cases are sporadic, but there have been well-documented small clusters of foodborne disease originating from infected Sika deer in Japan (Tei, Kitajima, Takahashi, & Mishiro, 2003). One outbreak of hepatitis E was linked to a cruise ship and consumption of shellfish (Said et al., 2009). In France, there have been outbreaks caused by consumption uncooked sausages that were made of pork products like liver and meat (Lapa, Capobianchi, & Garbuglia, 2015).

12.7.2.5 Likelihood of increased human burden

The increase in diagnosed cases in Europe could reflect increased awareness of and testing for hepatitis E (genotype 3). However, dietary reasons may also play a role, as food-borne transmission of HEV3 appears to be a major route in Europe (EFSA et al., 2017). The risk of food born transmission is primarily connected to consumption of raw or undercooked products made from pork liver and meat. There might be local food traditions which facilitates food borne transmission of HEV, which could result in serious infections, especially in persons with immune deficiency. HEV3 is presumed to be enzootic in the Norwegian pig population and there is an increasing focus on "raw food", which also includes hamburgers not fully heat treated. This trend makes an increase in HEV cases likely.

12.7.2.6 Scorecard

Table 12-7. Final scores for Hepatitis E virus, based on EKE of nine experts.

HEV	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	1	1	1	1	1	1	1	0	0	0.78
Acute morbidity severity	3	3	2	2	3	2	4	2	3	2.67
Chronic morbidity severity	3	3	3	3	3	3	3	3	3	3.00
Fraction of chronic illness	1	1	2	1	1	2	1	1	1	1.22
Case-fatality ratio	2	2	1	1	2	2	2	3	2	1.89
Probability for increased HBD	2	1	1	1	2	1	3	1	1	1.44
Total	12	11	10	9	12	11	14	10	10	11.00

12.8 Norovirus

12.8.1 Organism

Norovirus belongs to the family *Caliciviridae,* which are naked RNA viruses. This virus is classified into at least six genogroups (GI–GVI), of which three genogroups infect humans (GI, GII, and GIV) (Chhabra et al., 2019). GII.4 is the most common genotype and new variants that cause global epidemics are continuously emerging.

Norovirus causes a highly infectious gastroenteritis and norovirus is considered the most common cause of acute gastroenteritis worldwide (Glass, Parashar, & Estes, 2009). It has been estimated to cause 18% (95% CI: 17 - 20%) of acute gastroenteritis cases worldwide (Ahmed et al., 2014) leading to a substantial health and economic burden (Bartsch, Lopman, Ozawa, Hall, & Lee, 2016; CDC & Lopman, 2015).

The virus exhibits strong seasonality with most outbreaks occurring during the late autumn and winter months (Ahmed, Lopman, & Levy, 2013). The disease is therefore often called the "winter vomiting disease".

Norovirus is highly contagious, and some reports estimate that as few as ten virus particles can be enough to cause disease (Teunis et al., 2008). The virus is transmitted faecal-orally and vomit-orally by different routes such as directly from person-to-person, through contaminated food or water or from surfaces. It can easily be transmitted by aerosols from vomiting persons. Droplet and contact infections are probably the most common means of transmission during outbreaks in institutions and in households (NIPH, 2020a). Food-borne infections are estimated to account for approximately 15% of cases and 14% of outbreaks globally, but these estimates are mostly based on data from developed countries (CDC & Lopman, 2015).

There is no direct information on the survival of noroviruses on foods or in the environment due to the lack of methods to cultivate them. Heat treated foods do not appear to be an important source of infection. Problems usually arise when contaminated food is eaten without heat treatment. The virus is relatively resistant to acid treatment; a norovirus stool filtrate was infectious after exposure to pH 2.7 for three hours at room temperature (Dolin et al., 1972).

12.8.2 Illness and consequences

12.8.2.1 Acute morbidity

The incubation period is relatively short and varies between 12 - 48 hours. The symptoms include nausea, vomiting, abdominal pain, muscle aches, diarrhoea and fever and usually lasts for 1 - 2 days (Atmar et al., 2008; Glass et al., 2009). Illness from a norovirus infection is usually self-limiting, and healthy persons typically recover without sequelae (Robilotti, Deresinski, & Pinsky, 2015). Usually no specific treatment is needed except for relieving symptoms and preventing dehydration (NIPH, 2020a).

People of all age groups can be affected, with children experiencing the highest incidence. It is also known that some individuals are genetically more susceptible or protected against norovirus infections (Lindesmith et al., 2003). Severe outcomes, including hospitalization and deaths, are most common among children, immunocompromised individuals and the elderly (NIPH, 2020a).

Infected individuals are most contagious during the period of vomiting and diarrhoea but are also contagious for a short period before the onset of symptoms and a few days after recovery. Asymptomatic individuals can also excrete the virus. In experimental infections, 15-35% of adult volunteers that were confirmed positive for norovirus infection, either serologically or through detection of virus in stool samples, did not show symptoms associated with gastroenteritis (Atmar et al., 2011; Atmar et al., 2008; Graham et al., 1994; Lindesmith et al., 2003).

It is not clear how long the immunity after infection lasts. It is possible to become ill from norovirus infection several times during a lifetime, in part because there are many different types of the virus and because infection with one type may provide only limited or no cross-protection to another (CDC & Lopman, 2015; Wyatt et al., 1974).

12.8.2.2 Chronic morbidity

There is limited knowledge about chronic consequences as a result of Norovirus infections, but some data suggest that norovirus may be associated with chronic gastrointestinal problems such as irritable bowel syndrome (IBS), dyspepsia and gastroesophageal reflux syndrome (Porter et al., 2012; Zanini et al., 2012). IBS is the most frequently identified long-term consequence of norovirus infections and prospective studies have shown that ~3 to 36% of all enteric infections lead to an IBS diagnosis (CDC & Lopman, 2015). Norovirus

infections have also been reported to cause chronic diarrhoea in patients who are immunosuppressed such as transplant recipients.

12.8.2.3 Case-fatality ratio

Norovirus is estimated to cause about 200,000 deaths annually worldwide, 70,000 or more of these are among children in developing countries (CDC & Lopman, 2015). To the best of authors knowledge, no fataliiesy associated with norovirus infections have been reported in Norway.

12.8.2.4 Occurrence

Norovirus is usually detected in stools using a nucleic acid amplification method (PCR) or enzyme immunoassay (EIA) test. EIA tests are mainly suitable for the detection of outbreaks, due to their low sensitivity.

Although single cases and smaller outbreaks often remain unreported, norovirus is one of the most commonly registered causes of waterborne outbreaks of disease in Norway in recent years. In the period 2002 - 2018, the Norwegian Institute of Public Health collected monthly data for positive findings of noroviruses from most of the country's microbiological laboratories (NIPH, 2020a).

Outbreaks

The disease is usually recognized as outbreaks, often in environments where people are in close contact with each other, such as health care institutions, day care centres, cruise ships, military camps and hotels (NIPH, 2020a). These outbreaks are often amplified due to secondary transmission of the virus.

Ready-to-eat foods, including vegetables, shellfish and foods handled after cooking are the products most frequently associated with norovirus outbreaks (Hall et al., 2012). Noroviruses are particularly challenging for the production of bivalve shellfish such as mussels and oysters. If the water they grow in is faecally contaminated, the virus can be concentrated in the molluscs when they filter-feed and then transmitted to consumers if eaten without sufficient heat treatment (WHO, 2015).

In the period 2005 - 2018 there have been 1,126 food-borne Norovirus outbreaks in Norway, including 24,778 cases.

12.8.2.5 Likelihood of increased human burden

The global burden of norovirus infections is not expected to decrease as new variants emerge every □2–4 years, probably in response to population immunity from current variants. Multiple norovirus vaccines are currently in the pipeline, but it is unknown if they will provide cross-protection against different existing and emerging subtypes of the virus, nor is it known how long vaccine-induced immunity will last (Hall, Glass, & Parashar, 2016).

12.8.2.6 Scorecard

Table 12-8. Final scores for Norovirus, based on EKE of nine experts.

Norovirus	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illness	3	4	3	4	4	4	3	3	3	3.44
Acute morbidity severity	1	2	1	1	2	2	3	2	2	1.78
Chronic morbidity severity	1	0	1	0	1	1	2	1	1	0.89
Fraction of chronic illness	1	0	1	0	1	1	1	1	1	0.78
Case fatality ratio	1	0	0	0	1	1	1	0	1	0.56
Probability for increased HBD	1	2	1	2	1	1	2	1	1	1.33
Total	8	8	7	7	10	10	12	8	9	8.78

12.9 Bacillus cereus

12.9.1 Organism

Bacillus cereus is a Gram-positive, endospore (spore) -forming bacterium that is considered an important but under-reported cause of food poisoning. It causes food-borne illness mainly due to improper heat treatment and storage of foods (NIPH, 2020c).

The following violations of basic kitchen hygiene principles may contribute to propagation of *B. cereus* in foods (NIPH, 2020c):

- Heating at low temperature (<60 ° C)
- Insufficient or too slow cooling
- Storage at room temperature
- Insufficient heating of leftovers

B. cereus spores are metabolically dormant and exhibit extreme resilience towards environmental stressors due to their dehydrated state and unique multilayered cellular structure. *B. cereus* endospores can withstand wet heat (boiling), long periods of drought, starvation and exposure to disinfectants. Since *B. cereus* spores are ubiquitous in the environment, especially in soil and vegetation, they can contaminate foods at many stages along the value chains -at the farm, under transport, during processing and storage. *B. cereus* spores are common in a wide variety of food items such as grains, spices, pasta, vegetables, rice, milk, and meat (Soni, Oey, Silcock, & Bremer, 2016).

12.9.2 Illness and consequences

12.9.2.1 Acute morbidity

B. cereus causes two different types of food-borne disease mainly due to improper heat treatment and food storage (NIPH, 2020c):

Diarrhoeal syndrome, where toxins are formed during bacterial growth in the gut and emetic (vomiting) syndrome, which is an intoxication caused by consumption of foods containing the pre-formed toxin cereulide. All people are considered susceptible to *B. cereus* infections and intoxications.

The diarrhoeal syndrome is considered the most common form of *B. cereus* food poisoning in Norway. *B. cereus* produces different types of enterotoxins that are involved in development of gastroenteritis. The enterotoxins, which are actively secreted by the bacterium during vegetative growth in the gut, causes damage to the intestinal epithelium, resulting in abdominal pain and watery diarrhoea. The symptoms occur 6 - 24 hours after ingestion of contaminated food. The symptoms are usually self-limiting and last for up to 24 hours. It has been estimated that the infective dose for diarrhoeal syndrome is between 10^5-10^7 vegetative cells or spores per gramme of food ingested. Not all *B. cereus* strains causes diarrhoea, some are even claimed to have probiotic effects.

Emetic syndrome is an intoxication caused by the toxin cereulide that is formed during growth of *B. cereus* in food that has been stored at temperatures between 12 – 37 °C after heat treatment. It has been estimated that the infective dose for emetic syndrome is between 10^4–10^9 CFU vegetative cells or spores per gramme of food but, notably, pathogenicity arises from the preformed toxin cereulide, not from the bacteria themselves. According to studies in monkeys and based on the analysis of foods involved in foodborne intoxication in humans, from 5 to 10 µg of cereulide per kg of body weight is necessary to induce the emetic symptoms. This quantity of cereulide can be found in food when a *B. cereus* strain reaches a concentration of 10^6 cfu/g or greater (EFSA 2016; Granum & Lund, 1997; Logan, 2012).

The symptoms, which usually include nausea and vomiting, start between 30 minutes to 6 hours after ingestion of food containing pre-formed cereulide. They usually last for 8 - 16 hours and can be difficult to distinguish from *Staphylococcus aureus* food poisoning. Emetic syndrome is often associated with starchy products, such as boiled or fried rice, pasta, and potatoes. Cereulide is very heat resistant and rarely destroyed during heating of food.

Food poisoning can also be caused by toxins from other *Bacillus* species, e.g. *Bacillus thuringiensis* and *Bacillus cytotoxicus*, which are closely related to *B. cereus* (EFSA 2016; Guinebretière et al., 2013; Jackson, Goodbrand, Ahmed, & Kasatiya, 1995; Johler et al., 2018). Food-borne disease caused by *B. thuringiensis* is probably under-reported, as methods for identification of *B. cereus* in food and clinical settings do not distinguish between *B. cereus* and *B. thuringiensis* (EFSA & Hazards, 2016; Johler et al., 2018).

12.9.2.2 Chronic morbidity severity, fraction of chronic illness and case-fatality ratio

Symptoms are usually mild and do not last for more than 1 day. Severe intoxications are rare but can lead to acute liver failure and encephalopathy (Ichikawa et al., 2010). Intoxications

with fatal outcomes have been reported other countries, but not Norway (Naranjo et al., 2011).

12.9.2.3 Occurrence

B. cereus is confirmed as the source of a foodborne outbreak by isolation of the bacterium from a confirmed or suspected food source and the faeces or vomitus from at least two individuals affected by an outbreak (NIPH, 2020c).

Most cases likely go unreported because: 1) *B. cereus* food poisoning is not a reportable disease, 2) the symptoms are generally mild and subside on their own 3) the patients who do visit a doctor are often not tested to determine the etiological agent 4) the symptoms can be misdiagnosed as clostridial infections or intoxications with *S. aureus* enterotoxins

B. cereus food poisoning is not reported to MSIS, and the local medical officer and the Norwegian Institute of Public Health may not be notified during smaller outbreaks. Because of this, it is difficult to determine how often *B. cereus* food-poisoning cases and small outbreaks occur. The real importance of *B. cereus* group species as pathogens can therefore only be estimated using data from foodborne outbreaks.

Outbreaks

In the period 2005 - 2019, a total of 33 *B. cereus* outbreaks involving 278 cases were reported to Vesuv. Annual reports from EFSA estimate that "bacterial toxins other than *C. botulinum*, including those from *B. cereus,* account for approximately 16 - 20% of food poisoning outbreaks among the member states. In the period 2011 - 2015, several member states reported between 220 - 291 annual outbreaks associated with *B. cereus* and this accounted for approximately 3.9-5.5% of all annual food-poisoning outbreaks (Eurosurveillance editorial, 2013).

12.9.2.4 Likelihood of increased human burden

Record high temperatures have been measured worldwide, and there is an increasing number of intense rainfall events in the Northern Europe(EEA, 2017). The temperature increases and changes in rainfall patterns have an impact on the persistence and composition of bacteria in the environment (Li et al., 2018; Wang, Pan, Soininen, Heino, & Shen, 2016). A study from China showed that environmental temperature and humidity are important determinants for the composition of the raw milk microbiota. A higher abundance of bacteria belonging to the phylum Firmicutes, to which *B. cereus* belongs, was correlated with high temperature (Li et al., 2018).

12.9.2.5 Scorecard

Table 12-9. Final scores for *B. cereus*, based on EKE of nine experts.

Bacillus cereus	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	3	1	2	3	2	1	1	2	1.89
Acute morbidity severity	1	1	1	1	2	2	2	2	2	1.56
Chronic morbidity severity	1	0	0	0	1	1	1	1	1	0.67
Fraction of chronic illness	0	0	0	0	1	1	1	1	1	0.56
Case-fatality ratio	0	0	0	0	0	0	0	0	0	0.00
Probability for increased HBD	1	1	0	1	1	1	1	1	1	0.89
Total	5	5	2	4	8	7	6	6	7	5.56

12.10 Clostridium botulinum

12.10.1 Organism

Botulism is a rare but serious paralytic illness caused by six different *Clostridium* species, including *Clostridium botulinum* (Table 12-10). They belong to the family Clostridiae which include anaerobic, rod-shaped, spore-forming bacteria. Common to these species is that they produce closely related botulinum neurotoxins when they multiply in oxygen-free and moist environments.

For simplicity, all *Clostridium* species that produces botulinum toxin are referred to as *C. botulinum* in this chapter.

Table 12-10. The six *Clostridium* species that produce botulinum toxin and their non-toxin-producing equivalents

Toxin producing	Non-toxin producing equivalent
***C. botulinum* Group I (proteolytic)**	*C. sporogenes*
***C. botulinum* Group II (non-proteolytic)**	Not named
C. botulinum Group III	*C. novyi*
C. botulinum Group IV (C. argentinenense)	*C. subterminale*
C. baratii	*C. baratii*
C. butyricum	*C. butyricum*

C. botulinum strains are grouped genotypically and phenotypically into four distinct groups, designated I to IV. Generally, strains belonging to groups I and II cause human botulism, while group III strains cause animal botulism (exceptions occur). Group IV have generally not been associated with illness. Group I and II *C. botulinum* strains differ phenotypically from each other: Group I strains are often of terrestrial origin whereas group II strains are found in aquatic environments in the Northern hemisphere. There are also differences in heat resistance of spores and growth temperatures between groups I and II strains: group I

spores, which exhibits a high heat resistance, cause problems in canning and home preservation of foods, whereas group II spores, which exhibit somewhat lower heat resistance, are problematic in minimally processed packaged foods that have extended shelf lives at refrigerated temperatures.

The botulinum neurotoxin is proteinaceous and can be inactivated by sufficient heat treatment. After ingestion, toxin is absorbed in the small intestine by binding to receptors on gut epithelial cells. Thereafter, it is released into the blood and lymphatic circulations, from where it can reach peripheral cholinergic nerve endings throughout the body. The toxin binds to specific receptors on the nerve-endings and becomes internalized into the cytosol of the nerve terminus, where it blocks the release of acetylcholine, resulting in characteristic paralysis.

The botulinum neurotoxins are considered the most lethal natural toxins known. *C. botulinum* produce eight types (A - H) of neurotoxins, based on the serological specificity. Although the toxins are serologically diverse, they are structurally similar and have nearly the same biological effect on humans, warm-blooded animals, and fish. The most common types of botulinum toxin associated with human outbreaks are A, B, and E. Type F is rare, but has been involved in a few human outbreaks. In animal botulism outbreaks, types C and D predominate, but types A, B, and E have also been involved.

12.10.2 Illness and consequences

Three different forms of botulism are described, of which two can be foodborne:

Food-borne botulism is an intoxication caused by eating foods that contain pre-formed botulinum neurotoxin. Ingesting the bacteria themselves or their spores is usually not harmful to healthy individuals above 1 year of age. It has been estimated that botulism has the highest cost per hospitalized patient of all foodborne diseases (Roberts, 2000).

Infantile botulism is an intestinal colonization botulism and occurs when infants consume spores of *C. botulinum*. Colonization of infant intestine is facilitated by a lack of competition from a mature resident intestinal microbiota. In this case, botulinum neurotoxin is produced and released in the intestines unless the infant is treated with antibiotics. Infantile botulism occurs in children under the age of 1 year and the most common sources of the infection is honey and environmental exposure (dust or dirt). Although extremely rare, adults can acquire "infant botulism" due to intestinal abnormalities or after antibiotic treatment, as both conditions can weaken the natural intestinal microbiota.

Wound-related botulism has been increasingly diagnosed in people taking drugs with syringes. Wound botulism occurs when *C. botulinum* spores germinate in wounds or abscesses, that provide anaerobic conditions, for subsequent growth and production of botulinum neurotoxin.

12.10.2.1 Acute morbidity

The first symptoms of foodborne botulism usually appear 12 - 36 hours after eating toxin-containing foods, but there can be large variations from a few hours to several days.

All forms of botulism manifest as progressive neuronal paralysis, often starting with mild symptoms that may go away on their own, including abdominal pain, nausea, vomiting or diarrhoea (not in wound botulism), double and/or blurred vision, and drooping eyelids. In more severe cases, the symptoms progress to slurred speech, difficulty in swallowing, facial paralysis and dilated pupils. Limbs paralysis may occur and respiration fail. Botulism usually requires hospitalization, sometimes for a prolonged period. Respiratory muscle paralysis can lead to death. However, when treated effectively with antitoxin, mechanical ventilation, and other therapeutic measures, the survival rate is high. Physical therapy can facilitate recovery of muscle strength. Infantile botulism is also characterized by inability to suck, a weak cry, and poor head control. The onset is subacute to acute and the disease may progress to generalized hypotonia called "floppy baby syndrome" and respiratory failure.

The laboratory diagnostics of botulism is based on the detection of botulinum neurotoxin in the patient. Furthermore, detection of neurotoxin-producing clostridia in the patient and/or the source confirms the diagnosis.

12.10.2.2 Chronic morbidity

Paralysis symptoms of botulism often last for several weeks and then slowly go away in the following months. Fatigue and shortness of breath can last for several years. The recovery time is dependent on the amount of neurotoxin the patient has ingested and, to a lesser extent, on the toxin type. Type A toxin tends to be more potent than types B and E and causes the longest-lasting disease. Although botulism can cause severe and prolonged symptoms, most affected individuals recover completely from the illness.

12.10.2.3 Case-fatality ratio

Early treatment reduces the risk of permanent disability and death. However, even with treatment, botulism can be fatal. Patients who die tend to have a shorter reported median incubation period (1 day; range, 0.2 – 8 days) than patients who survive (1.5 days; range, 0.1 –12 days). Without treatment, more than 50% of people with botulism would die. Cases of sudden infant death syndrome have been related to infant botulism. The mortality rates from botulism have decreased drastically in recent years due to better treatment options and access to antisera. In Norway, nobody has died of foodborne botulism during the past 30 years and only one person has died since 1977.

12.10.2.4 Occurrence

C. botulinum prefers to grow in decaying organic matter and the spores are common in soil, mud, and sediments. *C. botulinum* spores are also present in the intestinal tract of fish and

other animals. The prevalence of spores varies in number and type from region to region due to differences in food preparation, food storage, and management practices. In the period 1995 - 2019 there have been 66 botulism cases in Norway. Most of them (52%) were in the age group of 40 - 59 years and the majority (77%) were infected in Norway. The great majority of cases (86%) required hospitalization.

Outbreaks

Two small outbreaks of botulism were registered in Norway between 2005 – 2019. An outbreak in 2005 included three cases and one in 2017 included two cases

12.10.2.5 Scorecard

Table 12-11. Final scores for *Cl. botulinum*, based on EKE of nine experts.

Clostridium botulinum	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	1	0	0	0	0	1	1	0	0	0.33
Acute morbidity severity	4	4	3	4	4	3	4	4	4	3.78
Chronic morbidity severity	3	2	2	2	4	3	4	4	2	2.89
Fraction of chronic illness	2	2	2	2	3	2	3	3	2	2.33
Case-fatality ratio	2	1	0	1	0	0	3	1	0	0.89
Probability for increased HBD	1	1	0	1	1	1	1	0	0	0.67
Total	13	10	7	10	12	10	16	12	8	10.89

12.11 Clostridium perfringens

12.11.1 Organism

Clostridium perfringens is a Gram-positive, spore-forming, anaerobic bacterial species that is found in soil, aquatic sediments, sewage, and in the intestinal tract of humans and other warm-blooded animals. Although this bacterium can be a natural member of the microbial community in the human intestinal tract, some strains may cause foodborne illness when foods contaminated with a large number of toxigenic *C. perfringens* are consumed *C. perfringens* food poisoning is one of the most common foodborne illnesses in the western world. The intestinal tract of animals was previously considered to be the main reservoir of toxigenic *C. perfringens,* with contamination occurring at slaughter. Although PCR analyses suggest a high prevalence of toxigenic *C. perfringens* in the intestines of food-producing animals, such strains have not been isolated from healthy production animals and very rarely from foods of animal origin. Toxigenic *C. perfringens* has, on the other hand, more frequently been isolated from humans and it has been suggested that the human gastrointestinal tract serves as an important source of contamination from healthy people

handling foods or food raw materials. Direct person-to person faecal-oral transmission has, however, not been considered to be an important transmission route.

C. perfringens also causes soft tissue infections and abscesses around injection sites in intravenous drug abusers. Toxin-producing species of type D can also cause gas gangrene during soil contamination of wounds. Non-foodborne *C-perfringens* infections will not be discussed further in this chapter.

C. perfringens represents one of the fastest multiplying organisms known; the generation time can be down to 8 minutes at 43 °C and 12 - 17 minutes at 37 °C when cultured in an optimal media. It grows in the temperature range of 15 - 50 °C, at a water activity down to 0.03 and at pH between 5.0 to 8.3. The spores can withstand cooking for several hours and will germinate as the temperature drops to 48 - 50 °C.

12.11.2 Illness and consequences

C. perfringens causes two types of food poisoning in humans: gastroenteritis and necrotic colitis. *C. perfringens* produces a range of different toxins and enzymes that may be involved in virulence and isolates are typed from A – E depending on which type of toxin they produce. Types A and C cause foodborne illness in humans.

Gastroenteritis, which is the most common form of *C. perfringens* food poisoning, is mainly caused by type A strains that produce the heat-stable, pore-forming enterotoxin CPE. Less than 5% of *C. perfringens* type A strains produces the CPE toxin. CPE is formed and released when the bacteria sporulate in the intestine. Production of CPE increases the spores heat resistance, and strains carrying the *cpe* gene are selected for in kitchen environments where the bacteria can be exposed to repeated heat treatments.

Laboratories diagnose *C. perfringens* food poisoning by detecting CPE toxin in patient faecal samples or by determining the number of bacteria in the faeces. At least 10^6 spores / gram stool is required to diagnose the infection. *C. perfringens* food-poisonings are, however, suggested to be underreported due to the short duration time and self-limiting symptoms.

C-type *C. perfringens* causes necrotic enteritis,a very serious form of food poisoning with high mortality. Necrotic enteritis is primarily caused by the pore-forming so called "β-toxin" or "CPB". The toxin is produced during vegetative growth of the bacterium in the small bowel (primarily the jejunum). Many type-C isolates also carry the *cpe* gene, and it has been shown that these two toxins can function synergistically in development of disease.

12.11.2.1 Acute morbidity

The symptoms of the common *C. perfringens* type A food poisoning are typically mild and self-limiting. They start suddenly and are almost indistinguishable from those caused by *B. cereus* food poisoning. After an incubation period of 6 to 24 hours (typically 8 to 12 hours), the infected person experiences severe abdominal pain and nausea, followed by watery diarrhoea often accompanied by headache. Fever and vomiting are unusual. The symptoms

usually last for 16 to 24 hours although stomach cramps can continue a little longer. The infective dose is often as high as 10^8 cells (10^6 cells / gram of food).

Everyone is susceptible to *C. perfringens* food poisoning. Very young, chronically ill, and elderly people are at the highest risk of *C. perfringens* infection and can experience more severe symptoms that may last longer (1 to 2 weeks) than in healthy adults. Complications, including dehydration, may occur in severe cases. Individuals who have had *C. perfringens* infections can shed spores for a long period after the symptoms have disappeared.

C. perfringens necrotic enteritis has an incubation time of less than 24 hours and the symptoms start with acute severe abdominal pain, vomiting and bloody stool. In the most severe cases, the symptoms develop into septic shock and necrosis in the intestine. Without treatment, death may occur within a short time. The infective dose is not known because external factors and nutritional status likely play an important role in disease progression. For example, C-type *C. perfringens* is extremely sensitive to trypsin and other proteolytic enzymes. Low protein diets reduce trypsin formation in the pancreas and increase the risk of developing necrotic enteritis. Furthermore, diets dominated by foods containing trypsin inhibitors (such as sweet potatoes and soybeans) can also make people particularly vulnerable. Human *C. perfringens* necrotic enteritis is endemic in Southeast Asia but extremely rare in Europe.

12.11.2.2 Chronic morbidity

To the best of authors' knowledge, no typical chronic morbidity following *C. perfringens* type-A food poisonings has been reported.

Little information is available about chronic morbidity after *C. perfringens* food poisonings. However, depending on the extent of intestinal damage, poor digestion and adsorption may result.

12.11.2.3 Case-fatality ratio

C. perfringens food poisoning very rarely leads to death but, when it occurs, it is often at nursing homes and hospitals where dehydration and other complications can occur in already weakened individuals.

In contrast, even when *C. perfringens* necrotic enteritis is diagnosed early, the mortality rate can be as high as 20%.

12.11.2.4 Occurrence

Sporadic cases of *C. perfringens* food poisoning are not reported to MSIS. *C. perfringens* type C is very rarely isolated in Norway and other parts of Europe.

Outbreaks

A large proportion of outbreaks of *C. perfringens* infection are probably never recognized or reported. Despite likely being underreported, *C. perfringens* is considered one of the most important causes of food poisoning in the Western world. In the period 2005 - 2019, a total of 12 *C. perfringens* outbreaks, including 293 cases, were reported to Vesuv. No outbreaks were reported between 2016 – 2019.

12.11.2.5 Scorecard

Table 12-12. Final scores for *Cl. perfringens*, based on EKE of nine experts.

Clostridium perfringens	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	3	1	2	2	1	1	0	2	1.56
Acute morbidity severity	2	2	2	1	2	2	2	3	2	2.00
Chronic morbidity severity	0	0	0	0	1	1	1	1	0	0.44
Fraction of chronic illness	0	0	0	0	0	1	1	0	0	0.22
Case-fatality ratio	0	0	1	0	1	1	1	1	0	0.56
Probability for increased HBD	1	0	0	1	1	1	1	0	0	0.56
Total	5	5	4	4	7	7	7	5	4	5.33

12.12 Staphylococcus aureus

12.12.1 Organism

Staphylococcus aureus food poisoning is caused by ingesting foods containing toxins produced by *S. aureus* growing in the food. *S. aureus* can also cause local and systemic infections in humans, where methicillin-resistant *S. aureus* (MRSA) is of particular concern; however, these infections are not caused by consumption of food and are not described further here.

S. aureus can produce several types of enterotoxins that can cause food poisoning. The bacterium is commonly found on human skin and in the nasal cavity, and 20-30% of adults are healthy carriers. The organisms can be transferred to food from food handlers that carry the bacterium or by cross-contamination from equipment and surfaces *S. aureus* is frequently isolated from unpasteurised milk and milk products, where animals with *S. aureus* mastitis are often the source. The disease arises after ingestion of food where *S. aureus* has grown and produced toxins. Growth and toxin production of *S. aureus* occurs when the food is not cooled properly or is kept warmed at a too low temperature. The toxins are heat-stable, so heating of food after the toxins are formed will not inactive them. Typical high risk products are meat and fish products, pre-peeled shrimps, salads, cream-filled pastry and cakes, and unpasteurized milk.

12.12.2 Illness and consequences

12.12.2.1 Acute morbidity

Symptoms have a rapid (30 min- 8 hours) onset after ingestion of food with preformed toxins. The most common symptoms are nausea, vomiting and abdominal cramping with or without diarrhoea. Symptoms are typically self-limiting and usually resolve within 24 hours.

12.12.2.2 Chronic morbidity

Infections are usually self-limiting, but complications occasionally occur, especially in the elderly, with the potential for dehydration and electrolyte imbalances, and, in extremely rare cases, *S. aureus* food poising can be fatal. In USA it was reported that 10% of cases involved in outbreaks with *S. aureus* food poisoning in 1977-1981, visited or were admitted to hospitals (Holmberg, 1975), while in UK it was reported that at least 14% of sporadic and reported cases from 1969-1990 required hospitalization (Wieneke, 1988).

12.12.2.3 Case-fatality ratio

The disease is rarely fatal, but deaths can occur. There is limited information available about case-fatality ratios, but in a study in USA of 7126 outbreak-associated cases from 1977-1981, the case fatality rate was 0.03%; all deaths were in elderly patients (Holmberg, 1975).

12.12.2.4 Occurrence

S. aureus food poisoning is not reported to MSIS and most sporadic cases are likely to go unreported. The disease is per definition 100% food borne.

Outbreaks

S. aureus is occasionally causing food-borne outbreaks in Norway.

12.12.2.5 Likelihood of increased human burden

Increasing temperatures due to climate change may lead to more situations in which food is not properly cooled.

12.12.2.6 Scorecard

Table 12-13. Final scores for *S. aureus*, based on EKE of nine experts.

Staphylococcus aureus	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	1	2	3	1	1	1	2	1.67
Acute morbidity severity	3	2	1	1	2	2	2	2	2	1.89
Chronic morbidity severity	0	1	1	0	2	2	3	2	1	1.33
Fraction of chronic illness	0	0	1	0	1	1	1	2	1	0.78
Case-fatality ratio	0	0	1	0	1	1	1	1	0	0.56
Probability for increased HBD	2	0	0	1	1	1	1	0	1	0.78
Total	7	5	5	4	10	8	9	8	7	7.00

12.13 Listeria monocytogenes

12.13.1 Organism

Listeria monocytogenes is a gram-positive bacterium that causes the illness listeriosis in animals and humans. Several serotypes of *L. monocytogenes* occur, all of which can cause listeriosis, but most human cases are caused by serotype 1/2a and 4b strains. During the last decade, PCR technology has replaced immunological methods for grouping of strains, and they are now grouped in molecular serogroups. Most isolates that have caused human illness cases belong to molecular serogroup IIa and IVb. Illness among animals is often related to serogroup IIc. Until a few years ago, the distribution of sporadic cases and outbreak cases of human listeriosis was assumed to be approximately 90 to 10. After the introduction of whole genome sequencing (WGS), this pattern has been reconsidered (EFSA & ECDC, 2018a; Schjorring et al., 2017). Typing of patient isolates from the last decades in different countries has indicated links between illness cases in several countries and different years which had not previously been recognised (ECDC, EFSA, & ANSES, 2021). Today, sporadic cases of human listeriosis are hardly mentioned in surveillance reports, but the definition of outbreaks has changed from being at least three cases over a few months period to outbreaks that can last for many years, in some cases with only a few new patients in some years. A recent example of an outbreak that was discovered years after it actually happened is a multinational outbreak associated with smoked salmon from a smokehouse in Poland that was distributed to several countries and used salmon from many suppliers, including some from Norway (EFSA & ECDC, 2018a).

L. monocytogenes is a ubiquitous bacterium. Typical reservoirs are soil, animals prior to slaughter, food-processing environments, food, and people. This widespread and high persistence of the bacterium appears contradictory to the relatively low number of registered listeriosis cases in humans (see below). However, most cases of human illness cases are related to intake of food with high concentrations of the bacterium (Buchanan, Gorris, Hayman, Jackson, & Whiting, 2017). The infective dose is not known, but risk models

indicate that the dose that leads to increased likelihood of illness among vulnerable consumers, like pregnant women, foetus, the elderly, and the immunocompromised, is 1000 cfu/g or higher, and 100000 cfu/g or higher for consumers not considered vulnerable (Pouillot, Hoelzer, Chen, & Dennis, 2015). These numbers are based on an intake of 100 g of the contaminated food.

L. monocytogenes can grow in many foods, even at cold storage temperatures, but is killed by pasteurization or heating to more than 55 ºC for a few minutes (Augustin, Zuliani, Cornu, & Guillier, 2005; Beaufort et al.). The bacterium can survive for years in low water activity foods, such as frozen, salt-cured, and dried food (Lorentzen, Wesmajervi Breiland, Cooper, & Herland, 2012). It can grow in air-packed, vacuum-packed, and modified-atmosphere-packed foods, but at different rates, partly due to different interfering effects of other microbes in the food (Cornu, Billoir, Bergis, Beaufort, & Zuliani, 2011; T. Skjerdal et al., 2021; VKM et al., 2019; VKM et al., 2018).

Legislation in EU and Norway focuses on the concentration of the bacterium in food, not only the presence. There is a microbial criterium for *L. monocytogenes* in ready-to-eat foods in the law (EU regulation 2073/2005, adopted in the Norwegian Food Law) that distinguishes between foods in which *L. monocytogenes* can and cannot grow.

12.13.2 Illness and consequences

Listeriosis appears in two versions. The less severe one causes flu-like symptoms and is called gastric listeriosis, the more severe version is called invasive listeriosis. In this case, the bacterium invades the body and causes meningitis, sepsis, and severe damage of infected organs. Invasive listeriosis has a higher fatality rate than most other foodborne illnesses and is therefore a major concern (EFSA & ECDC, 2019; EFSA, Ricci, et al., 2018). The number of registered invasive listeriosis cases in Europe is about 1500 per year, with most cases among the elderly and people with underlying diseases. Pregnant women and their foetus represent another vulnerable group, which also highlights the different symptoms of cases. Although the pregnant woman may not develop severe symptoms, the foetus may have severe, potentially fatal, symptoms from the same infection. EFSA carried out a large study in 2018 that considered various aspects regarding *Listeria* surveillance and models. This study indicates a possible overrepresentation of listeriosis cases in the age group 30-40 years that cannot be linked to the groups that have been considered as vulnerable until now. Another group with overrepresentation of listeriosis, was people medicated for acid regulation in the stomach.

The symptoms of gastric listeriosis are reported as flu-like. In families with members in different age groups and with different vulnerabilities, these are reflected in the strength of the symptoms. In recent outbreaks in Norway, it was observed that grandparents with underlying diseases had severe symptoms for weeks, grandchildren with underlying illness developed less-severe symptoms, while the parents had no apparent symptoms at all.

12.13.2.1 Acute morbidity

The symptoms of both invasive listeriosis and gastric listeriosis are severe. In the latter case, strong flu-like symptoms occur for weeks for the most vulnerable consumer groups.

12.13.2.2 Chronic morbidity

As *L. monocytogenes* invades organs, including vital organs, complications like blood infection, meningitis, or encephalitis occurs in up to 40 % of cases. The number of DALYs per illness case has been estimated as 2-29 years (de Noordhout et al., 2014)

12.13.2.3 Case-fatality ratio

The case fatality ratio of invasive listeriosis is assumed to be approximately 20 % based on outbreaks (EFSA 2018). This numbers are in line with observations in single outbreaks with more than 20 cases (Spain, South Africa, Norway Camembert cheese).

12.13.2.4 Occurrence

Total number of illnesses

In Europe, the number of cases of invasive listeriosis is normally around 1500 cases per year. The number of registered listeriosis cases has been stable for the last decade in Europe, but the number of cases increased in the years before. A possible reason is increased consumption of ready-to-eat foods with long shelf lives (EFSA, Ricci, et al., 2018). In Norway, 20-50 cases of invasive listeriosis cases are reported annually. Most cases are reported in elderly people.

The number of gastric listeriosis cases is not well documented, as healthy consumers can also be carriers of *L. monocytogenes* in their intestine and therefore the diagnosis cannot be made based on analysis of faeces samples. Underreporting of gastric listeriosis cases is, according to ECDC, likely to occur in all age groups. Cases of gastric listeriosis are not reported in MSIS due to the criteria for diagnosis. However, cases of gastric listeriosis are reported in informal ways, typically related to outbreak investigations. In a meat-related outbreak in Spain, there were more cases of gastric listeriosis than of invasive listeriosis.

Most cases of human illness are related to food.

Outbreaks

In Norway, these are some of the reported outbreaks associated with invasive listeriosis:

- "Rakfisk" – 2018 – 13 people ill – no deaths
- Imported brie cheese, – 2018 – 3 people ill, deaths not known.
- "Rakfisk" – 2013 – 3 people ill – no deaths
- Organic camembert cheese - 2007 – 19 people ill – 5 deaths

- Contaminated cold cuts – 2005 – 3 people ill – no deaths
- Heated meat spread – 1992 – 8 people ill – no deaths

Internationally, there has been several very large outbreaks in South Africa, Spain, Canada and USA over the last decade that have been related to various different foods.

- South Africa: 1060 cases of illness, 216 deaths. Processed meat
- Spain (2019): More than 220 confirmed cases in July 2019, at least 3 deaths. Meat product.
- USA: Cantaloupe – a melon with higher pH than other melons. Precut.
- USA: Caramel apples
- Canada (2008): 22 deaths, 35 ill. Sliced meat.
- Germany, Austria, Switzerland: Quargel cheese

Many smaller outbreaks have occurred, including some related to sandwiches at hospitals in the UK.

During the last few years, smaller, but international and long-lasting, outbreaks with cold smoked salmon have occurred. Two of these have been traced back to smokehouses in Poland and Estonia, and some of the fish used had been imported from Norway. The number of lost years due to human listeriosis is challenging as it also involves an assessment about what lost quality of life is. Further, the indirect burden of a lost unborn baby is hard to quantify. Based on data from 2010, it has been associated that the burden of listeriosis is 2-30 DALYs per case (de Noordhout et al., 2014).

12.13.3 Likelihood of increased human burden

Several consumer groups have elevated susceptibility to *Listeria*, and some of these groups are increasing in the population.

In parallel, there is an increased focus on food-loss reduction, new ways of processing foods, and new distribution channels. Among these is donation of food (e.g., on the last day of shelf life); such practices will not pose a risk for most consumers but may for vulnerable consumers.

Climate change appears not to have had a large impact of *L. monocytogenes* prevalence but may influence the concentration in food due to higher temperatures or more soil spread on e.g. vegetables due to heavy rain. Storage of food under abuse conditions (at higher temperatures than today), will increase the concentration of *Listeria*.

More processing of food is likely to increase both the prevalence and concentration of *Listeria* in foods, as recontamination from the product environment and removal of competing microbes are likely. Processing of food is also related to the desire of a longer shelf life, which, in turn, provides a longer growth period for *L. monocytogenes*. Mixed foods, which may provide niches with good conditions for growth of *Listeria,* will also lead to

increased concentrations. It should be noted that most outbreaks of listeriosis in Norway and Europe have been associated processed foods.

Thus, there is a considerable likelihood of the human burden of listeriosis increasing, not so much because of a rise in prevalence, but because processing, new ways of distribution of foods, and consumer habits have the potential to increase the concentration of the *Listeria* in contaminated food.

For risk factors in general, see also chapter 13.13.

12.13.3.1 Scorecard

Table 12-14. Final scores for *L. monocytogenes*, based on EKE of nine experts.

Listeriao monocytogenes	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	1	1	1	1	1	1	1	1	1	1.00
Acute morbidity severity	4	4	2	4	4	3	2	2	3	3.11
Chronic morbidity severity	3	3	3	3	4	3	3	4	2	3.11
Fraction of chronic illness	2	2	1	2	1	3	2	2	1	1.78
Case-fatality ratio	4	3	3	3	3	2	3	3	4	3.11
Probability for increased HBD	2	2	2	2	1	2	2	1	3	1.89
Total	16	15	12	15	14	14	13	13	14	14.00

12.14 Escherichia coli

12.14.1 Organism

Variants of intestinal pathogenic *Escherichia coli* that can produce *E. coli* enteritis have been described. The four most common are: enterohemorrhagic *E. coli* (EHEC), enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC), which is divided into typical EPEC (tEPEC) and atypical EPEC (aEPEC), and enterotoxic *E. coli* (ETEC). The reservoir for the human pathogens EIEC, ETEC and tEPEC are humans. For EHEC and aEPEC, the reservoir is ruminants. EHEC is defined as the human pathogenic variants of shiga-toxin-producing *E. coli* (STEC), also called verocytotoxin-producing *E. coli* (VTEC). Most STECs are not pathogenic and thus not classified as EHEC. EHEC is an increasing problem in high-income countries and poses a significant challenge for infection control. EHEC can belong to almost any serogroup. In Norway, about 20% of detected EHECs belongs to serogroup O157, while about 80% are non-O157 (of these, O103, O26, O145, and O91 are the most frequent). Smith et al. (2015) describe the importance of the non-O157 *E. coli* serogroups. Shiga-toxin production is an essential pathogenicity factor in all EHECs. This property can be lost *in vivo* or *in vitro*. The diagnosis of haemolytic-uremic syndrome (HUS) is based on detection of both *stx* and *eae* genes. For children who have HUS associated with diarrhoea, about 90 % is estimated to be due to EHEC.

Outbreaks with EPEC are rare in high-income countries today, but should not be forgotten as a possible cause of outbreaks, especially since EPEC has a significant infection potential. Globally, EPEC is one of the most frequent causes of bacterial gastroenteritis, affecting not only infants, but also adults, in developing countries. EPEC that causes this type of outbreak is now called tEPEC and is characterized by having the genes for both *eae* and several *bfp* genes that together encode a pathogenic protein (bundle-forming pili). EPEC that lacks *bfp* genes is called aEPEC, and is a heterogeneous group with an uncertain association with diarrhoea. Therefore, differentiation of EHEC that has lost its toxin genes and aEPEC as causes of diarrhoea or as a part of normal gut flora is very difficult.

12.14.2 Illness and consequences

12.14.2.1 Acute morbidity

EHEC: In 2017, 6,457 cases were reported in the EU / EEA area, most cases per 100,000 inhabitants were reported from Ireland, Norway, and Sweden. The incubation period for EHEC is mainly between 3-4 days, or even 1-14 days in some cases. The infectious dose of EHEC is very low. Infection caused by EHEC can cause different disease progression and severity. It can range from an asymptomatic course or uncomplicated diarrhoea to severe cases of massive bloody diarrhoea. In 10-15% of cases, especially in children, the elderly, and immunosuppressed, the infection may cause the development of HUS with renal failure and thrombotic thrombocytopenic purpura (TTP).

For the other intestinal pathogenic *E. coli,* the infectious dose is higher, ranging from 10^5 to 10^8. The incubation period and clinical picture for each pathotype are:

- EIEC: the incubation period is 10-12 hours. EIEC is enteroinvasive and is closely related to *Shigella flexnerii* and *S. sonnei*. Worldwide, several outbreaks and occasional cases of EIEC gastroenteritis has been reported, but EIEC is considered an uncommon cause of diarrhoea in high-income countries. Infections with EIEC usually cause mild diarrhoea, but some patients may develop dysentery-like symptoms with pus-containing, sometimes bloody, diarrhoea, severe abdominal pain, and fever. The bacteria invade the intestinal epithelial cells and spread to nearby epithelial cells. This gives rise to an acute inflammatory reaction in the intestinal mucosa, resulting in bleeding and necrosis of the epithelium.
- EPEC: the incubation period is unknown. Outbreaks with EPEC are rare in high-income countries today but should not be forgotten as a possible cause of outbreaks, especially since EPEC has a significant infection potential. Globally, EPEC is one of the most frequent causes of bacterial gastroenteritis in developing countries. The main symptoms are watery diarrhoea with fever.
- ETEC: the incubation period is 24-72 hours. ETEC is enterotoxin-producing and adheres to the intestinal epithelium using special fimbria on the bacterial surface. There are two types of enterotoxins, the heat-stable (LT) and the heat-stable (ST). The reservoir for this type of bacteria is people. ETEC is the most common cause of diarrhoea in children in low-income countries and is often isolated from patients with

"tourist diarrhoea". In recent years, domestically acquired foodborne infections with ETEC have become more common. The duration of the disease is from a few days to several weeks.

EAEC: the incubation period is 8-52 hours. EAEC is the latest addition to the group of diarrhoea-causing *E. coli*, and the clinical significance is still debated. EAEC adheres to the intestinal epithelium in a characteristic aggregate pattern. EAEC is associated with tourist diarrhoea, and acute and chronic diarrhoea in both adults and children. The major outbreak of HUS in Germany in 2011 was caused by an EAEC O104 strain (Beutin & Martin, 2012). However, infections with EAEC usually cause mild, self-limiting diarrhoea. There are indications that genetic factors in the host are important for the development of disease.

12.14.2.2 Number of foodborne illness including outbreaks

Total number of illnesses

Over the past 25 years, MSIS has registered a mean number of 447 (range 30-1704) *E. coli* enteritis cases each year. Most are seen in the age group 0-9 years of age (www.msis.no: Table 10-16) and are caused by EHEC (mean of 106; range 0-511). During the last 25 years, 1699/10279 (16%) of the *E. coli* enteritis cases were hospitalized and the fatality was around 0.07% (8 died out of 11197 cases). Of Norwegian patients for whom the place of infection is known, about 37% acquired their disease abroad. The incidence has significantly increased from 2014 for both EHEC and *E. coli* enteritis.

Proportion of illnesses attributable to food- and waterborne transmission

Regarding EHEC and aEPEC transmission through contaminated foodstuffs, including through meat and meat products from ruminants, vegetables, unpasteurized milk, products of unpasteurized milk, and drinking water, has been documented. Humans can also be infected by direct contact with animals (which are healthy carriers), or indirectly via animals' faeces, from bathing water, as well as directly from person-to-person through contaminated hands.

EIEC, ETEC, EAEC: Probably transmission through contaminated foods, including drinking water, but also from person to person.

Outbreaks

EHEC has caused several food and waterborne outbreaks in Norway. Since 2005, 24 outbreaks with around 480 persons have been reported to VESUV.

Many outbreaks of gastroenteritis caused by *E. coli* have been recorded in Norway. Since 2005, 157 outbreaks involving around 1970 persons have been reported to VESUV.

A major outbreak of HUS that started in Germany in 2011 was caused by an EAEC O104 strain that also produced shiga toxin (Beutin & Martin, 2012). Several European countries were affected by this epidemic. The source was believed to be contaminated fenugreek

seeds imported from Egypt and grown on a farm in Germany. A total of 4,397 cases, with 51 deaths, were reported in this outbreak, with 98 % of the cases were detected in Germany. Only one case was confirmed in Norway.

Since 1999, outbreaks, mainly caused by EHEC but also by ETEC and EPEC, have been reported in Norway. An outbreak of gastroenteritis at a conference in Oslo (2016) was related to the lunch serving. Cooked cod garnished with chives was found to be the most likely dish, and the most likely pathogen was ETEC, possibly in combination with EPEC. A total of 453 of the 590 participants (77%) completed a questionnaire and 110 (25%) met the case definition. An outbreak at a hotel at Ringerike (2012) involving more than 300 persons with gastroenteritis and was also possibly caused by ETEC from imported chives as one of the ingredients in scrambled eggs.

An outbreak of *E. coli* O103 in 2006 included 17 registered patients, including 10 children with renal failure (HUS), one with fatal outcome (Schimmer et al., 2008). Patients with HUS were aged 2–8 years, and patients with diarrhoea ranged from 1.5 to 18 years. The source of infection was cured mutton sausages.

Other smaller national outbreaks were mainly caused by EHEC, and many of them involved children that developed HUS. The sources of infection were often not identified, but contact with sheep and animals in general, unpasteurized milk, and contaminated salad were among the suspected sources.

12.14.2.3 Chronic morbidity severity and fraction of chronic illness

- EHEC: Approximately 10% of children with EHEC-associated HUS develop chronic kidney failure. The HUS cases had a high rate of complications and sequelae, including renal, CNS-related, cardiac, respiratory, serious gastrointestinal complications, and sepsis, consistent with other studies. This underlines the importance of attention to extra-renal manifestations in the acute phase and in renal long-term follow-up of HUS patients (Jenssen et al., 2016).
- EPEC: This pathotype appears to be one of the very few bacterial causes of chronic infant diarrhoea. aEPEC causes chronic diarrhoea in children under 2 years of age and there are examples of outbreaks of diarrhoea in nurseries.
- EAEC: Chronic diarrhoea may occur in children <1 year and in patients with immunodeficiency. The bacteria adhere to and colonize the intestinal epithelium with the help of fimbria, which also helps the bacterium to form biofilms. This produces an inflammatory reaction in the intestinal mucosa that is further enhanced by the excretion of toxins.

12.14.2.4 Case-fatality ratio

Three deaths have been recorded as a result of EHEC infection in Norway, all in children who had developed HUS. In 2004, a child died from infection with *E. coli* O86. In 2006, one child died after infection with *E. coli* O103, and in 2009 after infection with sorbitol-fermenting *E.*

coli O157. Mortality in children with HUS is 3–5%. In older people in nursing homes, outbreaks with EHEC have been associated with high mortality, partly independent of HUS.

During the European outbreak caused by an EAEC O104 strain in 2011, a total of 4,397 cases were confirmed and 51 persons died.

12.14.2.5 Probability for increased human burden of disease

Since drinking water and water used for growing vegetables on the ground, especially herbs and salad, are reservoirs and sources of infection, climate change may lead to greater infection pressure in humans. Increased precipitation with heavy rainfalls will cause run-off with contaminants from the environment to water reservoirs, and with shorter and milder winters, this will take place over a larger part of the year than now.

It is important that the hygiene routines during slaughtering and dressing of ruminants, such as preventing contamination from intestinal contents to the carcasses and the environment in the abattoir, are continued at Norwegian slaughterhouses and supervised by the Norwegian Food Safety Authority.

12.14.2.6 Scorecard

Table 12-15. Final scores for EHEC, based on EKE of nine experts.

EHEC	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	2	2	2	1	2	1	2	1.78
Acute morbidity severity	4	3	3	3	3	3	2	3	4	3.11
Chronic morbidity severity	4	4	3	4	3	4	2	4	4	3.56
Fraction of chronic illness	2	1	1	1	2	1	1	2	2	1.44
Case-fatality ratio	2	2	2	2	2	2	1	3	2	2.00
Probability for increased HBD	2	2	2	1	1	1	4	1	2	1.78
Total	16	14	13	13	13	12	12	14	16	13.67

Table 12-16. Final scores for other pathogenic *E. coli* based on EKE of nine experts.

Other pathogenic *E. coli*	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	2	2	2	2	2	1	2	1.89
Acute morbidity severity	3	2	3	2	2	2	3	2	2	2.33
Chronic morbidity severity	1	2	2	1	2	3	3	3	2	2.11
Fraction of chronic illness	0	1	1	1	1	1	2	1	1	1.00
Case-fatality ratio	0	1	2	1	1	1	1	1	1	1.00
Probability for increased HBD	1	1	2	0	1	1	4	1	2	1.44
Total	7	9	12	7	9	10	15	9	10	9.78

12.15 *Campylobacter* spp.

12.15.1 Organism

Several bacteria within the genus *Campylobacter* can cause food- and waterborne infection in humans. *Campylobacter jejuni* is responsible for the vast majority of cases in Norway (>90%); the remaining cases are mainly caused by *Campylobacter coli*. Campylobacteriosis is the most common zoonosis in Norway, as well as in other European countries (EFSA & ECDC, 2018a; NIPH, 2020.).

Campylobacter are transmitted through the faecal-oral route, usually via vehicles like contaminated foodstuffs and non-disinfected drinking water, or through contact with infectious animals and humans. The infective dose is very low: only a few bacteria (<1000) are sufficient to cause disease.

Unlike *Salmonella*, *Campylobacter* cannot grow in foods, but can survive for weeks at refrigeration temperature - in poultry products throughout their shelf life. The bacterium dies slowly (over months) by freezing, but a significant reduction is achieved after three weeks. The bacteria are also sensitive to desiccation.

In Norway, the reservoir for *Campylobacter* is a wide range of mammals and birds, both wild and domesticated (section 13.15 (Kapperud et al., 2008; NIPH, 2020.)). Only humans develop disease; other animals are healthy carriers

12.15.2 Illness and consequences

12.15.2.1 Acute morbidity

The disease varies from mild gastroenteritis to more severe enterocolitis, with abdominal pain and bloody diarrhoea (NIPH, 2020.). *C. coli* probably produces milder symptoms than *C. jejuni*. The disease usually presents as a self-limiting diarrhoea with abdominal pain and

fever that does not require antibiotic treatment or hospitalization. The illness normally lasts 1-2 weeks, but episodes of recurrent diarrhoea are not uncommon. Patients can shed the bacteria in their faeces for several weeks after the symptoms have resolved, but a prolonged carrier state is rare. Complications can occur, mainly in vulnerable individuals, and include septicaemia, meningitis, inflammation of the gall bladder (cholecystitis), urinary tract infections, and appendicitis.

In 2016 through to 2020, the annual number of hospitalizations recorded by MSIS varied from 800 to 1100.

12.15.2.2 Chronic morbidity

Post-infectious sequelae are relatively uncommon, but *Campylobacter* can provoke reactive arthritis (1-2% among Scandinavian patients) and Reiter's syndrome, a reactive arthropathy. Another sequela is Guillain-Barré's syndrome (GBS), a rare polyneuropathy leading to severe, local paralyses. A study from the United States supports other data documenting that *Campylobacter* is an important contributor to GBS, accounting for at least 5% and possibly as many as 41% of all GBS cases (Scallan Walter, Crim, Bruce, & Griffin, 2020). The estimated cumulative incidence of *Campylobacter*-associated GBS was at least 21.5 per 100,000 *Campylobacter* cases. Like many other food-borne infections, *Campylobacter* can give rise to chronic gastrointestinal disorders, including irritable bowel syndrome, dyspepsia, constipation, and gastroesophageal reflux disease (Pogreba-Brown et al., 2020).

12.15.2.3 Case-fatality ratio

The disease is rarely fatal, but deaths can exceptionally occur, mainly in particularly vulnerable persons (3 cases recorded by MSIS in the period 1995-2019).

12.15.2.4 Occurrence

Campylobacter is the most common causal agent of bacterial diarrhoeal disease recorded in Norway. Since 2010, the Communicable Diseases Surveillance System (MSIS) has registered 3000-4000 cases of campylobacteriosis each year (*www.msis.no*). However, the actual number of people affected is considerably higher (see Appendix III). About 50-60% of Norwegian patients, for whom the country of infection is known, have acquired their disease abroad. There is equal gender distribution. The number of cases increased sharply during the 1990s, and in 1998, campylobacteriosis passed salmonellosis for the first time. After the year 2000, the increase has continued, but not nearly as strongly as in the 1990s. The reason for the increase is unknown.

Proportion of illnesses attributable to food- and waterborne transmission

In 1990 through 2015, four analytic-epidemiological studies of domestically acquired campylobacteriosis have been carried out in Norway to identify preventable risk factors and the corresponding sources of infection, and estimate the relative importance of these factors

(Hauge, 1996; Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natas, et al., 2003; Kapperud et al., 1996; MacDonald, White, et al., 2015).

Four independent risk factors were identified in most studies (ranked by importance):

- Drinking untreated water (at home, at holiday cabins, or during outdoor activities)
- Preparing raw chicken in the kitchen at home, or eating undercooked chicken
- Eating at a barbecue outdoors
- Having contact with reservoir animals or their excrement (dogs, cats, poultry, sheep, or cattle)

The results indicate that more than 60% of the cases are caused by consumption of food or water, and waterborne transmission is more important in Norway than in most other European countries.

Outbreaks

Campylobacter is the second most common cause of food- and waterborne outbreaks recorded in Norway, following norovirus. In 2005 through 2019, 61 domestic outbreaks with more than 5000 cases of illness have been reported to Vesuv. Drinking water has been incriminated as the source of infection in several large outbreaks, some of which comprised more than a thousand persons. In 2019, a waterborne outbreak with ca. 2000 estimated cases was recorded; only about 200 of the cases were notified to MSIS. Likewise, a waterborne outbreak in 2007 with at least 1500 cases, resulted in only 30 notifications to surveillance. Other sources are listed in section 13.15.

12.15.2.5 Likelihood of increased human burden of disease

Climate change may lead to greater infection pressure for humans and animals. Since drinking water is a prominent source of infection for *Campylobacter,* increased precipitation and heavy rainfalls will cause more run-off with contaminants from the environment to drinking water reservoirs. With shorter and milder winters, this will take place over a larger part of the year than now. As the presence of *Campylobacter* builds up in the water sources, more people and animals will become infected, which in turn will lead to increased contamination of the watersheds in an escalating feedback process.

Gaardbo Kuhn et al. (2020) analysed the temporal and spatial relationship between climatic factors and the incidence of campylobacteriosis in the Nordic countries (Sweden, Finland, Denmark and Norway) by fitting national surveillance data and weather events in a statistical model. Their model showed that increased temperature and heavy rainfall in the week prior to illness onset were both independently related to increasing incidence of campylobacteriosis, suggesting a non-food transmission route not explained by consumption or handling of poultry. On the other hand, heat waves and winter precipitation were associated with decreased incidence. Using climate change projections, the authors predicted that the four Nordic countries may experience a doubling of *Campylobacter* cases by the end of the 2080s, caused by climate changes alone (Kuhn et al., 2020; NIPH, 2020.).

12.15.2.6 Scorecard

Table 12-17. Final scores for Campylobacter based on EKE of nine experts.

Campylobacter **spp.**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**Mean**
Number of foodborne illnesses	3	4	3	4	3	3	3	3	3	3.22
Acute morbidity severity	3	3	2	2	3	3	3	2	2	2.56
Chronic morbidity severity	3	3	3	2	3	3	3	2	2	2.67
Fraction of chronic illness	1	1	1	1	1	1	1	1	1	1.00
Case-fatality ratio	1	1	1	1	1	1	1	1	1	1.00
Probability for increased HBD	2	2	2	3	2	2	3	1	2	2.11
Total	13	14	12	13	13	13	14	10	11	12.56

12.16 *Salmonella* spp.

12.16.1 Organism

There are more than 2500 different serotypes of *Salmonella* described worldwide. The most common serotypes in Norway are *Salmonella* Enteritidis and *Salmonella* Typhimurium, constituting around 70% of the non-typhoid *Salmonella* isolates. Salmonellosis is the second most common zoonotic disease in Norway. The reservoir is a broad range of mammals and birds, including humans and pets, especially reptiles. For *Salmonella* Typhi, humans are the only known host. The infectious dose varies with serotype. For non-typhoidal salmonellosis, the infectious dose is approximately 10^3 bacilli. For enteric fever, the infectious dose is about 10^5 bacilli by ingestion. Patients with achlorhydria, depressed cell-mediated immunity, or who are elderly, may become infected with at a lower infectious dose. The infectious dose may also be dependent on the level of acidity in the patient's stomach. Human-to-human transmission occurs relatively rarely. Human infection usually occurs following ingestion of contaminated foods and water, contact with faeces from an infected individual, as well as contact with infective animals, animal feed, or humans. The bacterium needs to proliferate in foods in order to reach the infectious dose level and can proliferate in foods that are not chilled properly. *Salmonella* is not capable of proliferating at refrigerator temperatures and is easily killed by cooking and pasteurizing. The bacterium can, however, survive for long time in the environment and in dried foodstuff, such as spices and dried milk.

For non-typhoidal salmonellosis, the incubation period is variable, depending on inoculum size, and usually ranges between 5 and 72 hours. For typhoid fever, the incubation period can be between 3 and 60 days, although most infections occur 7-14 days after contamination. The incubation period for typhoid fever is highly variable and depends on inoculum size, host susceptibility, and bacterial strain.

12.16.2 Illness and consequences

12.16.2.1 Acute morbidity

Serotypes causing typhoid fever are transmitted between people, and typical symptoms include headache, stomach-ache, fever, diarrhoea or constipation, and loss of appetite, but other possible symptoms are respiratory problems, lethal neurological changes, perforation of the intestine, and hepatic and splenic injury. Salmonellosis is caused by all nontyphoid serotypes of the Salmonella genus, here typical symptoms are stomach-ache and diarrhoea, but other possible symptoms include vomiting, nausea, fever, shivers, muscular or articular pain, cramps and loss of appetite. After the disappearance of symptoms, *Salmonella* may still reside in the intestines of an adult for 4 weeks, and in children for up to 7 weeks. A small number of people demonstrate an asymptomatic carrier state for a year after the disappearance of symptoms. Bacteraemia develops in 5–10% of people infected with *Salmonella* spp. and may lead to focal infections, such as meningitis, endocarditis, arthritis, and osteitis.

12.16.2.2 Chronic morbidity

Salmonellosis infections are usually self-limiting with no chronic morbidity. However, occasionally septicaemia, and very seldom arthritis, may occur as sequelae.

12.16.2.3 Case-fatality ratio

Typhoidal Salmonella infections affect primarily developing countries, and the estimated annual prevalence of enteric fever caused by all typhoidal serovars is over 27 million cases, resulting in more than 200,000 deaths worldwide. (Gal-Mor, 2018). When treated, it has a mortality rate of less than 1%; whilst untreated cases can have a mortality rate greater than 10 %. Complications include myocarditis, encephalopathy, intravascular coagulation, infections of the biliary tree and intestinal tract, urinary tract infection, and metastatic lesions in bone, joints, liver, and meninges. The most severe complication is haemorrhage due to perforations of the terminal ileum of proximal colon walls.

From the first estimates of The Global Burden of Disease (2017): Non-typhoidal salmonella infections usually have low case fatality. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 estimated that salmonella enterocolitis resulted in 95·1 million cases (95% uncertainty interval [UI] 41·6–184·8), 50 771 deaths (2824–129 736), and 3·10 million DALYs (0·39–7·39) in 2017.

Mean all-age case fatality was 14·5% (9·2–21·1), with higher estimates among children younger than 5 years (13·5% [8·4–19·8]) and elderly people (51·2% [30·2–72·9], people with HIV infection (41·8% [30·0–54·0]), and in areas of low sociodemographic development (e.g., 15·8% [10·0–22·9] (GBD, 2017).

The understanding of the global burden is however incomplete, limited particularly by the breadth of blood culture-based surveillance systems that are able to accurately diagnose the aetiology of bacteraemia (Balasubramanian et al., 2019).

12.16.2.4 Occurrence

Total number of illnesses

Salmonella is the second most common causal agent of bacterial diarrhoeal disease recorded in Norway. Since 2009, the national incidence of salmonellosis has decreased substantially, due to a parallel reduction in imported cases of *S*. Enteritidis, which has been attributed to successful control programmes in poultry and eggs in the EU. Over the past 25 years, MSIS has registered a mean number of 1365 (range from 907-1942) cases of salmonellosis each year. However, the actual number of people affected is considerably higher, see chapter 3.2.1. Most cases are seen in the age groups 20-29 and 40-49 years of age. During the last 25 years 7699/34129 (23%) cases were hospitalized and the lethality is around 0.1% (37 died out of 34129 cases). Around 24% have acquired the disease in Norway. The incidence rate is around 18 (number of cases per 100 000 inhabitants).

Proportion of illnesses attributable to food- and waterborne transmission

The incidence of sporadic domestically acquired salmonellosis is low, and most frequently due to *Salmonella* Typhimurium. The low incidence of sporadic salmonellosis is primarily due to the negligible levels of *Salmonella* in Norwegian livestock and food*. S.* Enteritidis infections have most frequently been associated with consumption of poultry and eggs, while *S*. Typhimurium has been linked to a wide range of products, including beef, pork, and chicken. In addition to foodborne transmission, other exposures linked to infections have been associated with other factors, including foreign travel, drinking untreated water, contact with animals such as farm animals and pets (including reptiles), and contact with pet feed. There are two known domestic reservoirs for *Salmonella* in Norway, both of which harbour *S*. Typhimurium: wild birds and hedgehogs. Strains associated with these reservoirs have been implicated in earlier outbreaks. In 2018, a national case–control study investigated risk factors for domestically acquired salmonellosis. Eating snow, dirt, or sand, or playing in a sandbox (aOR 4.14; CI 2.15–7.97) were associated with salmonellosis. Consumption of red meat, poultry, or eggs was not associated with illness. Contact with hedgehogs, wild birds, or reptiles was not significantly associated with salmonellosis, but <1% of cases and controls reported such exposures. Only 34% of cases of salmonellosis due to *S*. Typhimurium between 2004 and 2015 could be linked to domestic reservoirs through MLVA genotyping; the results of the study support indirect or environmental exposure being the main sources of infection for salmonellosis. In 1990 through to 2018, four analytical epidemiological studies of salmonellosis have been carried out in Norway to identify preventable risk factors and estimate the relative importance of these factors (see 13.16.6).

Four risk factors have been identified in all studies:

- The use of non-disinfected drinking water

- Direct or indirect contact with wild birds or their faeces
- Direct or indirect contact with hedgehog or their faeces
- Eating meat consumed and/or bought abroad

12.16.2.5 Outbreaks

Since 2005, 54 outbreaks with around 685 persons recorded ill have been reported to Vesuv. Sources are primarily: 1) imported meat which has not been sufficiently heat-treated, 2) direct/indirect contact or contamination of food with wild birds and/or hedgehogs, and 3) use of non-disinfected drinking water.

The largest outbreaks are listed below, with the source or other information in parentheses:

- 1982: 126 cases due to *S.* Oranienburg (pepper)
- 1987: 349 cases due to *S.* Typhimurium (Norwegian-produced chocolate)
- 1989: 60 cases due to *S.* Enteritidis (imported chicken meat)
- 1999: 54 cases due to *S.* Typhimurium (drinking water)
- 2000: 30 cases due to *S.* Typhimurium (assumed to be hedgehogs)
- 2004: 70 cases due to *S.* Infantis (in a hospital)
- 2006: 62 cases due to *S.* Kedougou (salami)
- 2013: 26 cases due to *S.* Coeln (assumed to be salad; imported leaves)
- 2017: 21 cases due to *S.* Typhimurium (source not identified).

12.16.2.6 Likelihood of increased human burden of disease

Diarrhoeal disease is climate sensitive, showing strong seasonal variations (Kovats & Tirado, 2006). Higher temperature has been found to be strongly associated with increased episodes of diarrhoeal disease (Checkley et al., 2000). Climate change and global warming have contributed to the spread of several foodborne pathogens. Associations between extreme weather events and infectious waterborne disease also have been reported worldwide (Confalonieri et al., 2007). Climate factors act through many pathways, both directly and indirectly, and the net effect is difficult to predict regarding the future incidence of salmonellosis.

12.16.2.7 Scorecard

Table 12-18. Final scores for Salmonella based on EKE of nine experts.

Salmonella	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	3	3	3	2	3	2	3	3	2	2.67
Acute morbidity severity	3	3	3	2	3	3	3	3	3	2.89
Chronic morbidity severity	3	2	2	2	3	3	2	3	3	2.56
Fraction of chronic illness	1	1	1	1	1	1	1	2	2	1.22
Case-fatality ratio	1	2	1	1	1	1	2	2	1	1.33
Probability for increased HBD	2	1	2	1	2	1	4	2	1	1.78
Total	13	12	12	9	13	11	15	15	12	12.44

12.17 *Shigella* spp.

12.17.1 Organism

There are four species of *Shigella*: *S. dysenteriae* (formerly also called *S. shigae*), *S. boydii, S. flexneri,* and *S. sonnei*. The first two cause the most severe illness (the most severe is *S. dysenteriae* type 1) and occur most often in developing countries. The latter two usually result in milder disease and are the most common species in Norway. The disease mainly affects the colon and is also called bacterial dysentery. In low-income countries, most cases occur in children under the age of 10 years, while in high-income countries, illness is more common in adults. The reservoir for the bacterium is humans (Nygren & Bowen, 2013).

Today, the disease in Norway usually occurs as imported cases, especially from Egypt and Asia. Domestic infections can occur, either as secondary cases from contact with patients infected abroad or in connection with imported contaminated foods.

12.17.2 Illness and consequences

12.17.2.1 Acute morbidity

Initially often manifest as a watery "small intestine diarrhoea" which, in a short time, can develop to colitis with fever, nausea, and abdominal cramps. Typical dysentery is diarrhoea with blood and mucus and sometimes pus. Dehydration can occur. The disease picture depends on the type of bacteria that causes the disease. *S. dysenteriae* and *S. boydii* result in the most severe symptoms, while *S. flexnerii* and *S. sonnei*, which occur most commonly in Norway, have a milder disease picture. Bacteraemia is unusual. Secondary cases occur relatively often when children are infected. The infectious dose is low (10–200 cells according to DuPont et al., (1989)). Infection may also occur through sexual practices, such as oral-anal contact. A carrier condition is rare but can occur and can also be long-lasting.

The person is contagious during acute illness and as long as the bacterium is present in the faeces. Incubation period is 1-7 days, usually 1-3 days.

12.17.2.2 Occurrence

Total number of illness

Over the past 25 years, the Communicable Diseases Surveillance System (MSIS) has registered a mean number of 136 (range from 77-198) cases of shigellosis each year (www.msis.no). Most cases are caused by *S. sonnei* and *S. flexnerii* and seen in the age groups 20-29 years, followed by 0-9, 40-49 and 30-39 years of age. During the last 25 years 745/3359 (22%) cases were hospitalized and the lethality is not listed. Around 79% of Norwegian patients, for whom the place of infection is known, have acquired their disease abroad.

Proportion of illnesses attributable to food- and waterborne transmission

Contact infection by faecal-oral contact in unhygienic conditions or vehicle infection through contaminated water or food such as imported salads and herbs are both possible. Food may be contaminated through handling by infectious persons or washed with contaminated water.

Outbreaks

Shigella spp. has been a cause of food and waterborne outbreaks in Norway. Since 2005, 11 outbreaks with around 182 persons recorded ill have been reported to VESUV.

2011: The same strain of *S. sonnei* was detected in a total of 46 people who had eaten fresh basil from the same batch in Tromsø and Sarpsborg. The basil was imported from Israel and was used as an ingredient in homemade pesto.

Also 2011: At least 33 people became ill due to *S. sonnei* after eating at a canteen in Oslo. Epidemiological studies showed that those who had eaten from a salad buffet on a particular day became ill and had more than three times the likelihood of being sick compared to those who had not eaten the salad. However, it was not possible to identify which ingredient in the salad buffet that was contaminated.

2010: Five cases of shigellosis were reported in which studies showed that the infection had probably been through sexual contact among men who have sex with men.

2009: A possible outbreak of *S. sonnei* infections with 4 people infected at home was reported. In addition, five suspected cases in two different households in the same municipality were detected. In total, the outbreak strain was detected in 23 persons, mainly resident in the counties of Hordaland and Trøndelag. All had eaten sugarsnap peas imported from Kenya. Based on the results of the investigation, the Norwegian Food Safety Authority reduced the ban on sales of all sugarsnap peas from Kenya.

2004 and 2006: Outbreaks of shigellosis among Norwegian personnel in the International Security Assistance Force force in Afghanistan in 2004 with an estimated 35 sick (*S. flexneri*) and in 2006 with approx. 100 sick (*S. sonnei*) were reported.

2001: Ten people were infected with *S. sonnei* after eating at a kebab restaurant in Oslo.

1994: An increase in the number of domestically acquired cases of *S. sonnei* infection was detected in several European countries, including Norway, Sweden, and the United Kingdom. In all three countries, epidemiological studies showed that iceberg lettuce imported from Spain was the likely source of infection. In Norway, a total of 110 people were identified in the outbreak; two-thirds were adults between 30 and 60 years. The bacterium was not detected in salad samples.

12.17.2.3 Chronic morbidity, severity and fraction of chronic illness

Complications of *S. flexnerii* can include reactive arthritis and Reiter's syndrome. Complications of *S. dysenteriae* can include an enlarged colon due to toxins, haemolytic uraemic syndrome (HUS) and sepsis.

12.17.2.4 Case-fatality ratio

S. dysenteriae causes more severe disease than other species of *Shigella* with higher death rates.

12.17.2.5 Probability for increased human burden of disease

Since drinking water and water used for growing vegetables, especially herbs and salad, are reservoirs and sources of infection, climate change may lead to greater infection pressure. Increased precipitation with heavy rainfall will cause run-off with contaminants from the environment to water reservoirs, and with shorter and milder winters, this will take place over a larger part of the year than now.

12.17.2.6 Scorecard

Table 12-19. Final scores for *Shigella* based on EKE of nine experts.

Shigella spp.	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	2	1	2	1	2	2	1	1.67
Acute morbidity severity	2	2	2	2	2	2	3	3	2	2.22
Chronic morbidity severity	2	2	2	2	2	2	1	2	2	1.89
Fraction of chronic illness	1	1	1	1	1	1	1	2	1	1.11
Case-fatality ratio	1	1	1	1	1	1	1	1	1	1.00
Probability for increased HBD	1	1	1	1	2	1	2	1	1	1.22
Total	9	9	9	8	10	8	10	11	8	9.11

12.18 *Vibrio* spp.

12.18.1 Organism

Bacteria in the Vibrionaceae family can cause a variety of diseases in both humans and fish but only 10 are known to cause disease in humans (Abbott, Janda, & Farmer III, 2011).

In humans, the most famous species is *Vibrio cholerae* serogroup O1 and serogroup O139 that causes epidemic cholera. Annually 3-5 million cases resulting in 120000 deaths occur worldwide (CDC, 2019a; WHO, 2017). These serogroups usually cause diarrhoeal disease that is severe and have great epidemic potential and thus represent substantial threats to community health if not readily controlled. Mechanism of action is exerted by the combined effect of cholera toxin which is a complex of two toxin components A & B. The microbes adhere to intestinal epithelium and the toxin actions renders the epithelium extremely leaky, producing a watery diarrhoea in the patients who needs extensive fluid replacement. The number of bacteria necessary for producing disease is high i.e. 10^8 bacteria. Much lower numbers are sufficient in cases of hypo- or achlorhydria (Ali, Nelson, Lopez, & Sack, 2015).

V. cholerae non-O1 / non-O139. This collective concept covers different serogroups of *V. cholerae* that does not cause epidemic cholera (Harris, LaRocque, Qadri, Ryan, & Calderwood, 2012; Schwartz, Hammerl, Gollner, & Strauch, 2019). These serogroups usually cause diarrhoeal diseases that are less severe than cholera. They do not have epidemic potential. Reservoir for the bacterium is sea- and brackish water. Non-O1 / non-O139 strains can also cause septicaemia and wound infections, especially in immunosuppressed individuals. A number of other species occur naturally in seawater and can be a risk to humans bathing at persistently high sea temperatures in areas with low salt content, e.g. brackish water. The bacteria multiply best at water temperatures above 20ºC, in brackish water and in sea areas with low salt content and can act together with water flower (algae

bloom). Most cases of serious illness have been reported from coastal areas near Taiwan, South Korea, Japan and the Gulf of Mexico.

Vibrio spp. which cause disease in humans are very uncommon in Norway as sea temperature is too cold. They are present as part of the environmental flora in tempered or tropic areas and thus also in seafood from these areas. Oysters from these areas may contain high numbers of Vibrio-bacteria as they filter large volumes of seawater and thus easily acquire Vibrio bacteria from the water. In fish, the bacteria might be found on the gills, but also in the gut and on the skin. They are all killed by heat. In areas with higher temperatures in seawater and brackish water numerous different vibrios might be present but only a small fraction of these may produce illness. Rain and pollution increase the risk of contamination of seafood by *Vibrio* ssp. Other Vibrio bacteria that do not produce disease in humans are common along the Norwegian coast. They may cause fish diseases such as cold water vibriosis and winter ulcers. Increase in number of patients due to climate change should be anticipated.

V. vulnificus infection is the most common cause of deaths related to shellfish in the United States (Jacobs Slifka, Newton, & Mahon, 2017; McLaughlin et al., 2005; A. Newton, Kendall, Vugia, Henao, & Mahon, 2012; A. E. Newton et al., 2014; Slayton, Newton, Depaola, Jones, & Mahon, 2014). It overcomes our natural defence mechanisms using pili, outer membrane proteins and flagella to enter the human body. In recent years, several serious cases caused by *V. vulnificus* in bathing areas in Nordic coastal areas, including South Norway, have been reported (Bonnin-Jusserand et al., 2019; Morris Jr., 2020). The pathogenicity is likely to rely on several bacterial factors, but the mechanisms are not clearly known (Bonnin-Jusserand et al., 2019; Morris Jr., 2020). The bacterium is best multiplying at water temperatures above 20ºC in brackish water and in sea areas with low salt content and can act together with water flower (algae bloom). Most cases of serious illness have been reported from coastal areas near Taiwan, South Korea, Japan and the Gulf of Mexico. In recent years, several serious cases caused by *V. vulnificus* in bathing areas in Nordic coastal areas, including South Norway, have been reported (Baker-Austin et al., 2016; Herriman, 2018; Levy, 2018; Morris Jr., 2020; Semenza et al., 2017).

V. parahaemolyticus (Slayton et al., 2014) is found in seawater, plankton and larger marine organisms such as fish and shellfish. The bacterium was first described as the cause of food poisoning in Japan in 1951. The symptoms are associated with the production of thermostable direct haemolysin (TDH) or related proteins (Slayton et al., 2014). It occurs in coastal areas around the world and is one of the most common causes of outbreaks of shellfish poisoning in Asia and the United States. In Japan, the bacterium is a main cause of foodborne infections. The bacterium is thus found mainly in warmer seawater but is also sometimes isolated in colder areas. The bacterium can occur in Norway during warm summers when the water temperature is high or during import of contaminated food products (i.e. oysters and crabs).

V. alginolyticus is found in seawater and was identified as the human pathogen *Vibriobacter* in 1961 (Jacobs Slifka et al., 2017). It is rarely seen in Northern Europe but infections may

occur (Schwartz et al., 2019) it usually causes ear canal infection and wounds after bathing, even in Nordic coastal areas at high sea temperatures. It can also, in rare cases, cause sepsis usually in people with proven immunodeficiency or other underlying diseases (Jacobs Slifka et al., 2017).

12.18.2 Illness and consequences

12.18.2.1 Acute morbidity

In humans, the most famous species is *V. cholerae s*erogroup O1 and serogroup O139 that causes epidemic cholera which is a major threat to public health (Abbott et al., 2011; Slayton et al., 2014; WHO, 2017). *V. cholerae* group. As of Feb 29 2020, 13 cases of *V. cholerae O-1 / O-139.* infection has been reported since 1977, all cases acquired outside Norway.

V. cholerae non-O1 / non-O139. This collective concept covers different serogroups of *V. cholera* that does not cause epidemic cholera. These serogroups usually cause diarrhoeal diseases that are less severe than cholera. They do not have epidemic potential. The reservoir for the bacterium is sea and brackish water. These sero-groups can also cause septicaemia and wound infections especially in immunosuppressed patients.

According to reports, most cases have been of a milder nature, and very few of them are linked to consumption of contaminated seafood, but projects are in progress to define the role of these microbes in a Norwegian context. High water temperatures for a long period of time occur relatively rarely in Norwegian coastal areas. Should the swimming temperature still stay close to or above 20ºC in Norwegian coastal areas for several days, there may be a risk of infection with *Vibrio* , including in southern Norwegian coastal areas. Most relevant are areas in the Oslo fjord, as well as the Telemark and Southern coasts (Herriman, 2018; Morris Jr., 2020; Semenza et al., 2017).

12.18.2.2 Chronic morbidity

Some *Vibrio* infections have devastating consequences for the patients. Table 12-20 provides an overview of the basic types of illnesses. Data from Scandinavia, and Norway in particular, are scarce, as diseases besides *V. cholerae* were only notifiable beginning June 19th, 2019. Thus, information on the chronic morbidity is limited.

Table 12-20. 5 Diseases caused by *Vibrio* spp. (i.e., *V. vulnificus, V. parahaemolyticus, V. alginolytuicus*) Clinical findings in cases according to type of infection and outcome.

	Major Clinical Symptoms			
Species	Acute morbidity		Chronic morbidity	
	Gastroenteritis	Wound infection	Mortality	Chronic disease entities
V. cholerae	Severe	No	>5%	
V. cholerae **non-toxigenic O1/ non-O139**	Moderate/ Severe	No	Ca 5%	
V. vulnificus **and other species**	Moderate/ Severe	Yes	>15%	A high percentage require prompt and advanced medical treatment including intensive care and surgery and sometimes amputation

Table 12-21. Incidence of *Vibrio* infections and acute mortality. Data compiled based on MSIS (incidence) and CDC, USA (mortality) (8)

Pathogen	**% Mortality in USA (CDC data)**	**Annual incidence pr 10^5 inhabitants in Norway (MSIS data)**
V. cholerae **(classic)**	5	0.008
Other *Vibrio* **spp. (***V. vulnificus***)**	18	1.1

Other *Vibrio* species known to cause mild disease in humans include *V. mimicus*, *V. fluvialis,* and *V. furnissii*. Other species such as *V. harveyi*, *V. metschnikovii* and *V. cincinnatiensis* are reported to cause mild, sporadic cases of disease.

12.18.2.3 Occurrence

Total number of illnesses

The disease burden in Norway of *Vibrio* infections beyond *V. cholerae*, is difficult to define as this disease group was only recently made notifiable (by June 19th, 2019). Thus, cases in 2019 and earlier may have been missed. Altogether 55 cases were reported from Jan 1st 2019 until Feb 29th 2020. Further clinical details are not readily available.

Proportion of illnesses attributable to food- and waterborne transmission

Since *V. cholerae* is very rare in Europe (Ali et al., 2015; CDC, 2019b; WHO, 2017), it represents an important, but highly unlikely, pathogenic agent in the food chain in Norway. However, vibriosis in general causes an estimated 80,000 illnesses and 100 deaths in the United States every year (CDC, 2019b). People with vibriosis become infected by consuming raw or undercooked seafood or exposing a wound to seawater. Most infections occur from

May through October when water temperatures are warmer. The other bacteria mentioned may contaminate seafood, usually raw oysters.

Outbreaks

Just one outbreak in Norway has been recorded in VESUV with 5 persons reported infected.

12.18.2.4 Likelihood of increased human burden

The bacterium is found mainly in warmer seawater but is also sometimes isolated in colder areas. The bacterium can occur in Norway during warm summers when the water temperature is high or during import of contaminated food products (i.e., oysters and crabs). *V. alginolyticus* is rarely seen ,but infections do occur and shall probably increase in numbers if climate changes elevate summer temperatures in costal seawaters and local production of seafood (i.e., oysters) is increasing in such areas (Baker-Austin et al., 2016; Herriman, 2018; Levy, 2018; Morris Jr., 2020; Semenza et al., 2017).

12.18.2.5 Scorecard

Table 12-22. Final scores for *Vibrio* based on EKE of nine experts.

Vibrio **spp.**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**Mean**
Number of foodborne illnesses	1	1	1	1	1	1	1	0	0	0.78
Acute morbidity severity	2	2	1	2	2	3	3	3	2	2.22
Chronic morbidity severity	2	1	2	1	2	3	3	3	2	2.11
Fraction of chronic illness	1	1	1	1	1	1	2	2	1	1.22
Case-fatality ratio	1	1	0	1	1	2	2	2	1	1.22
Probability for increased HBD	3	2	2	3	2	3	4	2	3	2.67
Total	10	8	7	9	9	13	15	12	9	10.22

12.19 Yersinia enterocolitica

12.19.1 Organism

Yersinia enterocolitica can cause food- and waterborne infection in humans. *Y. enterocolitica* serotype O:3 is responsible for the vast majority of cases in Norway. The remaining cases are mainly caused by serotype O:9. Globally, serotypes O:5,27 and O:8 should be noted, and other serotypes not carrying virulence plasmids might be added since the role of some of these serotypes regarding disease is discussed. Yersiniosis is the third most common bacterial zoonosis in Norway, as well as in most other European countries. Like *L. monocytogenes*, *Y. enterocolitica* can grow in foods, even at refrigeration temperatures, and survives freezing. Human infection due to *Y. enterocolitica* is most often acquired by the oral

route. Regarding serotypes O:3 and O:9 only humans develop disease, and pigs are healthy carriers and the main reservoir.

The view that *Y. pseudotuberculosis* might be a cause of foodborne disease has been encouraged by reports of isolation from vegetables and by implication in some foodborne outbreaks (Nesbakken, 2015). In Norway, one outbreak has been reported, although the source was not detected.

12.19.2 Illness and consequences

12.19.2.1 Acute morbidity

The minimal infectious dose required to cause disease is unknown. In one volunteer, ingestion of 3.5×10^9 organisms was sufficient to produce illness (Szita, Káli, & Rédey, 1973). The incubation period is uncertain, but has been estimated as being between 2 and 11 days (Szita et al., 1973), usually 3 to 7 days (msis.no). Gastroenteritis is by far the most common symptom of yersiniosis. The clinical picture is usually one of a self-limiting diarrhoea associated with mild fever and abdominal pain. Occasionally, the infection is limited to the right fossa iliaca in the form of terminal ileitis or mesenterial lymphadenitis, with symptoms that can be confused with those of acute appendicitis. People with impaired immunity or generally weakened conditions can develop sepsis. During the last 25 years, 568 of 2475 (23%) cases were hospitalized and the lethality around 0.1% (3 died out of 2537 cases).

12.19.2.2 Occurrence

Total number of illnesses

Over the past 25 years, the Communicable Diseases Surveillance System (MSIS) has registered a mean number of 101 (range 43-211) cases of yersiniosis each year (www.msis.no). However, the actual number is considerably higher. Most cases are seen in the age groups 0-9 and 20-29 years of age. Domestic infection predominates and only around 24% of Norwegian patients for whom the place of infection is known acquired their disease abroad. The incidence in Norway was significantly reduced from the mid-1990s, probably because of changes in pig-slaughter routines. The routines prevent contamination of the carcasses.

Proportion of illnesses attributable to food- and waterborne transmission

The following risk factors were identified in the study of Ostroff et al. (1994) (ranked by importance):

1. Consumption of pork and products from pork (73 %)
2. Drinking untreated drinking water (25 %)

National outbreaks in recent years have been dominated by mixed salads being the transmission vehicle.

Outbreaks

Y. enterocolitica has been a cause of several food and waterborne outbreaks in Norway. Since 2005, 9 outbreaks with around 202 persons recorded ill have been reported to VESUV. In 2018, 2014, and 2011 outbreaks caused by *Y. enterocolitica* serotype O:9 in mixed salad were reported. A total of 133 patients were confirmed in the 2014 outbreak, and 117 of the infected persons were associated with four different military camps. Even smaller outbreaks in 2013 and 2006 associated with brawn made from pork were caused by serotype O:9 (Grahek-Ogden, Schimmer, Cudjoe, Nygard, & Kapperud, 2007). Brawn made from pork was also involved in small 2006 and 2000 outbreaks caused by serotype O:3. In 2017, the first outbreak caused by *Y. pseudotuberculosis* in Norway was reported, but the source of infection was not detected.

12.19.2.3 Chronic morbidity, serverity and fraction of chronic illness

In some cases, especially in infections caused by serotypes O:3 or O:9, the primary enteritis is followed by reactive arthritis; this is most common in patients possessing the tissue type HLA-B27 (Aho et al., 1981). Reactive arthritis is seen especially in adults, occurring in 10-30 % of cases. Such effects usually last from a few days to months, occasionally up to a few years; knees, ankles, wrists, toes or fingers are usually affected. Elderly and middle-aged women may develop erythema nodosum (nodule) located to the calves or abdominal area. Some of these patients have no recollection of prior gastrointestinal involvement.

12.19.2.4 Case-fatality ratio

The disease is rarely fatal, but deaths can exceptionally occur, mainly in particularly vulnerable persons.

12.19.2.5 Probability for increased human burden of disease

It is important that specific hygiene routines during slaughtering and dressing of pigs, such as preventing contamination of the carcasses and the environment in the abattoir from the oral cavity and intestinal contents (Nesbakken, 2015) are continued in the future by the Norwegian slaughterhouses, and supervised by the Norwegian Food Safety Authority.

As drinking water and water used for growing vegetables on the ground, especially salads, are a reservoir and source of infection for *Y. enterocolitica*, climate change may lead to greater infection pressure in humans. Increased precipitation with heavy rainfall will cause run-off with contaminants from the environment to water reservoirs, and with shorter and milder winters, this will take place over a larger part of the year than now.

12.19.2.6 Scorecard

Table 12-23. Final scores for *Y. enterocolitica* based on EKE of nine experts.

Yersinia enterocolitica	A	B	C	D	E	F	G	H	I	Mean
Number of foodborne illnesses	2	2	1	2	2	2	1	2	2	1.78
Acute morbidity severity	2	2	2	2	3	2	3	2	3	2.33
Chronic morbidity severity	2	3	2	3	3	3	3	3	2	2.67
Fraction of chronic illness	2	2	2	3	1	2	2	1	3	2.00
Case-fatality ratio	1	1	1	1	1	1	1	1	1	1.00
Probability for increased HBD	1	1	1	2	1	1	1	1	1	1.11
Total	10	11	9	13	11	11	11	10	12	10.89

13 Appendix II – Source attribution

13.1 Anisakidae

13.1.1 Literature

String used for search in Pubmed:

(Norway[Title/Abstract]) AND (Anisaki*[Title/Abstract] OR Pseudoterranova[Title/Abstract]) – 16 results

13.1.2 Surveillance and monitoring programmes

The prevalence of *Anisakis simplex* or other members of the Anisakidae family is not included in any surveillance or monitoring programmes of food or food-producing animals.

13.1.3 Rapid Alert System for Food and Feed (RASFF) notifications

In the period January 2001 to October 2020, the Rapid Alert System for Food and Feed (RASFF) received 559 notifications and alerts on foods containing *Anisakis* (RASFF 2020); 538 in fish and fish products and 21 in cephalopods or products thereof. Parasitic infestation with *Pseudoterranova* in fish products was reported in 10 notifications and 5 of the products harboured *Anisakis* as well.

Table 13-1. Notifications on *Anisakis* in fish, fish products and cephalopods by country of origin, RASFF 2001-2020 [1]

Origin of product [2]	No. of notifications	Origin of raw material (if different from final product) [3]
Albania	2	
Argentina	16	
Belgium	1	
Bulgaria	2	Spain (1), Denmark (1)
Canada	8	
Chile	1	
China	15	
Croatia	46	
Denmark	46	UK (1), Norway (12), UK (2)
Faeroe Islands	3	
Falkland Islands	1	
France	84	Norway (1), Spain (1)
Germany	2	Faeroe Islands (1), Argentina (1)
Greece	5	
Iceland	9	

Origin of product [2]	No. of notifications	Origin of raw material (if different from final product) [3]
Ireland	4	
Italy	5	Spain (1)
Latvia	2	Spain (1)
Lithuania	1	Argentina (1)
Morocco	68	
Netherlands	12	Spain (1)
New Zealand	23 [4]	
Norway	39	
Poland	6	Faeroe Islands (1), Norway (2)
Portugal	7	Morocco (1)
Russia	2	
Senegal	2	
Slovakia	1	Ireland (1)
Slovenia	3	Croatia (2)
South Africa	1	
South Korea	1	
Spain	114	Portugal (2)
Switzerland	1	Croatia (1)
Taiwan	1	
Tunisia	4	
Ukraine	1	
hUnited Kingdom	46	Denmark (2)
United States	13 [5]	Canada (3)
Uruguay	2	Spain (2)

[1] The RASFF Portal was accessed 10 October 2020.

[2] Countries flagged as product origin in the RASFF Portal (RASFF 2020), which include both origin of final products and of raw materials. Since more than one country may be flagged as product origin, the total number of notifications exceeds 559.

[3] Origin of raw material if different from the origin of the final product. Number of notifications in parentheses.

[4] 20 notificatiosn involved squids.

[5] One notification involved squids.

The 39 notifications in which Norway was identified as the country of origin, comprised the following fish species and products: Mackerel (*Scomber scombrus*) (33), redfish (*Sebastes marinus*) (1), tusk (*Brosme brosme*) (1), monkfish (*Lophius piscatorius*) (1), frogfish (probably misnamed) (1), herring (*Clupea harengus*) (1), and cod liver in oil (1). Farmed fish or products thereof were not incriminated in any notification, irrespective of the country of origin. In two notifications, Norway was identified as one of the countries to which the product was distributed: cod filet from Latvia and mackerel from Norway. Norway did not forward any notifications on *Anisakis* in the period.

13.1.4 Surveys – prevalence studies

Surveys on the prevalence of Anisakidae in wild and farmed marine fish from Norwegian waters are described below.

13.1.5 Reservoir

13.1.5.1 Wild-caught fish

Anisakis simplex is common in many marine fish species in Norwegian waters. This applies to pelagic, as well as benthic, species, including the most common food fishes (e.g., herring, mackerel, cod, saithe, other cod fishes, and flounder). Anadromous salmonids can also be infected, notably salmon, which have a relatively long period in the seas compared to sea trout and sea char (Gjerde, 2015; Levsen & Lunestad, 2010; NVI, 2020; Rahmati et al., 2020; Strømnes & Andersen, 1998).

The distribution of *Anisakis* larvae in viscera vs. muscles has been shown to vary considerably between different fish groups and species. In marine species in general, the majority (> 80%) of the larvae are found in and on the abdominal viscera, and are consequently removed by gutting if it is done shortly after capture before the parasites migrate to the muscle tissue (NVI, 2020).

Strømnes and Andersen (1998) investigated the distribution of *A. simplex* L3 larvae between host tissues in three fish species sampled monthly in 1990 at one locality on the west coast of Norway: saithe (*Pollachius virens*), cod (*Gadus morhua*), and redfish (*Sebastes marinus*). The overall prevalence of infection was 97.2% (saithe), 92.2 (cod), and 60.1 (redfish). In all three species, larvae were most frequently detected in the viscera, the percentages of visceral infection for saithe, cod and redfish were 99.6%, 97.8% and 88.0%, respectively. In general, the distribution patterns of *A. simplex* L3 between muscle and viscera were not significantly affected by host size.

In anadromous salmonids, a large proportion of the parasites are detected in the muscles. In various species of Pacific salmon (including rainbow trout), the majority (> 80%) of the larvae occur in the musculature. In Atlantic salmon, almost 40% of the *Anisakis* larvae are detected in the fish meat (NVI, 2020).

Strømnes and Andersen (2000) examined seasonal variations in the infection of saithe, cod, and redfish, from a coastal area of central Norway over a period of one year. In all three host species there was an increase in the abundance of *A. simplex* third-stage larvae in spring, with a peak in March and April. Cod displayed the most distinct seasonal variation.

Levsen and Lunestad (2010) studied the prevalence of *Anisakis* larvae in trimmed and skinned filets of Norwegian spring-spawning herring caught in the north-eastern Norwegian Sea in October 2004 and in the outer basin of Vestfjorden, northern Norway, in November 2007. The larval prevalence varied from 42 to 70% and 8 to 10% in the manually- and

industrially produced fillets, respectively. They concluded that any product based on industrially produced fillets of Norwegian spring-spawning herring may still carry nematode larvae when put on the market.

The larvae of *Pseudoterranova* spp. are less prevalent in fish in Norwegian waters than *Anisakis* larvae, but a considerable proportion is encapsulated in the muscles (10% in cod) and are not removed by gutting (Gjerde, 2015).

13.1.5.2 Farmed fish (salmon or rainbow trout)

Studies confirm that it is unlikely to find Anisakidae in farmed Atlantic salmon or rainbow trout from Norway (NFSA, 2018), probably because those species are exclusively fed on heat-treated dry feed, which does not contain any viable parasites. Accordingly, the Food Safety Authority has implemented exemptions from the regulations requiring that fish products intended to be eaten raw or undercooked must undergo freezing before consumption.

On the other hand, roundworm infestation is a common finding in routine autopsies and histopathological examinations of runts ("loser fish") from fish farms (NVI, 2013b). Runts are individual fish showing clear signs of poor performance and abnormal appearance; they are discarded at the slaughter line and are not processed for human consumption (Mo et al., 2014; NVI, 2013b). Likewise, *A. simplex* has been detected in small wild-caught wrasse (Labridae spp.) that are used for delousing purposes ("cleaner fish") in Norwegian fish farms (Hansen & Solgaard, 2011). Such species represent a possible source of infection for farmed salmon and trout.

Lunestad (2003) examined 1,180 samples of muscle or viscera from Norwegian-farmed salmon for the presence of nematode larvae. The samples represented all salmon-producing counties in Norway. None of the samples contained nematodes.

Mo et al. (2014) examined 100 farmed Atlantic salmon (*Salmo salar*) for the presence of nematodes. All fish were sampled from one cage in a fish farm on the Norwegian south-west coast. No nematodes were found in the musculature or viscera of 50 harvest quality salmon. In contrast, 75 nematodes were found in 10 (20%) of 50 runts; 53 nematodes in the viscera and 22 in the musculature. Nematodes in the musculature were identified as *A. simplex*, while nematodes in the viscera were identified as *A. simplex* and the non-zoonotic *Hysterothylacium aduncum*. Thus, the prevalence of anisakid nematodes in farmed runts was approximately equal to the prevalence found in wild-living Atlantic salmon.

In 2014-2015, a total of 4184 farmed Atlantic salmon from 37 different farms along the Norwegian coast were examined for nematodes (Levsen & Maage 2015). All samplings took place at processing facilities during regular slaughtering and consisted of salmon processed for human consumption (3527), but also discarded fish (657, incl. runts and fish discarded for other quality defects). No Anisakidae were found in any of the food quality salmon intended for human consumption. The only nematode findings were from three runts, each

originating from different farms in northwestern and southern Norway. Two of the runts harboured the non-zoonotic *H. aduncum* in their intestines, the third contained *A. simplex*.

In 205-2016, a total of 1038 farmed rainbow trout from 15 farms along the Norwegian coast were examined for nematodes (Roiha, Maage, & Levsen, 2017). All samplings took place at processing facilities during regular slaughtering and consisted of rainbow trout processed for human consumption (860), but also discarded fish (178, incl. runts and fish discarded for other quality defects). No Anisakidae were found in any of the food quality rainbow trout intended for human consumption. The only nematode findings were from five runts, originating from three different farms. Two runts harboured *A. simplex* and three contained the non-zoonotic *H. aduncum.*

The two studies described above show that actual sources of infection were present in the cages where the infested runts were found. Although only the non-zoonotic, and thus harmless (to humans), nematode *Hysterothylacium* was detected in some localities, this parasite has the same basic life cycle at the intermediate host level as *Anisakis.* One possibility is that infected copepods, krill, or small fish may have gained access to the cages. It is also worth noting that wild-caught wrasse were used as cleaner fish on several of the farms concerned. The question remains why only runts were infected but probably reflects reduced access to the feed provided by the unit.

13.1.6 Sources of infection in outbreaks

As of 15 October 2020, there are no reported outbreaks of anisakiasis in Norway.

13.1.7 Risk factors and sources of infection for sporadic cases

Anisakiasis is acquired when people ingest raw, pickled, smoked, undercooked, lightly salted, or improperly frozen wild marine fish or squid harbouring the larvae (EFSA, 2010b). The nematodes will die, however, following freezing, frying, boiling or strong salting for extended periods. Many traditional marinating and cold smoking methods are not sufficient to kill *A. simplex* and freezing or heat treatments remain the most effective processes guaranteeing killing (EFSA, 2010b). Larvae in fish muscle are killed by appropriate cooking, heating the fish to > 60 °C for at least one minute, freezing at -20 °C for a minimum of 24 hours, or hot smoking. When salting the fish, it takes time for the musculature to be salted and all larvae killed. Hence, light salting for a short time is not sufficient.

13.1.8 Conclusions

The evidence presented in this report suggest that wild-caught marine and anadromous fish represent a significant potential for anisakid exposure in the Norwegian population, unless the preventive actions mentioned above are applied. Consumption of raw or undercooked fish is infrequent in Norway. Although current food preferences are favourable, there is a growing demand for raw or lightly cooked food.

13.1.9 Data gaps and research needs

The following topics needs further investigation:

- The incidence of anisakiasis in the Norwegian population.
- Which fish products and cooking practices that cause human anisakiasis in Norway.
- The consumption of risk products in the population.
- The significance of wild wrasse as a possible source of infection with anisakids when used for delousing on fish farm.
- Which sources of infection and other factors cause anisakid infection in runts, and why food quality fish are apparently not affected.
- Whether runts can be suitable as a marker for localities that are particularly exposed to anisakids and which should therefore be followed up at regular intervals.
- The effects of different farming practices on the prevalence of anisakids in aquaculture.

13.2 Echinococcus multilocularis

13.2.1 Literature

A literature search (PubMed – no date restrictions) was carried out in October 2020, using the search terms "echinococc* AND source attribution" and identified 9 publications, the titles of all of which were scanned. Five were excluded due to focus on Iran (4 publications) and China (1 publication). A further article was excluded as the focus was solely on companion animals rather than food. The remaining 3 articles are presented in Table 10-2 below.

Table 13-2. Summary of relevant literature.

Article	Summary
(Robertson, 2018)	In this article, which considers 6 different foodborne parasites, the spread of *E. multilocularis* globally, but particularly in Northern/Central Europe and North America is discussed and considered to be due to increasing fox populations and import of dogs. The article states a lack of evidence of increasing foodborne transmission but notes the difficulty of source attribution when symptoms occur many years after infection
(Koutsoumanis et al., 2018)	This EFSA document provided information on 3 different genera of foodborne parasites, including *Echinococcus* spp. This article also notes the difficulty of source attribution in a pathogen with a long incubation period and considers the feasibility of 4 different approaches for source attribution assessment of this parasite, including: epidemiological studies, subtyping, comparative risk assessment, and EKE. Not all these approaches were found appropriate for *E. multilocularis* and the authors conclude that although the potential for foodborne transmission is incontrovertible, the extent to which it occurs remains impossible to determine at present.

Article	Summary
(Torgerson et al., 2020)	This study, which considered both CE and AE, identified 10 cross-sectional studies and 5 case-control studies with suitable data for examining source attribution associated with *E. multilocularis* infection. However, most of the data were not from Europe. The authors acknowledge that the transmission epidemiology in Europe is likely to be different from that of China and Kyrgyzstan where the disease is more common. The authors conclude that, globally, transmission is mostly due to dog contact and waterborne transmission; foodborne transmission was found to be of minor significance in regions of high incidence, but is a more convincing transmission route in regions of relatively low human incidence, such as Europe

13.2.2 Surveillance and monitoring programmes

Detection of *E. multilocularis* in food has never been included in the NFSA surveillance and monitoring programmes.

13.2.3 RASFF notifications

There is a single report of *Echinococcus* (species not stated) in RASFF from 2018. However, given that the report refers to detection in red meat from Poland, this is very unlikely to be *E. multilocularis* (as this usually cycles between rodents and canids).

13.2.4 Occurrence in food or water

Data on the occurrence of *E. multilocularis* eggs in food or water in Scandinavian countries, particularly Norway, is scarce. An outbreak of echinococcosis in 7 western lowland gorillas, all held at a Swiss zoo, and which resulted in 6 fatalities (mortality rate of 86%) (Wenker et al., 2019), resulted in an investigation of fruit and vegetable samples harvested from Basel region, Switzerland, for taeniid eggs (Federer et al., 2016). Of 141 samples investigated, 30 (21%) were found positive for taeniid DNA. None of these were found to be from *E. multilocularis*, but *E. granulosus* DNA was identified, and also DNA from various canid or fox taeniids, indicating the potential for fresh produce to act as a vehicle of infection for *E. multilocularis*. An ongoing survey of berries on the Norwegian market (674 imported samples, 86 Norwegian samples) for contamination with various parasites, including *E. multilocularis*, has so far, not detected such contamination with this parasite (Temesgen, 2020). However, a similar study from Italy that investigated both berries and fresh produce found evidence of contamination with *E. multilocularis* (by both microscopy and molecular techniques) in an RTE-salad grown in Italy (Barlaam et al.).

13.2.5 Reservoir

The source of contamination is infected canids, particularly foxes. In mainland Norway, *E. multilocularis* has not (yet) been detected in the red fox population, and a monitoring programme is in place. It is compulsory for dogs entering Norway to have been treated

against this tapeworm. In both Sweden and Denmark, the fox population has been shown to harbour this parasite, and a previous risk assessment (VKM et al., 2012) has considered it to be only a matter of time before the parasite enters mainland Norway.

13.2.6 Sources of infection in outbreaks.

Partially due to the prolonged incubation period (months or years), outbreaks of AE have not been identified in the human population.

13.2.7 Sources of infection for sporadic cases

Due to the prolonged incubation period (months or years), determining how individuals have become infected AE is very difficult. See comments under 13.2.1 literature.

13.2.8 Relative importance of different food sources

Fresh produce is most likely to be contaminated with canid, particularly fox, faeces, and therefore is more likely to be of importance than other food sources. Water may also be a relevant infection vehicle.

13.2.9 Risk factor identification

For Scandinavian countries, no risk factors for infection have been identified.

13.2.10 Data gaps

An absence of data is acknowledged in all the literature considering source attribution of infection with this parasite. Although foodborne and waterborne transmission are acknowledged potential routes of infection, the long incubation period between infection and symptoms mean that it is very difficult to trace how people became infected. In addition, as pointed out in the EFSA document, there is a paucity of information on the occurrence of food contamination with *Echinococcus* eggs.

13.3 *Cryptosporidium* spp.

13.3.1 Literature

A literature search (PubMed – no date restrictions) was carried out in November 2020, using the search terms "Cryptosporidi* AND source attribution" and identified 52 publications, the titles of all of which were scanned, followed by the abstracts. Of these, 41 were excluded because the topic did not include source attribution or it was a review over a decade old, 26 were excluded because the studies were relevant to countries not considered relevant (13 from USA, 4 each from China and Australia, 2 from New Zealand, and 1 each from Nigeria, Kenya, and Iran), and 11 were excluded as the focus was animal infections (6 on cattle, 2 on

avian hosts, and 1 each on sheep, rabbit, and quenda). Several articles were excluded for more than one of these reasons, and of the 52 articles originally identified only 7 were retained for further consideration. None of the articles are from Norway or Scandinavia; whereas two have a multinational focus, two are from the UK and 3 from Canada. These are presented in the Table 10-3 below.

Table 13-3. Summary of the relevant literature.

(Chalmers, Robinson, Elwin, & Elson, 2019)	This article is from the UK, but it was included due to being from Northern Europe. The sources of 178 outbreaks involving 4031 laboratory-confirmed cases of cryptosporidiosis are provided. The source of 5% of the outbreaks were unknown. However, the majority were considered to be due to recreational water (46%) or animal contact (42%). Environmental contact and person to person spread each were considered to be responsible for 2%. Food was considered to be the source for 3 outbreaks (2%) and drinking water for 2 outbreaks (1%).
(Robertson, 2018)	In this article, which considers 6 different foodborne parasites, changes in the predominance of source of *Cryptosporidium* infections are discussed, with particular emphasis on foodborne outbreaks. It is noted that between 1993. and 2003 just 10 foodborne outbreaks were recorded, with fewer than 450 cases in total, but from 2005 to 2015 the number of foodborne outbreaks recorded has increased by 50% (15 outbreaks) with over 1800 cases recorded, an increase of over 400%. In addition, the specific foods associated with outbreaks seem to have changed; dairy products and apple cider were the main transmission vehicles between 1993 and 2003, whereas more recently over 45% of outbreaks and more than 90% of cases were associated with salad ingredients or garnish. The reasons for these transmission routes are discussed in the article.
(EFSA, Koutsoumanis, et al., 2018)	This EFSA document provided information on 3 different genera of foodborne parasites, including *Cryptosporidium* spp. Four different approaches for source attribution assessment of this parasite were considered, including: epidemiological studies, subtyping, comparative risk assessment, and EKE. Of these, epidemiological studies and EKE were found to be most relevant. Epidemiological studies indicated waterborne transmission to be most commonly reported probable source of infection (48% of cases), followed by contact with livestock (21%), person-to-person contact (15%), food-borne transmission (8%), and contact with pets (8%). Among foodborne outbreaks, fresh produce was considered the most usual implicated food, followed by milk and dairy products. Data cited from the FERG study, indicated that in the region of Europe that includes Norway, water was the main transmission route (38%), followed by person-to-person (30%), animal contact (14%) and food (10%). However, wide credible intervals indicate the extent of uncertainty. The authors conclude that the predominant baseline/background transmission pathway involves water, although other transmission routes can also be important.

(Murphy et al., 2016)	This article is from Canada and was included due to being from the northern hemisphere, with some social, economic, and geographical similarities with Norway. In this article, that focuses solely on waterborne transmission, a QMRA model is described and used to predict cases of waterborne infection from different water sources. For *Cryptosporidium*, an annual waterborne infection rate of 13354 cases is calculated, despite the reported infection incidence being actually around half that, indicating that cases of cryptosporidiosis are probably vastly under-reported. Most cases are expected to be from water from small supplies and private wells.
(Butler, Thomas, & Pintar, 2015)	This article is also from Canada and describes an EKE exercise regarding sources attribution of 28 different enteric pathogens. In this study, 11 experts provided information for *Cryptosporidium* and waterborne transmission was considered the most common source (median of 36.8%). Animal contact and person-to-person contact were similar (medians of 23.0% and 24.2%, respectively), and foodborne was 11.3%. For 4.7%, sources were grouped as "other". Again, wide 90% credible intervals indicated the large uncertainty.
(Davidson, Ravel, Nguyen, Fazil, & Ruzante, 2011)	The 3rd article from Canada also uses EKE, but this time to investigate the types of food associated with foodborne transmission of *Cryptosporidium*. The mean of the fitted Beta-distribution for attribution estimates put produce (fruit, vegetables etc.) as highest at 34.5%, beverages (excluding water, which was not included) as next highest at 14.7%, and third highest beef at 13.2%. All other food categories, except "other", which included food categories not listed, were all below 5%. The relatively high beef percentage seems slightly unusual, but presumably reflects that *C. parvum* is a common pathogen of cattle. However, that would suggest that dairy should also be high, but was only 4.7%.
(Doria, Abubakar, Syed, Hughes, & Hunter, 2006)	This 2nd article from UK is based on the "perceptions" of infected people (n=411) regarding where they had been infected, and therefore the information should be treated with caution as the respondents are unlikely to have wide expertise on cryptosporidiosis. Nevertheless, water was given as a likely source by about 1/3 of respondents (divided approximately equally between drinking water and recreational). Transmission from other infected people (or animals) was also mentioned by about 1/3 of respondents, with children particularly implicated. Travel-associated infection and transmission from food were each mentioned by about 20% of respondents.

13.3.2 Surveillance and monitoring programmes

Surveillance and monitoring programmes: *Cryptosporidium* has been included in the NFSA Surveillance and monitoring programmes over several years (2012, 2015, 2016, 2017, 2018), with samples of imported and Norwegian fresh produce (soft fruits, leafy greens, herbs) analysed for contamination. According to the data available, the number of samples analysed ranged from 40 in 2013 to 232 in the period 2017-2019. The majority of fresh produce was imported. *Cryptosporidium* contamination was not reported from any of the samples analysed.

13.3.3 RASFF notifications

There are no reports of detection of *Cryptosporidium* in food or feed in RASFF.

13.3.4 Occurrence in reservoir animals

There are around 40 different species of *Cryptosporidium* described, but the majority of human infections are associated with two species, *Cryptosporidium hominis* and *Cryptosporidium parvum*. Whereas *C. hominis* infects predominantly only humans, with just a few reports of detection in animals, *C. parvum* infects a wide range of animals and is particularly associated with infections in young ruminants. In Norway, infections of lambs and calves with *C. parvum* is known to occur relatively frequently (Gulliksen et al., 2009; Lange et al., 2014; Robertson, Gjerde, Forberg, Haugejorden, & Kielland, 2006).

13.3.5 Occurrence in food or water

Drinking water in Norway is regularly examined for contamination with *Cryptosporidium* oocysts, and water sources are known to be contaminated widely, albeit with low numbers of oocysts (VKM et al., 2020). As described under section 13.3.2, investigations organised by the OK programme have not identified any cases of contamination, but separate research projects have reported low level contamination levels in both lettuce and bean sprouts (Robertson et al., 2006; Robertson & Gjerde, 2001).

13.3.6 Sources of infection in outbreaks

In Norway, several small outbreaks of cryptosporidiosis have been reported. Most of these have been associated with contact with infected animals, particularly young ruminants (e.g., (Lange et al., 2014; Robertson et al., 2006)). An outbreak associated with self-pressed (non-commercial) apple juice has also been reported (Robertson, Temesgen, et al., 2019)). Although no waterborne outbreaks of cryptosporidiosis have been reported from Norway, large waterborne outbreaks have been reported from Sweden (e.g., (Widerström et al., 2014), and there is no obvious reason why, under particular circumstances in which water supply protection is compromised, such outbreaks would not occur in Norway.

13.3.7 Sources of infection for sporadic cases

Due to the relatively long incubation period of around 7-days, it is often difficult to determine sources of infection for sporadic cases of cryptosporidiosis, although municipal water supply contamination is less likely (as would probably result in an outbreak). Animal-to-person and foodborne transmission have both been documented and could occur (see section 10.3.7 above). However, an analysis of the data indicated that foodborne cryptosporidiosis is no more likely to occur in Nordic countries than elsewhere (Robertson & Chalmers, 2013). Person-to-person transmission of *Cryptosporidium* infection has also been documented in Norway (Johansen Ø et al., 2015). According to an EFSA opinion (EFSA, Koutsoumanis, et

al., 2018), see section 13.3.1 above, epidemiological studies indicated waterborne transmission to be most commonly reported probable source of infection (48% of cases), followed by contact with livestock (21%), person-to-person contact (15%), foodborne transmission (8%), and contact with pets (8%). Data cited from the FERG study (Torgerson et al., 2015), indicated that in the region of Europe that includes Norway, water was the main transmission route (38%), followed by person-to-person (30%), animal contact (14%) and food (10%). However, wide credible intervals indicate the extent of uncertainty.

13.3.8 Relative importance of different food sources

Apart from water (see above), those food products that are eaten raw (without heat treatment) and are at risk of contamination from either infected humans or animals are more likely to be more important as transmission vehicles. According to an EFSA opinion (EFSA, Koutsoumanis, et al., 2018), see section 13.3.1, above, fresh produce is the most usual food implicated in foodborne outbreaks of cryptosporidiosis, followed by milk and dairy products. Another article (Robertson, 2018), notes a change in specific foods associated with foodborne outbreaks of cryptosporidiosis over time, with dairy products and apple cider the main transmission vehicles between 1993 and 2003, whereas in more recent times over 45% of outbreaks and more than 90% of cases were associated with salad ingredients or garnish.

13.3.9 Risk factor identification

A risk factor analysis for cryptosporidiosis in Norway has not been conducted, but a study from the Netherlands (Nic Lochlainn et al., 2019) indicated that for *C. parvum* infection (the species most often identified in human cases in Norway), the following risk factors were relevant in a multivariable model: taking immunosuppressant medication and visiting a farm. Furthermore, those with a higher frequency of consuming water from sources other than taps had greater odds of being a case. A study from USA (Benedict et al., 2019), using almost 11,000 cases of cryptosporidiosis found that, compared with cases of salmonellosis, exposure to treated recreational water (aOR 4.7, 95% CI 4.3-5.0) and livestock (aOR: 3.2; 95% CI: 2.9-3.5) were significantly associated with cryptosporidiosis. It would seem likely that these will be risk factors for infection in Norway also. A study from Canada also noted that extreme precipitation, particularly following a dry period, was particularly associated with an increase in cryptosporidiosis (Chhetri et al., 2017); this could also be a relevant risk for Norway.

13.3.10 Data gaps

Although outbreak data from various countries, including Scandinavia, make it clear that waterborne transmission is important, the extent to which water contributes to sporadic cases is unclear. It is obvious that under-reporting of cases occurs. Food and transmission from infected hosts (both animals and human) are also clearly relevant transmission routes, and, to date, both these routes have also been documented in Norway.

13.4 Giardia duodenalis

13.4.1 Literature

A literature search (PubMed – no date restrictions) was carried out in November 2020, using the search terms "Giardi* AND source attribution" and identified 28 publications, the titles of all of which were scanned, followed by the abstracts. Of these, 25 were excluded because the topic did not include source attribution or it was a review over a decade old, 14 were excluded because the studies were relevant to countries not considered relevant (4 each from USA and Australia, and 1 each from China, New Zealand, Nigeria, Kenya, Iran and "developing countries"), and 4 were excluded as the focus was animal infections (1 each on sheep, cattle, companion animals, and quenda). Several articles were excluded for more than one of these reasons, and of the 28 articles originally identified only 2 were retained for further consideration. Neither of these articles are from Norway or Scandinavia – both are from Canada were also included in the source attribution consideration for *Cryptosporidium*. These are presented in the Table 10-4below.

Table 13-4. Summary of the relevant literature

(Murphy et al., 2016)	This article is from Canada, due to being from the northern hemisphere, with some social, economic, and geographical similarities with Norway. In this article, that focuses solely on waterborne transmission, a QMRA model is described and used to predict cases of waterborne infection from different water sources. For *Giardia*, an annual waterborne infection rate of 3616 cases is calculated. Given that the reported infection incidence is actually around 4000 cases, it appears that, based on this model, most cases of giardiasis are waterborne from water from small supplies and private wells.
(Butler et al., 2015)	This article, also from Canada, and describes an EKE exercise regarding sources attribution of 28 different enteric pathogens. In this study, 13 experts provided information for *Giardia* and waterborne transmission was considered the most common source (median of 48.0%). Person-to-person contact was second, with a median of 29.5%, followed by animal contact (median of 13.9%) and foodborne transmission (median of 7.2%). For 1.4%, sources were grouped as "other". The relatively high route of animal transmission, although considerably under that of *Cryptosporidium*, is slightly unexpected and may reflect uncertainty around the zoonotic potential of *Giardia*. Again, wide 90% credible intervals indicated the large uncertainty.

13.4.2 Surveillance and monitoring programmes

Surveillance and monitoring programmes: *Giardia* was included in the NFSA Surveillance and monitoring programmes in 2013 and 2015-2016 (fresh produce on each occasion). In 2013, 40 samples (20 salad, 10 sugar snap peas, 10 fresh raspberries) were analysed, and 55 samples of imported fresh berries were analysed in 2015 and 2016 (25 and 30 samples, respectively). Among the samples analysed in 2013, a single *Giardia* cyst was identified in a

50 g sample of sugar snap peas imported from Kenya. None of the samples from 2015 were found to be contaminated with *Giardia*, but *Giardia* cysts were identified in a strawberry sample imported from Spain. Follow up samples from the same batch were also positive for *Giardia* cysts (each with 3 cysts).

Although the viability status of the *Giardia* cysts detected in these analyses could not be determined, those in the Spanish strawberries were determined to be of a genotype with potential for infection to people (Assemblage A).

13.4.3 RASFF notifications

There is one report of detection of *Giardia* in RASFF, and this refers to a single sample of strawberries imported from Spain in 2016. This is the same batch of samples found positive in the Norwegian OK programme mentioned above.

13.4.4 Occurrence in reservoir animals (if relevant)

Giardia duodenalis is currently considered as a species complex consisting of 8 recognised genotypes, some of which are further divided into subtypes; these have also been described as separate species (Thompson & Ash, 2019). Of these, only two have been shown to infect humans commonly, and therefore detection of *Giardia* infection in an animal does not necessarily represent a risk to humans. In Norway, the majority of *Giardia* infections identified in domestic animals have been of subtypes that are not associated with human infections (e.g. Assemblage E, also termed *Giardia bovis*, in sheep and cattle; Assemblage F, also termed *Giardia cati*, in cats; Assemblages C and D, also termed *Giardia canis* in dogs). However, the data are not extensive, and some animals have been found to harbour *G. duodenalis* types that may be zoonotic (e.g., Assemblages A and B in foxes (Robertson, Clark, et al., 2019); Assemblages A and B in cervids – moose and reindeer, and also cattle (Robertson, Forberg, Hermansen, Hamnes, & Gjerde, 2007); Assemblage A, and to a lesser extent B, in dogs (Robertson et al., 2015). Thus, although different animals in Norway may be reservoirs of *G. duodenalis* isolates that are infectious to humans, zoonotic transmission probably occurs relatively rarely compared with human-to-human transmission.

13.4.5 Occurrence in food or water

Drinking water in Norway is regularly examined for contamination with *Giardia* cysts, and water sources are known to be contaminated widely, albeit with low numbers of cysts (VKM et al., 2020). As described under section 10.4.2, investigations in regi of the OK programme have identified a few cases of contamination, and, in addition, separate research projects have reported low level contamination levels in herbs, lettuce, strawberries, radish sprouts, and bean sprouts (Robertson & Gjerde, 2001; Robertson, Johannessen, Gjerde, & Loncarevic, 2002).

13.4.6 Sources of infection in outbreaks

In Norway, one large outbreak of giardiasis (involving several thousand cases) has been reported, which was associated with contamination of drinking water in Bergen (Robertson et al., 2006). The source of the water contamination was most probably human sewage that had leaked into the raw water source (Robertson et al., 2006; Robertson et al., 2015). Other minor outbreaks have been noted, such as one that occurred in a childcare setting in Trondheim in 2004 (Wahl & Bevanger, 2007). Although the source of infection was not determined for this outbreak, person-to-person spread seems likely in this setting. Foodborne outbreaks of giardiasis have not been reported in Norway.

13.4.7 Sources of infection for sporadic cases

Due to the relatively long incubation period of around 7-days, it is often difficult to determine sources of infection for sporadic cases of giardiasis, although municipal water supply contamination is less likely (as would probably result in an outbreak). However, as occurred in the Bergen outbreak, it took several months for even this outbreak to be identified (Robertson et al., 2006).

Person-to-person transmission of *Giardia* infection has also been documented in Norway (Wahl & Bevanger, 2007), and is likely to be the source of many of the sporadic infections reported. As noted from the literature review (Section 10.4.1), contaminated drinking water, person-to-person spread, infected animals, and contaminated food, are all possible sources of infection.

13.4.8 Relative importance of different food sources

Apart from water (see above), those food products that are eaten raw (without heat treatment) and are at risk of contamination from either infected humans or animals are more likely to be important as transmission vehicles.

13.4.9 Risk factor identification

A risk factor analysis for giardiasis in Norway has not been conducted, but a study from the States (Reses et al., 2018) identified the following risk factors: international travel (aOR = 13.9; 95% CI 4.9-39.8), drinking water from a river, lake, stream, or spring (aOR = 6.5; 95% CI 2.0-20.6), swimming in a natural body of water (aOR = 3.3; 95% CI 1.5-7.0), male-male sexual behaviour (aOR = 45.7; 95% CI 5.8-362.0), having contact with children in nappies (aOR = 1.6; 95% CI 1.01-2.6), taking antibiotics (aOR = 2.5; 95% CI 1.2-5.0) and having a chronic gastrointestinal condition (aOR = 1.8; 95% CI 1.1-3.0). Eating raw produce was inversely associated with infection (aOR = 0.2; 95% CI 0.1-0.7). The same study found that eating raw produce had a protective effect (aOR = 0.2; 95% CI 0.1-0.7). Another study from USA (Benedict et al., 2019), using around 17,500 cases of giardiasis found that, compared with cases of salmonellosis, exposure to untreated drinking (aOR 4.1, 95% CI 3.6-

4.7) and recreational water (aOR 4.1, 95% CI 3.7-4.5) were significantly associated with giardiasis.

A study from UK (Waldram, Vivancos, Hartley, & Lamden, 2017) regarding risk factors for within household transmission found the presence of children younger than 5 years in the household was a risk factor. A study from the Netherlands investigated risk factors for giardiasis in children attending day-care centres, and divided the cases between Assemblages A and B (Pijnacker et al., 2016). They found that Assemblage B giardiasis seemed to be mostly related to anthroponotic transmission risks, for Assemblage A there was some suggestion of potential zoonotic transmission with sandpits and cats being a risk factor (OR 13.5; 95% CI 1.8-101.3).

A study from Canada also noted that extreme precipitation, particularly following a dry period, was particularly associated with an increase in giardiasis (Chhetri et al., 2017); this could also be a relevant risk for Norway.

One aspect worth noting is that the algorithm for testing for giardiasis may miss cases; a study from Scotland (Currie et al., 2017) noted that up to 95% cases of giardiasis would have been missed should the algorithm for testing be based on travel to areas of the world perceived as high risk, or with particular clinical symptoms. Such testing bias may give an incorrect impression of risk factors.

13.4.10 Data gaps

Although outbreak data from various countries, including Norway, make it clear that waterborne transmission is important, the extent to which water contributes to sporadic cases is unclear. Under-reporting of cases is likely to occur also.

13.5 Toxoplasma gondii

13.5.1 Literature

Search string used for search in Pubmed:

(Norway[Title/Abstract]) AND (Toxoplasm*[Title/Abstract]) – 48 results

13.5.2 Surveillance and monitoring programmes

The prevalence of *Toxoplasma* in food or food-producing animals is not covered by any surveillance or monitoring programmes. There is no routine inspection at abattoirs or vegetable-processing plants to ensure the safety of meat and fresh produce with regards to this parasite.

13.5.3 Rapid Alert System for Food and Feed (RASFF)

As of 15 October 2020, RASFF has not received any notifications or alerts on food contaminated with *Toxoplasma* (RASFF 2020).

13.5.4 Surveys – prevalence studies

No status surveys or inspection project have been carried out in Norway to determine the prevalence of *Toxoplasma* in food. An ongoing research project investigates the presence of *Toxoplasma* oocysts on imported and domestic berries (13.5.4). Serological surveys of sheep, pigs, cattle, cats and wild animals are presented below (13.5.5). At an international level, EFSA has reviewed the occurrence and survival of *T. gondii* in different types of food including meat, milk, dairy products, seafood and fresh produce (EFSA, Koutsoumanis, et al., 2018).

13.5.5 Reservoir

Toxoplasma-infection is common among many wild and domesticated animal species in Norway.

13.5.5.1 Cats

Kapperud (1978) found a significant antibody titer in 21 (24%) of 87 domestic cats from Oslo, all of which were outpatients at the Norwegian School of Veterinary Science. In a more recent investigation, Sævik et al. (2015) examined 478 Norwegian cats and found that 196 (41.0%) were seropositive for *T gondii*. The seroprevalence among cats living in Oslo was significantly reduced (OR 0.51) when compared with the rest of Norway.

13.5.5.2 Wild animals

The seroprevalence inn wild-living mammals and birds in mainland Norway, Svalbard and Sweden, including marine mammals, has been well published (Akerstedt et al., 2010; Gjerde & Josefsen, 2015; Kapperud, 1978; Prestrud et al., 2007).

13.5.5.3 Cervids

Kapperud (1978) detected antibodies to *T. gondii* in sera from 12 of 99 red deer (*Cervus elaphus*) (12%), and 5 of 8 roe deer (*Capreolus capreolus*) (63%), while 68 domestic reindeer from one herd (*Rangifer tarandus*), and 21 wild reindeer, tested negative.

Vikøren et al. (2004) tested serum samples collected from 4339 wild cervids collected in Norway during 1992-200 for antibodies against *T. gondii.* The seroprevalences differed significantly between the species: Positive titers were found in 33.9% of 760 roe deer (*Capreolus capreolus*); 12.6% of 2142 moose (*Alces alces*); 7.7% of 571 red deer (*Cervus elaphus*); and 1.0% of 866 reindeer (*Rangifer tarandus*). For roe deer and male moose,

significant geographical differences in prevalence were found. The prevalence increased with age in roe deer, moose, and red deer, except from the age group yearling to adult in red deer. In moose, a significant age–gender interaction was identified, the effect of age being most distinct for females. No association between seropositivity and gender was found for roe deer and red deer. In conclusion, the survey documented a widespread exposure to *T. gondii* in Norwegian cervids, and meat from Norwegian cervids, particularly roe deer, should be regarded a potential source of infection for humans.

13.5.5.4 Sheep, pigs and cattle

The likelihood of meat animals being infected varies by species, and by the animal husbandry and management practices (EFSA, Koutsoumanis, et al., 2018).

In the 1970s, Waldeland published a series of studies indicating that 42-50% of ewes and 20-39% of slaughtered lambs were seropositive for *Toxoplasma* (Waldeland, 1976a, 1976b, 1977). Tissue cysts were detected in carcasses from 25-37% of the ewes and 10-15% of the lambs examined.

In a study published in 1996, serum samples from randomly selected slaughtered pigs, sheep and cattle were analysed for antibodies against *Toxoplasma* (Skjerve, Tharaldsen, Waldeland, Kapperud, & Nesbakken, 1996). A high seroprevalence was found in sheep from all regions in Norway. Of 207 herds examined, 91 (44.0%) were defined as infected, and 17.8% of 2070 individuals were seropositive. A much lower prevalence was detected in slaughtered pigs; the herd prevalence was 5.3% (17 of 321 herds), and 2.6% of 1605 individuals tested positive. According to the authors, there seems to have been a decrease in prevalence among pigs, when compared with results reported by Hellesnes et al. (1978) who found 16% seropositive. They argued that the difference could be explained by a change from traditional small-scale farming to larger management systems. Although pig production in Norway still consists of relatively small units, the hygiene, management procedures and housing has changed dramatically since the 1970s. For cattle, 55 (5.1%) of 1053 animals from nine slaughterhouses were seropositive. According to the authors, the lower prevalence in cattle compared to sheep, may be explained by differences in grazing areas and grazing strategies. A considerable geographical variation in the prevalence was observed in all three species.

13.5.5.5 Water

Harito et al. (2017) used lectin-magnetic separation combined with PCR and DNA-sequencing for detecting *Toxoplasma gondii* oocysts in environmental water. In a pilot project, *Toxoplasma* was found in one of 20 water samples, indicating that *Toxoplasma* oocysts occur in Norwegian drinking water supplies. The samples were collected from raw (untreated) water to be used for potable supply after treatment and came from a total of 9 different water sources.

13.5.6 Sources of infection in outbreaks

As of 15 October 2020, there are no reported outbreaks of toxoplasmosis in Norway.

13.5.7 Risk factors and sources of infection

13.5.7.1 Risk factors for Toxoplasma-infection in sheep herds

Skjerve et al. (1998) carried out a study to identify risk factors for *T. gondii* infection in sheep herds. Lambs from 194 herds slaughtered in 1993 at the two largest abattoirs in Norway, were examined for antibodies against *T. gondii*. The animals originated from the four most densely populated sheep districts. In all, 44.3% of the herds were infected and 16.2% of the 1940 individual animals were seropositive. The following risk factors were independently related to herd infection in multivariate logistic regression analysis:

- daily presence of a young cat in the sheep house
- atypical grazing strategy (i.e. the lambs were grazed close to the farm)
- use of mouse poison in the sheep house
- farm situated at an altitude >100 meters above sea level, with the highest risk of infection being detected between 250 to >500 m.

Two factors were associated with reduced risk: having perforated metal floors in the sheep house and timber construction of the house.

The authors concluded: Based on these findings it was recommended that farmers avoid keeping young cats in the sheep houses, that close-to-farm grazing be kept to a minimum and that perforated metal floors be used in the sheep houses. However, with such a high seroprevalence, the proposed measures alone would not reduce the occurrence of *Toxoplasma* in lambs to a level where undercooked lamb can be consumed without posing an unacceptable risk for some consumer groups.

In accordance with that conclusion, a Nordic project on risk-based meat inspection advocated that risk management efforts should generally be directed at meat products, rather than live animals. Post-harvest measures focusing on processing might be more effective, than pre-harvest measures consisting of, for example, herd certification. Such measures may be based on herd categorization and involve freezing of carcasses from infected herds before de-boning or freezing of risk products after de-boning is completed). Strategies to prevent and control infection in food-producing animals have been discussed by EFSA (2018).

13.5.7.2 Risk factors and sources of infection among pregnant women

In 1992-1994, a nationwide case-control study was conducted to identify risk factors and sources for *T. gondii* infection in pregnancy (Kapperud et al., 1996). Most cases were identified through serological screening of 36,000 pregnant women. In conditional logistic

regression analysis, the following independent factors were associated with increased risk of primary infection during gestation (estimates of attributable fractions are given in parentheses; figures indicate the relative importance of the factors):

- Eating raw or undercooked minced meat products (29%)
- Eating raw vegetables or fruits that have not been washed (28%)
- Eating raw or undercooked mutton or lamb (22%)
- Eating raw or undercooked pork (18%)
- Cleaning the cat litter box (16%)
- Washing the kitchen knives infrequently after preparation of raw meat, prior to handling another food item (11%)

The principles for design, conduct and analysis of case-control studies, and how to interpret the results, are explained in chapter 14. EFSA (2018) has reviewed epidemiological studies and comparative risk assessment on the relative importance of meatborne toxoplasmosis vs other transmission routes, including the feasibility of employing oocyst-specific antibody assays.

13.5.7.3 Consumption of raw or undercooked meat

Calculation of attributable fractions shows that a large majority of the cases could be explained by ingestion of raw or undercooked meat or meat products, including tasting raw meat while preparing food. In stratified analysis, persons who had eaten raw or undercooked meat purchased in Norway were at significantly increased risk of infection. Except for beef, few respondents reported having eaten undercooked meat in foreign countries. Although an elevated odds ratio was noted for several meat items consumed abroad, statistical significance was not achieved.

Among the study participants, consumption of undercooked beef was far more frequent than that of pork or mutton: 73% of the case-patients reported consumption of undercooked beef, while only 24% and 25% had eaten undercooked mutton or pork, respectively. However, consumption of undercooked mutton and pork was found to be independently associated with an increased risk of infection, whereas eating undercooked beef was not, despite the seroprevalence in cattle being twice as high as in pigs (5.1 vs 2.6%). In comparison, sheep had by far the highest seroprevalence (17.8%) (Skjerve et al. 1996). One probable explanation is that cattle are less likely to develop long-term latent infection with tissue cysts after the acute phase of infection, compared to sheep and pigs (cited by Kapperud et al. 1996).

Nevertheless, consumption of raw or undercooked minced meat or products thereof, which mainly contain beef, was identified as an independent risk factor. Moreover, the study revealed that 25 of the case-patients who reported consuming undercooked red meat had tasted raw meat while preparing food. A majority had nibbled raw minced meat, a factor contributing to the comparatively high attributable fraction associated with minced meat consumption. Recently, more studies showed that cattle can harbour viable tissue cysts in

their meat and quantitative risk assessment studies in the Netherlands and Italy have shown that undercooked beef contributes substantially to human infections (cited by EFSA 2018).

The number of participants who ate undercooked venison or undercooked meat from other cervids, was too low to enable meaningful analysis (data are not shown in the publication).

13.5.7.4 Consumption of unwashed fresh produce

According to EFSA (2018), consumer preferences for raw, fresh produce may contribute to increasing the likelihood of infection, since cooking inactivates the oocyst. This factor has been underemphasised previously. In the Norwegian study, cases and their matched controls did not differ significantly with regard to consumption of raw vegetables, unpeeled fruits, strawberries, or other berries, whether in Norway or abroad. However, the cases were more likely to report ingestion of raw vegetables or fruits *that had not been washed*. Eating strawberries or other types of berries unwashed was not associated with infection. The attributable fraction obtained strengthen the evidence that consumption of unwashed produce is a major factor contributing to maternal infection in Norway. Even though the percentage of vegetables, fruits and berries contaminated with *Toxoplasma* may be small, the frequency with which these foods are consumed may result in an appreciable exposure. Interestingly, preliminary results from an ongoing research project indicate that *Toxoplasma* oocysts are not uncommon on imported berries and occur in domestically produced berries as well (L. Robertson, personal communication). A high proportion of vegetables, fruits and berries consumed in Norway are imported, accounting for 27% of the economic value of all imported foods in the period 2014-2019 (Statistics Norway 2020). In 2018, imported vegetables accounted for 54% of the total consumption, compared with 94% for fruits and berries (Hjukse 2020).

A scientific opinion from EFSA concluded that on-farm measures that reduce the contamination of fresh produce may be a more effective control strategy than post-harvest interventions (EFSA 2018).

13.5.7.5 *Cat contact*

T. gondii oocysts survive for many months in the environment, including for weeks at freezing temperatures, in water (54 months) and in the soil (18 months) (EFSA, Koutsoumanis, et al., 2018). It has been debated whether pet cats should be banished from the household for the duration of pregnancy. The study reinforces the suggestion that living in a household with a cat *per se*, is not an important risk factor for *Toxoplasma* infection. On the other hand, cleaning the cat litter box was an independent risk. Living in a household with a kitten and feeding the cat raw meat scraps were associated with increased risk in univariable analysis but did not attain statistical significance in the regression model.

13.5.7.6 Consumption of untreated water

Contaminated drinking water has been the source of infection in a few outbreaks of toxoplasmosis abroad. In the case-control study, drinking untreated water, including from a private well, was marginally related to *reduced* risk in univariable analysis. In the multivariable model, however, this exposure showed no hope of becoming significant when combined with other, stronger risk factors, like undercooked meat consumption. There is no reason to believe that untreated water is genuinely protective. Rather, the observation indicates a reverse correlation between the factors: it is conceivable that persons living in rural areas with undisinfected drinking water are reluctant to embrace the urban habits of eating undercooked meat and using cat litter trays. Interestingly, the incidence of toxoplasmosis peaked in Oslo, the most urbanised region in Norway (section 12.5.2.4). It is notable that among the study participants, those residing in Oslo were more likely than residents of other areas to report consumption of undercooked meat and foreign travel.

Norwegian drinking water supplies largely use surface sources. Although a pilot project indicates that *Toxoplasma* oocysts occur in Norwegian drinking water (Harito et al., 2017), most reservoirs are located in remote areas where contamination from cat faeces is less likely.

13.5.7.7 Foreign travel

Although travelling outside of Scandinavia was identified as an appreciable risk in univariable analysis, this factor was not independently associated with infection after factors more directly related to modes of infection were controlled for.

13.5.8 Conclusions

In conclusion, most infections with *T. gondii* in pregnancy are caused by consumption of foods containing tissue cysts or contaminated with oocysts. The risk factors responsible for the highest proportion of cases are eating raw or undercooked meat, including tasting raw meat while cooking, and eating fresh produce that has not been washed.

As underlined in section 12.5, congenital toxoplasmosis can be regarded as indirectly foodborne when resulting from a primary foodborne infection in the mother. The consequences of congenital toxoplasmosis may be severe (12.5.2). These consequences make toxoplasmosis a public health problem of greater magnitude than the actual number of cases would suggest (Torgerson & Mastroiacovo, 2013). The findings indicate that modification of meat-consumption preferences, food-handling practices, including washing of fresh produce, cat contact patterns, kitchen hygiene, and travel habits during gestation offer the potential for substantial reduction of the burden of congenital toxoplasmosis in Norway. The results support initiatives that encourage implementation of post-harvest measures focusing on processing of red meat products, based on herd categorization.

13.5.9 Data gaps and research needs

The following issues need further consideration:

- The clinical, psychological and socio-economic consequences of
    - congenital toxoplasmosis, including case-fatality ratios.
    - *Toxoplasma*-related abortions, stillbirths and neonatal deaths, including incidence rates.
- Formal calculation of the burden of disease.
- Post-harvest measures regarding processing of red meat products with the aim of reducing human exposure.
    - The practical and economic feasibility of implementing such measures (i.e. cost-benefit analyses).
    - Parasitological or serological methods needed to identify infected flocks, carcasses or products.
- The effects of different farming practices in Norway on the prevalence of *Toxoplasma* in meat-producing mammals.
- Application of oocyst-specific antibody assays to quantify the risk of acquiring *T. gondii* from environmental sources (including fresh produce) vs meat.

13.6 Hepatitis A virus

13.6.1 Literature

Search string used for search in Pubmed:

(((hepatitis A) AND (Clinical disease,)) AND (Source attribution)) AND (Food)

13.6.2 Occurrence in reservoir animals (if relevant)

Not relevant, as the human intestine is the sole reservoir.

13.6.3 Occurrence in food or water

13.6.3.1 Surveillance and monitoring programmes

Hepatitis A virus has been included in the NFSA OK programme "Smittestoffer i bær" (frozen, imported samples) in 2015 (n=22) and 2016 (n=30) and in the program "Smittestoffer i vegetabilsk mat" (imported leafy greens and herbs) in 2017, 2018 and 2019 with 75 samples yearly. Contamination with HAV was not reported from any of the samples analysed.

13.6.3.2 International studies

Nestlé analysed 2015 samples of frozen berries for HAV RNA, in the period 2009 to 2016. Of these, 2 samples (0,1 %) were positive (Li, Butot, Zuber, & Uyttendaele, 2018).

13.6.4 RASFF notifications

From 1999 to August 2020 there have been 49 RASFF notifications on presence of HAV in foods:

- Bivalve molluscs – 25
- Cake with mixed berries – 1 (Norway notifying country)
- Cake with strawberries – 1
- Fruits and vegetables – 22 (mostly frozen berries)

13.6.5 Sources of infection in outbreaks

During the period 1977 to 2020 a total of 6364 cases of hepatitis A were registered in Norway, with domestic infections in 2703 cases (MSIS). The HAV reservoir is the human intestine and the virus can transmit directly among close contacts (probably most common infection route) and with contaminated water and food that is consumed raw. A single foodborne outbreak in Norway has been described in the literature.

In 2013-14, a total of 33 cases of hepatitis A in Norway were linked to mixed berries on an imported cake (Guzman-Herrador et al., 2015). The viral strain that caused this outbreak was detected in the berries and identified as the agent behind a multination European outbreak caused by frozen berry mix (Severi et al., 2015). According to EFSA, more than 1300 cases, with 240 confirmed, were related to this prolonged outbreak (EFSA, 2014).

The epidemiology of HAV transmission varies between regions worldwide and depends on economic and hygienic conditions. The possibility of HAV outbreaks in Norway caused by domestically produced food is low. Contamination of food with HAV can occur at any point of the food chain, from farm to fork. Contact with incorrectly treated sewage or sewage-polluted water, with infected food handlers and, to a lesser extent, with contaminated surfaces represent the most common routes of HAV contamination in food. Ready-to-eat foods that do not undergo further processing, bivalve molluscs, fresh leafy greens, fresh and frozen berries have frequently been implicated in HAV outbreaks (Randazzo & Sánchez, 2020), as can also be seen from the RASFF notifications. Examples mentioned in the literature, other than shellfish and frozen berries, are pomegranate seeds (Franklin et al., 2019), fresh dates (Rajiuddin, Midgley, Jensen, Müller, & Schultz, 2020), sun dried tomatoes (Gallot et al., 2011), and bakery products (Harries et al., 2014). A particularly large outbreak caused by HAV was registered in Pennsylvania in 2003. The outbreak was linked to a single restaurant that had prepared salsa with green onions imported from Mexico. Of 601 patients, three died and at least 124 were hospitalized (Wheeler et al., 2005).

13.6.6 Sources of infection for sporadic cases

The same sources as for outbreaks.

13.6.7 Relative importance of different food sources

Imported ready-to-eat food like oysters, frozen berries, and leafy greens are the most common food transmission vehicles.

13.6.8 Risk factor identification

Consumption of raw shellfish is considered a risk factor for infection.

13.6.9 Data gaps

The true number of domestic hepatitis A cases in Norway is not known, as many patients are uncertain of where or how they got infected. Of the cases registered from 1977 to 2020, 29 % has an unknown site of infection. Also, although hepatitis A is a reportable disease, cases are probably underreported. Regarding foodborne disease, sporadic cases and smaller outbreaks are probably not detected. Finding the source of a HAV outbreak is a demanding task due to the long incubation period, which puts patient memory to the test.

The prevalence of HAV in different food matrices is difficult to assess, and even more the prevalence of infectious virus. Molecular detection (RT-qPCR) is the only option as sensitive methods are needed and cultivation of environmental strains in order to find infective HAV is very limited. Despite using sensitive molecular methods, detection of HAV in food matrices is difficult, even in outbreak situations where epidemiological investigations clearly indicate a certain food item. The reason for this is the low amount of HAV necessary to cause infection, combined with low recovery of virus during sample preparation prior to RT-qPCR. An additional hinderance is the content of RT-qPCR inhibitors that can be found in, e.g., berries and foods rich in lipids.

13.7 Hepatitis E virus

13.7.1 Literature

Search string used for search in Pubmed:

(((hepatitis E) AND (Clinical disease,)) AND (Source attribution)) AND (Food)

13.7.2 Occurrence in reservoir animals (if relevant)

Pigs and wild boars are the main reservoir animals in Europe. No information is available regarding the presence of HEV in these animals in Norway. However, in a seroprevalence

study of 663 individual swine serum samples from 153 herds, 73 % of the samples tested positive for anti HEV antibodies. The positive samples represented 90 % of the herds.

In Spain organs from 45 healthy pigs in a slaughterhouse were analysed for the presence HEV RNA. Different organs were found positive, with liver (16 %) showing the highest detection rate (García et al., 2020).

In Sweden, HEV RNA was detected in 13 out of 159 (8%) blood samples from wild boars. Sequencing showed relatedness between these HEV strains and strains collected from piglets and from humans with clinical hepatitis E (Widén et al., 2011).

In France 6565 sera and 3715 livers were randomly sampled from 186 pig farms throughout the country. The individual prevalence of HEV RNA positive livers was 4% and 24% of the farms had at least 1 positive liver (Rose et al., 2011).

13.7.3 Occurrence in food or water

13.7.3.1 Surveillance and monitoring programmes

There have been no monitoring programmes for hepatitis E virus in foods in Norway.

13.7.3.2 International studies

In USA, of 127 packages of commercial pig liver sold in grocery stores samples from 14 samples (11 %) were positive for HEV RNA (Feagins, Opriessnig, Guenette, Halbur, & Meng, 2007). Inoculation of pigs with two of three liver homogenates showed that the RNA represented infectious virus.

13.7.4 RASFF notifications

There have been no RASFF notifications of hepatitis E virus.

13.7.5 Sources of infection in outbreaks

There have been no reports on foodborne HEV infections in Norway. In other European countries, food seems to be a major transmission route for HEV (genotype 3) and outbreaks have been identified (EFSA, Ricci, et al., 2017). The main reservoirs of HEV are faeces, muscle, and liver from pigs and wild boar, with the source of outbreaks being raw or undercooked meat and liver from such animals. In Italy, the consumption of raw seafood, wild boar meat, and liver sausage were identified as risk factors for locally acquired HEV infection (La Rosa et al., 2011). Consumption of pork products (pie, pâté, ham, and sausages) was identified as a risk factor for HEV infection in the UK (Said et al., 2014). Outbreaks described in the literature include consumption of pig liver sausage (Colson et al., 2010) and shellfish (Said et al., 2009).

Although products of pig and wild boar are the main causes of HEV outbreaks, deer must be included on the list of sources, as deer meat consumed as sushi has caused HEV infections (Takahashi, Kitajima, Abe, & Mishiro, 2004).

13.7.6 Sources of infection for sporadic cases

Same as for outbreaks.

13.7.7 Relative importance of different food sources

Products of pork and wild boar, especially those that contain liver are the most important.

13.7.8 Risk factor identification

The consumption of raw or undercooked shellfish and pig liver-based products are risk factors for infection.

13.7.9 Data gaps

Hepatitis E is not a notifiable disease in Norway; only a few cases have been diagnosed and little is known about the prevalence. Although most infections are asymptomatic, there are probably cases of hepatitis E that are not diagnosed or registered as non-A or non-B hepatitis. A seroprevalence study in Norway showed that 90 % (137 of 153) of blood donors tested positive. The assumption is that contact with swine is the main route of infection.

There is no information on the prevalence of HEV in pig liver and food products from domestic swine in Norway.

The number of wild boars is increasing in Norway and in the 2018/2019 hunting season, 310 animals were killed in Østfold and Hedmark. There is no information on consumption of meat from wild boars in Norway, nor about the prevalence of HEV in animals killed in Norway.

Generally, there is a lack of in-depth information about the spread of HEV from animals to humans. The extent of foodborne transmission is poorly understood. The infectious dose is unknown. There is a lack of a sensitive *in vitro* system for cultivation of the virus. Diagnostic tools need to be validated and standardized. There is no standardized method for detection of HEV in food matrices.

13.8 Norovirus

13.8.1 Literature

Search string used for search in Pubmed:

(((norovirus) AND (Clinical disease,)) AND (Source attribution)) AND (Food)

13.8.2 Occurrence in reservoir animals (if relevant)

Not relevant, as the human intestine is the only source.

13.8.3 Occurrence in food or water

13.8.3.1 Surveillance and monitoring programs

Norovirus has been included in the following NFSA Surveillance and monitoring programmes:

- «Smittestoffer i vegetabilske næringsmidler» (salad n=20, frozen raspberries n=20) in 2013.
- «Smittestoffer i bær" (frozen, imported samples) in 2015 (n=22) and 2016 (n=30)
- "Smittestoffer i vegetabilsk mat" (imported leafy greens and herbs) in 2017, 2018 and 2019 with 75 samples yearly.

Contamination with norovirus was not reported from any of the samples analysed.

13.8.3.2 Studies

Berries

Nestlé analysed 2015 samples of frozen berries for norovirus RNA, in the period 2009 to 2016. Of these, 5 samples (0.2 %) were positive of either NoV GI or GII (Li et al., 2018).

Commercial fresh/frozen berry fruits collected from 2016 to 2017 in the Heilongjiang Province of China were analysed for NoV. Among 900 frozen and 900 fresh domestic retail samples, the prevalence of NoV was 9 % and 12 %, respectively. NoV was not detected among the 677 frozen berry samples for export (Li et al., 2018).

In Belgium, 130 samples of frozen raspberries from 26 batches imported from Poland were tested for NoV. Six out of 70 samples (9 %) taken from 14 batches used for raspberry puree production, were positive. The mean NoV level in 20 g of sample was 4.3 log genomic copies. For 12 batches of individually quick-frozen berries, one was positive with a NoV copy number level below the limit of quantification (De Keuckelaere, Li, Deliens, Stals, & Uyttendaele, 2015).

Leafy greens

In Canada 275 samples of imported packaged leafy greens bought from retail stores were analysed for NoV RNA. Using sequencing in order to confirm NoV detection, a total of 40 samples (15 %) were positive (Mattison et al., 2010).

Shellfish

Common blue mussels, horse mussels, and flat oysters obtained from various harvesting and commercial production sites along the Norwegian coast were screened for the presence of norovirus by a real-time reverse transcription (RT)-nested PCR. Noroviruses were detected in 6.8% of the samples (Myrmel, Berg, Rimstad, & Grinde, 2004).

A European baseline survey of norovirus in raw oysters took place between 1. November 2016 and 31. October 2018 (EFSA, 2019). Oysters were collected from production areas (2180 samples) and dispatch centres (2129 samples) in 12 EU Member States. The prevalence in production areas was estimated to be 34.5% (CI: 30.1 – 39.1%), while for dispatch centres it was 10.8% (CI: 8.2 – 14.4%). There was a strong seasonal effect with higher contamination in the period November – April. The lowest contamination was found in Class A areas. Norway participated with 24 samples from production areas, of which 9 samples (38%) were positive. Five of the samples had results above limit of quantification, with NoV copy numbers from 160 to 830 per 20 g of shellfish. All but one positive sample had been collected in the period January – April.

13.8.4 RASFF notifications

From February 2001 until October 2020 there have been 355 RASFF notifications on norovirus in foods:

- Bivalve mollusks – 266 (11 notified by Norway, all from oysters. Countries of oyster origin and the number of alerts: Spain-1, The Netherlands-2, France-2, Ireland-3, UK-3)
- Fish – 1
- Fruits and vegetables - 88 (mostly frozen berries) (1 notified by Norway, seaweed imported from China)

13.8.5 Sources of infection in outbreaks

The reservoir for NoV is the human intestine. Water for production of drinking water and oysters can be contaminated with sewage. Food can be contaminated with fecal material in irrigation water, on hands of food handlers and people that pick berries and leafy greens. The risk products are water and food that are consumed raw. As NoV easily transmits between people, outbreak investigation and finding the source can be demanding. Outbreaks are often registered during the cold part of the year, probably due to NoV infections in general, being most common in this period.

13.8.5.1 NoV foodborne outbreaks in Norway

Food handling - Outbreak of gastroenteritis after a memorial service, 2016

A total of 33 participants reported that they had become ill, and norovirus was detected in the two stool samples that were analysed. An epidemiological study indicated **salmon**

slices. Although salmon cuts are suggested as a possible source of infection in this outbreak, it cannot be ruled out that the infection was also spread from person to person.

Frozen raspberries - Outbreak of gastroenteritis following meetings at a conference centre, November 2013

Overall, 74 of 148 (50%) that were included in the investigation had gastroenteritis and five stool samples provided were norovirus positive. No kitchen staff reported being sick. The epidemiology indicated **raspberry mousse,** which had been consumed by 70 cases (95%). Frozen berries used for the mousse were imported and not heat-treated. Contamination by a food handler could not be excluded (Einöder-Moreno et al., 2016).

Shellfish soup – Christmas party 2013

A total of 29 of the 43 party participants (67 %) reported gastrointestinal symptoms, including stomach pain, vomiting, diarrhoea, and light fever in the period between 24 and 48 h post celebration. Consuming carpet-shell soup was the only significant risk factor for infection. Norovirus GI and GII were detected in the remaining raw shellfish. The soup was prepared by adding raw chopped shellfish tissue in porcelain cups tempered to 20 °C, followed by boiling soup base. The heat-absorbing capacity of cold ingredients, utensils and porcelain should not be underestimated during food production (Lunestad et al., 2016).

Oysters - Christmas party at a hotel in Oslo, December 2012

After Christmas dinners at a hotel in Oslo, at least 41 people became ill with symptoms of gastroenteritis. Both the epidemiological study and the laboratory study showed that oysters were the source of the outbreak. None of the patients had seen a doctor, but the clinical picture indicated norovirus, and norovirus was detected in **oysters** (FHI).

Oysters - Oslo in February 2010

Six outbreaks with a total of 37 patients at six different restaurants in Oslo were detected. Norovirus was detected in imported **oysters** served in the restaurants, and they came from the same producer in France (FHI). There were simultaneous outbreaks of NV infection in several countries linked to the consumption of raw oysters. Since January 2010, 334 cases in 65 clusters were reported from five European countries: United Kingdom, Norway, France, Sweden, and Denmark. The oysters involved were cultivated within EU (Westrell et al., 2010).

Lettuce - National outbreak in January 2010

In January, NoV was detected in green coral lettuce in Denmark. The lettuce was produced in France and some of the batches were sent on to Norway. Norovirus was detected in the lettuce after an outbreak with 15 patients in a canteen in Nordland. It was assumed that at least nine other outbreaks of norovirus infection in Norway were caused by the contaminated lettuce (FHI).

Food handling – Hotel at Gardermoen, September 2008

More than 200 people fell ill in the outbreak. Many of them were diabetics, which led to several hospitalizations. The infection was probably spread via sick kitchen employees with inadequate routines for sick leave and hand hygiene as contributing causes (FHI).

Drinking water - Eikedalen in 2001

More than 400 people became ill after a visit to a ski resort. Norovirus was found in patient samples and it was concluded that contaminated drinking water was the probable cause of the outbreak (FHI).

13.8.6 Sources of infection for sporadic cases

Same as for outbreaks.

13.8.7 Relative importance of different food sources

Ready-to-eat food, such as oysters, frozen berries and berries, are most often involved in outbreaks of disease, but disease is also caused by consumption of cold food that has been handled by infected persons.

13.8.8 Risk factor identification

Consumption of raw shellfish is considered a risk factor for infection.

13.8.9 Data gaps

As NoV infections are quite acute and resolves after 24-48 hours, most cases of NoV disease are not registered and the fraction of foodborne NoV disease is difficult to estimate due to frequent person-to-person transmission. Sporadic foodborne cases of disease and smaller outbreaks are probably not detected.

The prevalence of NoV in different food matrices is difficult to assess and even more the prevalence of infectious virus. Molecular detection (RT-qPCR) is the only option as sensitive methods are needed and cultivation of NoV in commercial cell line is not possible. A few laboratories are cultivating the most prevalent GII4 virus in human, intestinal organoids, but this method is complicated, expensive and not suitable for routine diagnostics. Important data on NoV stability in food matrices, in the environment, and during treatment processes is therefore limited as they are mostly based on molecular detection.

As molecular methods detect infectious and non-infectious viruses, positive NoV results in food matrices is difficult to interpret for risk assessment. However, due to the low NoV infectious dose, NoV positive food are usually treated as risk food. This is a delicate situation regarding shellfish. The EFSA baseline study on NoV in oysters shows a high prevalence,

especially during the winter period. As there is no demand for analysis of oysters that are to put on the market, huge numbers of raw oysters that contain NoV are eaten each year. Sometimes they cause large outbreaks of NoV disease, but most often they do not. Although competence has been built regarding NoV RNA copy numbers in oysters and the possible outcome of consuming them, there is still a risk connected to this practice. The scientific community dealing with this problem is divided regarding whether a demand for NoV analysis of oysters should be introduced and what the limit of NoV copy numbers should be for the shellfish to be considered fit for consumption.

Despite using sensitive molecular methods, detection of NoV in food matrices is difficult, even in outbreak situations with epidemiologic studies clearly indicating a certain food item. The reason for this is the low amount of NoV necessary to cause infection, combined with low recovery of virus during sample preparation prior to RT-qPCR. An additional hinderance are the RT-qPCR inhibitors that occur in, e.g., berries and foods rich in lipids. This adds to the knowledge gap as results may be false negatives or indicate a low number of virus copies. Optimization of detection methods is therefore still an ongoing process.

13.9 Bacillus cereus

13.9.1 Literature

Search strings used for search in Pubmed and Cited Reference Search in Web of Science:

(Food[Title/Abstract]) AND (Bacillus cereus[Title/Abstract]). The search was limited to the period between 2010-2020: 1003 results

(Norway[Title/Abstract]) AND (Bacillus [Title/Abstract]): 53 results

13.9.2 Surveillance and monitoring programmes

There is no routine surveillance of *B. cereus* in animals and food.

13.9.3 RASFF notifications

In the period 2000 to 2019, RASFF received 199 notifications and alerts on food contaminated with *B. cereus*. The data indicated that spices and dried powdered herbs have frequently been associated with *B. cereus* with 44 notifications, and various processed products. Other processed foods, such as canned or bottled products, falafel, syrups (maple, sugar-cane and corn), pesto, tahini, tapenade, tomato sauce, tomato soup, vegetables in oil, and vegetable soups are also represented with a total of 50 notifications. In addition, there were 28 notifications for various dried products, such as dehydrated vegetable soups, dried fruits, porcini mushrooms, and (sun)-dried tomatoes with 28 notifications, and 12 notifications for other dry legumes, cereals, edible seeds and grain, flours and products thereof (processed products).

13.9.4 Reservoirs

The major habitat of *B. cereus* is soil and occurrence is particularly abundant on roots, tubers, and mycorrhizae of plants, but can also be found within soil organisms, such as in the digestive tracts of different arthropods and worms (Ehling-Schulz, Frenzel, & Gohar, 2015; B. Kim et al., 2014; Margulis et al., 1998). Warm-blooded animals, including humans, can also carry *B. cereus* in their digestive tracts (Wilcks, Hansen, Hendriksen, & Licht, 2006).

13.9.4.1 Occurrence in food or water

From its environmental habitats, *B. cereus* spores are easily spread to raw materials for food. It is virtually impossible to obtain food materials free of *B. cereus* spores, and this is important to take into consideration during further processing and storage. Foods may also be contaminated during processing; the hydrophobic nature of *B. cereus* spp. spores allows them to adhere efficiently to stainless steel and they can therefore accumulate on food processing equipment, which can become reservoirs for spores and vegetative cells. Good hygienic practices at all steps in the food chain is, therefore, important to minimize the level of *B. cereus* spores in production facilities, especially in the dairy industry. *B. cereus* has been isolated from broad diversity of foods, such as cereals, milk, fresh and dried spices, edible insects, fruits, meat, and vegetables; the spores seem to be particularly common in dried or dehydrated foods such as spices, rice, pastas and flours (reviewed in (Rouzeau-Szynalski, Stollewerk, Messelhäusser, & Ehling-Schulz, 2020)).

Norwegian surface waters have been examined for the presence of *B. cereus* spores and a low number of cytotoxic strains were found in samples from several rivers (Ostensvik, From, Heidenreich, O'Sullivan, & Granum, 2004). As filtration and chlorination have little effect on removal of *B. cereus* spores, they may pass through water treatment procedures such as filtration and chlorination. Indeed, Østensvik *et al*., showed that spores of *B. cereus* spp. may be present in drinking water that satisfies microbiological requirements (Østensvik et al., 2004).

13.9.5 Sources of infection in outbreaks

According to EFSA (EFSA & ECDC, 2017) mixed foods were most often involved in outbreaks with strong evidence of being caused by *B. cereus* spp. toxins (23% of the strong evidence outbreaks), followed by cereals such as rice and seeds. Gilbert and Kramer suggested that no type of food with a pH above 4.8 could be excluded as a source for *B. cereus* food poisoning (Gilbert & Kramer, 1986). This suggestion is supported by the large variety of foods that have been involved in *B. cereus*-associated foodborne outbreaks. However, it has been suggested that emetic strains are mainly associated with starch-rich foods, such as pasta, rice, and pastries, and in milk products, while enteropathogenic strains are present in all types of foods (Altayar & Sutherland, 2006).

Table 13-5. Examples of food poisoning outbreaks caused by *B. cereus* from 2010-2019. When no year of incidence was indicated, the publication year is given in (). The table is modified from Jessberger et al., 2020 (Jessberger, Dietrich, Granum, & Märtlbauer, 2020).

Year	Country	Food	Symptoms od illness	Reference
2010	Japan	Fried rice	1 child (11 years), gastroenteritis, acute encephalopathy, liver failure	(Ichikawa et al., 2010)
2010	Korea	Cooked and fried rice	Emesis	(Kim, Jeong, Park, Kim, & Oh, 2010)
2010	Japan	Reheated fried rice	3 family members, vomiting, acute encelopathy, one dead (1 year old child)	(Shiota et al., 2010)
2012	Italy	Basmati rice	12 cases, mostly vomiting, nausea, abdominal pain; diarrhoea	(Martinelli et al., 2013)
2007-2013	Germany	Different foods	Emetic B. cereus in 32 samples, vomiting	(Messelhäusser et al., 2014)
2014	China	Fermented black beans	139 people, nausea, vomiting, diarrhoea; 2 emetic isolates	(Zhou et al., 2014)
2015	Germany	Rice meal	Vomiting, abdominal pain, liver failure	(Tschiedel et al., 2015)
2007-2014	France	Mostly starchy food and vegetables	74 outbreaks, often mix of emetic and diarrhoeal syndrome, abdominal pain	(Glasset et al., 2016)
2001-2013	Australia	Fried rice and honey chicken	1 outbreak, vomiting	(May, Polkinghorne, & Fearnley, 2016)
2012	Great Britain	Pearl haricot beans	Several nurseries (182 children, 18 adults), vomiting	(Nicholls et al., 2016)
2015	Belgium	mashed rice–cucumber–chicory meal	20 toddlers, vomiting	(Delbrassinne, Botteldoorn, Andjelkovic, Dierick, & Denayer, 2015)
2016	USA	Refried beans	179 cases, 6 emetic isolates, mostly vomiting, some diarrhoea	(Carroll et al., 2019)
2018	Australia	Multi-course dinner	15 cases, vomiting or diarrhoea	(Thirkell, Sloan-Gardner, Kacmarek, & Polkinghorne, 2019)
2019	Germany	Buck wheat	Massive vomiting, diarrhoea, oesophageal perforation, Boerhaave syndrome	(Dichtl et al., 2020)

As it is nearly impossible to avoid the presence of *B. cereus* spores in many types of food, EFSA recommends that the level should not exceed 10^3-10^5 CFU/g food (EFSA & Hazards, 2016). Cereulide is very heat and acid stable and can remain intact in food after the vegetative bacteria that have produced it have been killed or it can be introduced to food via ingredients in which *B. cereus* may have multiplied. Counting *B. cereus* in a food product is therefore not a sufficient indicator for the risk of intoxication.

13.9.6 Sources of infection for sporadic cases

As *B. cereus* usually causes notifiable diseases with relatively mild symptoms, there is no available data on the sources for sporadic disease in Norway.

13.9.7 Relative importance of different food sources

Generally, foods with a minimum a_w of 0.91-0.97, a pH between 4.6 - 8.8, little or no competing microflora (for example, prepared meals, mixed salads, certain pastries etc.), that have been insufficiently re-heated or insufficiently cooled can be considered as high-risk foods for *B. cereus* food poisoning (Carlin et al., 2013). High cereulide production has been observed in foods with high content of starch, carbohydrates, vitamins, a medium/high a_w value as well as a pH value around 7 (Messelhäusser et al., 2014). Examples of foods supporting high levels of cereulide production are potato puree (pH 5.9-6.4) and pasta (pH 7.4) while toxin production is dramatically reduced in more acidic food, such as dishes containing vinegar (Agata, Ohta, & Yokoyama, 2002). Reheating of food does not necessarily reduce the risk, since the emetic toxin cereulide is not destroyed by heating.

13.9.8 Risk factor identification

B. cereus food poisoning is often related to the growth of *B. cereus* when foods are stored at unsuitable temperatures. Most cases of *B. cereus* food poisoning in Norway are due to food produced in canteens or large households. Foods associated with *B. cereus* foodborne outbreaks have often not been sufficiently cooled or not kept sufficiently heated after preparation. If not consumed immediately after preparation, foods must be kept at temperatures above 63 °C or deep-frozen or refrigerated to prevent or slow the growth of *B. cereus*.

Cereulide is pre-formed in the food within a temperature range of 12 – 40 °C and is heat stable at 100 °C for >2 hours (Apetroaie-Constantin et al., 2008). The optimum temperature for cereulide production is between 20-37 °C and it is strongly reduced or stops at 40 °C (Guérin et al., 2017). However, small amounts of cereulide production by a psychrotolerant *B. weihenstephanensis* strain have been detected during growth on agar media at 8 °C (Guérin et al., 2017). At 10 °C and higher, this emetic *B. weihenstephanensis* strain produced cereulide at levels implicated in emetic poisoning (Guérin et al., 2017). Although *B. weihenstephanensis* strains are predominant in Norwegian drinking milk stored at abused temperature (8 °C) until the end of the storage period, emetic strains were not detected among 59 isolates tested. All strains were, on the other hand, positive for at least one

gene/gene cluster encoding diarrhoeal toxins (Porcellato et al., 2021). Although psychrotrophic strains often carry diarrhoeal toxin genes they seem to pose a minor risk for diarrhoeal food poisoning; the diarrhoeal potential of 39 Norwegian *B. cereus* dairy isolates was investigated and it was found that at 37 °C (human body temperature) none of the strains were highly cytotoxic (Stenfors Arnesen, O'Sullivan, & Granum, 2007). The low risk associated with psychrotrophic *B. cereus* species is also supported by several studies from elsewhere in Europe and Australia ,reporting that minimally processed chilled foods contain very low levels of *B. cereus* contamination when stored at correct temperature (reviewed in (Webb, Barker, Goodburn, & Peck, 2019)). Furthermore, there are no outbreaks associated with *B. cereus* and correctly stored commercially produced minimally processed foods (EFSA, 2016; Kennedy, 2004). Remarkably, in UK alone, more than 10^{10} packages of these foods have been sold in 1995-2005 without reported foodborne illness, which suggests that the risk associated with this type of food is very low (Peck, Goodburn, Betts, & Stringer). EFSA stated that refrigerated foods have seldom been linked to outbreaks of *B. cereus*-associated food poisoning (EFSA & Hazards, 2016).

According to studies in monkeys and based on the analysis of foods involved in *B. cereus* intoxications in humans, approximately 5 to 10 µg of cereulide per kg of body weight is necessary to induce emetic syndrome. It has been estimated that a level of *B. cereus* of 10^5 CFU/g food can produce sufficient cereulide to cause illness a few hours after ingestion. Notably, the disease symptoms arise from the pre-formed toxin cereulide, not from the bacteria themselves.

13.9.9 Conclusions

B. cereus is common in soil but can also grow in the gut of mammals. Almost any type of food can be liked to *B. cereus* food poisoning. The main causative factors for *B. cereus* food poisoning are:

- Inadequate cooling of food
- Improper storage of food.

The most important measures to prevent *B. cereus* food associated disease is to keep the number of spores as low as possible and to ensure proper heating, cooling and storage regimes. In mass catering and restaurants, it is particularly important to cool cooked foods rapidly and sufficiently to prevent spores from germinating and vegetative cells from growing. Good cleaning practices are important to minimize spore-related problems in food-production facilities and, particularly, in the dairy industry. Based on a few studies, psychrotrophic *B. cereus* strains pose a minor risk for diarrhoeal food poisoning and properly stored commercially produced minimally processed food products have never been associated with *B. cereus*-associated food poisoning.

13.9.10 Data gaps

- There is a knowledge gap on which foods are involved in sporadic cases of *B. cereus* food poisoning in Norway.
- The true incidence of *B. cereus* food poisoning in Norway is unknown.
- There is a need for better understanding of the course of enteropathogenic *B. cereus* infections to evaluate the potential risk associated with different subtypes of this group of bacteria, particularly the psychrotrophic species.
- Considering the wide and largely uncontrolled use of *B. cereus* in commercial probiotic preparations, we need a better understanding on the potential health risks imposed by *B. cereus* strains that are sold as dietary supplements.
- There is a lack of systematic studies where the role of different extrinsic factors on cereulide production has been determined under standardized conditions. Such data would facilitate predictive microbiology and improve HACCP studies. Currently there are no models are available to predict both growth and cereulide production by *B. cereus* spp. in food.

13.10 Clostridium botulinum

13.10.1 Literature

Search string used for search in PubMed and Cited Reference Search in Web of Science:

(Food[Title/Abstract]) AND (Clostridium botulinum[Title/Abstract]). The search was limited to the period between 2005-2020: 308 results

13.10.2 Surveillance and monitoring programmes

There is no routine surveillance of *C. botulinum* in animals and food.

13.10.3 RASFF notifications

In the period 2001 to 2019, RASFF received 34 notifications and alerts on food contaminated with *C. botulinum*. *C. botulinum* has been associated with processed products, such as sauces and dressings, purées, soup, and pastes (including canned and bottled products), and syrups (11 notifications), fish (8 notifications) and other seafoods (2 notifications), vegetable oil (3 notifications), poultry (2 notifications) and red meat (1 notification), baby food (1 notification), and beverages (1 notification).

13.10.4 Reservoir

In nature, *C. botulinum* prefers to grow in decaying organic matter and its spores are common in soil, mud and sediments in lakes, streams or coastal waters. *C. botulinum* spores are also present in the intestinal tract of fish, birds and mammals (not humans). However, neurotoxigenic Clostridia are considered to be saprophytic and are not dependent upon a

host organism (Doyle, 2011). As *C. botulinum* spores are common in natural environments, they are easily spread to food raw materials during harvesting, processing or subsequent storage. The presence of *C. botulinum* spores in foods varies depending on their distribution and prevalence in the environment which, in turn, varies between different geographical regions (Doyle, 2011).

13.10.5 Sources of infection in outbreaks

In Norway, only a few cases of foodborne botulism have been diagnosed during the last 20 years, but mild cases may have occurred undiagnosed. Home-canned foods and traditional local foods are the major sources of foodborne *C. botulinum* intoxications. The botulinum toxin has been detected in a variety of foods, including low-acid preserved vegetables, such as green beans, spinach, garlic mushrooms, olives and beets; fish, including canned tuna, fermented, salted and smoked fish; and different meat products, such as ham and sausage. The food implicated in foodborne botulism differs between countries and often reflects local eating habits and food preservation methods. Only occasionally, commercial food products are involved. In 2006, four cases of foodborne botulism associated with carrot juice were reported to the CDC. *C. botulinum* probably proliferated in the juice as a result of poor refrigeration during transport or storage (CDC, 2006). In 2007, five cases of foodborne botulism associated with commercially canned chili sauce were reported to CDC. The outbreak investigation identified production deficiencies that might have allowed *C. botulinum* spores to survive the canning process (CDC, 2007).

13.10.6 Sources of infection for sporadic cases

Most cases of food-borne botulism in Norway are sporadic, involving only 2-3 persons. The food sources are not expected to differ from those involved in outbreaks.

13.10.7 Risk factors

Vegetative *C. botulinum* can be easily destroyed by boiling, while the spores can remain viable even after boiling for several hours. Foodborne botulism often occurs after ingestion of improperly processed low-acid food that has been stored insufficiently chilled for a longer period (Doyle, 2011). A very high temperature is required to ensure *C. botulinum* spores are killed and failure to apply enough heat to canned foods has often led to foodborne botulism. Home-canned or fermented foods without adequate salt or acidity, and that are eaten without further heat treatment, are often involved in botulism. The closed jars create an anaerobic environment where *C. botulinum* spores can germinate and the revived bacteria grow in the absence of competing microorganisms if the jars are not stored sufficiently chilled. Psychrotrophic Group II *C. botulinum* strains can grow, and even produce toxins, at temperatures down to 3 °C, although their optimal growth temperature is reported to range between 26–30 °C (Graham, Mason, Maxwell, & Peck, 1997). The upper temperature limits for growth of group I and group II strains are approximately 50 and 45 °C, respectively (Doyle). Industrially canned foods, that are not required to be stored chilled, are seldom

involved in foodborne botulism. They undergo a "botulinum cook" in a pressure cooker at 121 °C (250 °F) for 3 minutes.

High salt and/or acidity are often combined with low temperature to prevent growth of C. botulinum. Under otherwise favourable conditions, Group I strains can grow in brine with a maximum NaCl concentration of 10% w/v (Lynt, Kautter, & Solomon, 1982). It is generally accepted that *C. botulinum* grows in low-acid foods with pH values higher than 4.6. Low-acid foods with pH values higher than 4.6 include red meats, various types of seafood, poultry, milk, and fresh vegetables (except for most tomatoes). Mixtures of low-acid and acid foods may have pH values above 4.6 unless enough lemon juice, citric acid, or vinegar has been added to make them acidic. These foods need suitable processing and preservation methods to prevent growth of *C. botulinum*. Growth of *C. botulinum* in canned or fermented food may not cause any visual defects to the container or jar (such as bulging) or organoleptic defects to the food. Only strict control during of processing (and absence of subsequent contamination), as well as control of other hurdles such as acidity, salinity, and refrigeration temperature, is sufficient to ensure food safety.

High-acid foods have occasionally been involved in outbreaks of foodborne botulism. When acids are not sufficiently mixed or allowed to spread by diffusion throughout the food, the resulting product could contain localized areas of high pH that permits growth of *C. botulinum* and toxin production. Furthermore, growth of yeast and mould in foods can metabolize acids and create growth niches for of *C. botulinum* (Doyle, 2011). For this reason, the presence of yeast and mould in high-acid canned foods should be considered as a serious defect and the contaminated food should be discarded.

Outbreaks of foodborne botulism in Norway are relatively often caused by ingestion of contaminated home-produced "rakfisk", a Norwegian fish dish made from trout or char, salted and fermented for two to three months before being consumed without prior heating (Skåra, Axelsson, Stefánsson, Ekstrand, & Hagen, 2015). The production of rakfisk is based on mild (4-6% w/w) salting of the gutted fish and layering of the fish under pressure in tight containers. The containers are then stored at 3-7 °C for 3-12 months, during which period fermentation takes place. As long as strict hygienic practices are followed, the salt concentration is not lower than 5%, and the storage is at a maximum temperature of 10 °C, rakfisk is considered safe regarding botulism. Commercially produced rakfisk has not been the source of botulinum intoxications (Skåra et al., 2015).

13.10.8 Conclusions

Foodborne botulism is a severe intoxication that is of high importance to food safety due to the severity of the disease symptoms. It results from consumption of food in which *C. botulinum* spores have been allowed to germinate and the resulting vegetative bacteria to grow and produce toxin under low-oxygen conditions. This typically occurs in improperly prepared home-canned foods and fermented dishes without adequate salt or acidity and that are stored insufficiently chilled. Proper heat treatment and preservation conditions are important for preventing growth and toxin production by *C. botulinum* in food. Although *C.*

botulinum typically will not grow in high acid food with pH <4.6, other contamination or factors in the food can have a protective effect on the bacteria by providing localized areas or pockets of high pH, thus allowing for growth in high-acid foods.

13.10.9 Data gaps

- There is a lack of knowledge regarding the effect of newer processing methods such as high pressure and high intensity light and sound on *C. botulinum* spores.
- It is not known how climate changes will influence the presence of *C. botulinum* spores in the environment.

13.11 Clostridium perfringens

13.11.1 Literature

Search strings used for search in PubMed and Cited Reference Search in Web of Science:

(Food[Title/Abstract]) AND (Clostridium perfringens[Title/Abstract]): The search was limited to the period between 2005-2020: 480 results

(Norway[Title/Abstract]) AND (perfringens [Title/Abstract]): 15 results

13.11.2 Surveillance and monitoring programmes

There is no routine surveillance of *Cl. perfringens* in animals and food.

13.11.3 RASFF notifications

In the period 2000 to 2015, RASFF received 19 notifications and alerts on food contaminated with *C. perfringens.* Among these, *C. perfringens* was associated with processed products such as sauces and dressings, purées, soup, and pastes (including canned and bottled products) (4 notifications), syrups spices and dry powdered herbs (3 notifications), fresh pods, legumes, grains and other dry legumes, cereals, edible seeds and grain, flours and products thereof (3 notifications), white fish (2 notifications), fermented, salted, or acidified vegetables or fruit (2 notifications), fresh herbs (2 notifications), dehydrated vegetables and fruits (1 notification).

13.11.4 Occurrence in food or water

C. perfringens is present in almost every natural environment examined so far, including soil, water, plant material, and dust (Allaart, van Asten, & Gröne, 2013). As *C. perfringens* is ubiquitous in the environment, it can contaminate almost any food raw material. In the spore form, *C. perfringens* can survive in water for many years and is therefore used as an indicator of faecal contamination. However, *C. perfringens* can also growing soils and sediments where it breaks down organic material. Therefore, the presence of low

concentrations of this bacterium in water could also emanate from sources other than faecal contamination.

13.11.5 Occurrence in reservoir animals (if relevant)

Most warm-blooded animals used for food carry a high number of CPE-positive *C. perfringens* in their intestines and are considered a natural reservoir for this bacterium (Tschirdewahn, Notermans, Wernars, & Untermann, 1991).

13.11.6 Sources of infection in outbreaks

Meat and meals containing meat are the most common types of food causing *C. perfringens* outbreaks in various countries, including Norway. In 2012, there was a large *C. perfringens* outbreaks among swimming club members staying at a hotel in Trondheim. The outbreak included 43 cases who showed symptoms typical for *C. perfringens* infection. All but one of the affected individuals had eaten a beef stew containing a high number of *C. perfringens* of the same protein profile. Cohort analysis showed that eating beef stew and rice was significantly associated with symptoms of *C. perfringens* food poisoning. No pathogens were detected in the rice. It was found that the temperature control of the stew, but not of the rice, was poor. Interestingly, the individuals who fell ill reported a median duration of the symptoms of 35 hours (range 8 - 96 hours), which is markedly longer compared with that described in most other reports (usually not longer than 24 hours) (Wahl, Romma, & Granum, 2013).

13.11.7 Sources of infection for sporadic cases

Individual cases of *C. perfringens* food poisoning are not reported to MSIS.

13.11.8 Relative importance of different food sources

C. perfringens is not able to produce 13 of 20 amino acids. It therefore needs to acquire most amino acids from its environment. This broad nutritional requirement is the reason why it grows better in nutrient-rich foods, such as meat, and approximately 75% of *C. perfringens* foodborne outbreaks can be traced to meat and meat products. Meat dishes, such as beef, poultry, sauces and pre-cooked foods, are common sources of *C. perfringens* infections, but *C. perfringens* can also multiply quickly in other proteinaceous foods. The contaminated food is almost always heat-treated, which kills competing bacterial flora while *C. perfringens* spores survive. *C. perfringens* will then, sometimes together with other spore-forming bacteria, such as *Bacillus cereus,* become the dominating flora. *C. perfringens* infection often occurs when foods are prepared in large quantities and slowly cooled or re-heated. Therefore, outbreaks often occur in large institutions, such as hospitals, nursing homes, school cafeterias, and prisons.

13.11.9 Risk factor identification

The following food safety violations may contribute to propagation of *C. perfringens*:

- Heating at low temperature (<60 °C)
- Insufficient cooling
- Storage of foods at room temperature
- Insufficient heating of leftovers

13.11.10 Conclusions

C. perfringens food poisoning outbreaks commonly occur in restaurants and canteens that prepare and store large quantities of food. People become sick after consuming insufficiently heated or improperly stored food where contaminating *C. perfringens* has been given the opportunity to proliferate and sporulate, producing sufficient levels of CPE toxin. Preventive measures must therefore be focused on hindering growth of this bacterium in cooked foods. As the spores are expected to be present in many types of food raw materials, cooking/heating at appropriate temperatures, combined with rapid cooling followed by refrigeration, is the most efficient way to avoid *C. perfringens* food poisoning.

13.11.11 Data gaps

It is not known how climate changes will influence the presence of *C. botulinum* spores in soils.

13.12 Staphylococcus aureus

13.12.1 Literature

A literature search was performed in Pubmed 30th November 2020 with the search string: (staphylococc*) AND (enterotoxin*)) AND (Norway). The search generated 29 hits, from relevant information, included below, was extracted.

13.12.2 Surveillance and monitoring programmes

The Norwegian Food Safety Authority has, through their Surveillance and monitoring programmes, analysed for *S. aureus*/enterotoxin in cheese, almost exclusively unpasteurized cheese. Testing was performed in 2014, 2015, 2016, and 2018. A total of 168 cheeses from Norway, France, Italy and Switzerland were analysed, all were negative for *S. aureus*.

13.12.3 RASFF notifications

In the period 2000 to 2018, the Rapid Alert System for Food and Feed (RASFF) received 25 notifications and alerts on food contaminated with *S. aureus* (RASFF 2020). The most

frequently associated food was red meat (6 notifications), followed by cheese (4) and seafood (4).

13.12.4 Occurrence in reservoir animals (if relevant)

Mastitis caused by *S. aureus* in the cow, goat or sheep udder can lead to contaminated unpasteurized milk or dairy products. Many types of animals, as well as humans, can be carriers for *S. aureus*.

13.12.5 Occurrence in food or water

In Norway, studies in 2003 and 2005 showed that the prevalence of *S. aureus* in raw cow milk and raw goat milk was about 70% and 90%, respectively. In 2018, 38% of 71 unpasteurized milk products were positive, while enterotoxins A-E were not detected in any of these samples (NFSA, 2020a).

13.12.6 Sources of infection in outbreaks

In the period 2005-2019, there were 20 outbreaks with a total of 88 cases of *S. aureus* food poisoning in Norway. In 2011, there was an outbreak associated with soft-ice, where enterotoxin was detected. In 2003, there was an outbreak with 8 persons, after eating leftovers of mashed potato made with raw milk (Jorgensen et al., 2005). In addition, in 2001, 18 persons became ill after consumption of white goat cheese bought at a local market.

In 2018, there was a total of 114 outbreaks in the EU (including both strong- and weak evidence outbreaks) in 17 reporting countries (including two non-member states), with a total of 1124 cases, caused by staphylococcal enterotoxins (Amore, 2020). The most commonly associated foods were "other foods" (38 outbreaks, included milk and milk products and cereal products and legumes), "mixed food" (21), meat and meat products (19, of which 8 from poultry), egg and egg products (9), milk and milk products (7), and fish and fish products (5). The majority of the outbreaks were associated with canteens or catering for workplaces, schools, hospitals etc (EFSA & ECDC, 2018a; Scallan et al., 2011).

13.12.7 Sources of infection for sporadic cases

In principle all types of food that can be contaminated during preparation and handling and where *S. aureus* can grow when food is inappropriate cooled or stored at too high temperature.

13.12.8 Relative importance of different food sources

Non-pasteurized dairy products stand out as a food category especially linked to *S. aureus* food poisoning, but otherwise many types of food may be vehicles of infection.

13.12.9 Risk factor identification

Consumption of unpasteurized dairy products Temperature abuse when storing food, resulting in possible growth and toxin production of *S. aureus,* are main risk factors:

- Keeping hot food warm at too low temperatures (< 60°C)
- Insufficient or too slow cooling of food
- Prolonged storage of food at room temperature
- Inadequate heating of previously cooked foods

Eating food contaminated from human or animal carriers and insufficient personal hygiene and hygiene when handling food are also risk factors.

13.12.10 Data gaps

As in most cases (beside non-pasteurized dairy-products), persons handling food and not raw materials are the source of *S. aureus*. Thus, extensive analysis of different types of foods other than dairy products may not be very informative, except for in outbreak situations. When performing analyses, food should be analysed for both *S. aureus* and toxins. Research is needed to develop sensitive detection methods for all types of enterotoxins.

13.13 Listeria monocytogenes

13.13.1 Literature

Surveillance data for *Listeria* is collected in official reports, and the sources to a large extent known. The need of literature search was therefore limited to recent studies on connections between strain variation, dose response and symptoms of illness.

The search strings Listeria AND Dose response models; Listeria AND virulence AND genome; Listeria AND illness symptoms gave several thousand hits after 2020.

EFSA reports the prevalence and fraction of non-compliant products in terms of *L. monocytogenes* in ready-to-eat foods every year (EFSA & ECDC, 2018b, 2019). These correspond well with the results from the Norwegian surveillance programmes during the last years. The prevalence is highest in the fish category, being about 10 times higher than in meat and dairy. About 90 % of the samples are within the legal limit regarding concentration, but the remaining fraction may have several million bacteria per gram. High concentrations are found within all food segments. Interestingly, an EFSA study from 2018 concluded that there was a higher prevalence of *L. monocytogenes* in products where two or more preservatives were added than in products with no additives (EFSA 2018). This should not be taken as an indication of that preservatives increase the prevalence, but rather that preservatives are used when contamination is hard to avoid and limiting the growth of *Listeria* is therefore necessary.

The products with the highest concentrations are related to food matrixes with a high growth potential of *Listeria* (i.e. pH, water activity, and few additives), a process where contamination is likely to occur, long shelf life, and/or abuse of temperature conditions for storage. This is in accordance with the literature. It has been well documented that the growth rate of *L. monocytogenes* in foods depends largely on temperature, atmosphere, food matrix, water activity, pH, additives like lactate and acetate, and presence of other microbes (Augustin et al., 2005; Beaufort et al.; Cornu et al., 2011).

Ready-to-eat foods were previously considered as single food products, like smoked salmon, cooked ham, soft cheese, etc. Nowadays, complex foods consisting of several ingredients have become a larger fraction of ready-to-eat foods. Outbreaks and literature studies have revealed that complex food represent a mixture of microenvironments where some have favourable conditions for growth of *Listeria*. Some examples are "rullepølse" (rolled sausage) (Kvistholm Jensen et al., 2016), mixed salads (Stratakos et al., 2015), and caramel apples (Angelo et al., 2017).

13.13.2 Surveillance and monitoring programmes

Surveillance programmes have been carried out at least every second year since 2010 in Norway. These have been focused on these groups of samples:

- Dairy and dairy products, both pasteurised/unpasteurised and Norwegian/imported products
- Classical ready-to-eat categories of smoked and graved (cured) fish, cold cuts of meat, and soft and semisoft cheeses
- A wide range of ready-to-eat foods, including the classical categories, mixed foods like salads and sandwiches, and unintended ready-to-eat foods like meat balls intended to be consumed heat treated, but used as cold cuts.

The number of samples per programme has been from 200-400 per year.

In 2010-2012 a Europewide surveillance programme was carried out that was designed to cover those products with the highest consumption; i.e., associated with large cities, large shops, large producers, and the classical ready-to-eat food categories.

The results from the Norwegian samples were:

- Soft and semi-soft cheeses: 60 samples, no positives.
- Meat cold cuts: 60 samples, no positives
- Cold smoked and gravad fish, 120 samples, 6 positives, 1 noncompliant with criteria (>100 cfu/g)

In 2012, nearly 300 samples of imported cheese were analysed

In 2013, a variety of products on the Norwegian market were analysed:

- Meat products: 145 samples from Norway, 4 positive;

- Dairy products: 164 samples, 1 positive;
- Pelagic fish: 169 samples, 14 positive;
- Leaves: 63 samples, 2 positive;
- Other processed foods: 21 samples, no positive.

Nearly all positive samples were found in Norwegian products.

In 2016, 294 samples of dairy products were analysed: no positive samples.

In 2018, 188 samples of dairy products were analysed: no positive samples

In 2019, 400 samples of a wide range of ready-to-eat foods were analysed: *L. monocytogenes* was found in 8 samples

- Minced meat products: 4 positive samples: 20-30000 cfu/g
- Smoked salmon: 1 positive sample, concentration <10 cfu/g
- "Rakfisk": 2 positive samples, concentration <10 cfu
- Sandwich with chicken: 1 positive sample, concentration <10 cfu/g

In 2020, approximately 330 samples of a wide range of ready-to-eat foods were analysed, with 4 positive samples

- Frozen vegetables
- Baked product with cheese and ham
- Smoked salmon
- An unpasteurised cheese, more than 100 cfu/g

Typical for all these programmes is that the prevalence is low, even at the last day of shelf life, but positive samples are found in some food categories. However, this category varies from year to year. Mostly, the concentrations are low, but some samples have very high concentrations, reaching up to 1000 times higher than the legal limit.

13.13.3 Summary for product groups

13.13.3.1 Rakfisk, smoked and graved (cured) fish:

Positive samples have been found in nearly all programmes where the category is included. For rakfisk, concentrations of up to several millions per gram are found.

13.13.3.2 Meat products:

Found in only some programmes, but high concentrations found.

13.13.3.3 Dairy products

Table 13-6. Number of samples in surveillance programmes

Year	Total number of samples	Norway pasteurised	EU pasteurised	Norway non-pasteurised	EU non-pasteurised	Treatment unknown
2018	189	73	20	71	25	
2016	184	71	31	52	30	
2013	82	50	8	16	1	7
2012	388	1	314		73	
2010	60	18	38		4	
SUM	903	213	411	139	133	7

Listeria monocytogenes was detected in only one of these samples, concentration less than 100 cfu/g

13.13.3.4 Vegetables:

Few samples analysed, but positive samples are found

13.13.3.5 Mixed foods

Only included in a few programmes. Positives found in all programmes in which this category is included.

13.13.4 RASFF notifications

There are numerous RASFF notifications about *Listeria* in food every year, so many that only trends can be described here.

- The number of countries reporting *Listeria* in foods has increased over the years. Countries from several continents are present.
- The number of reports increases every year.
- The main categories of foods are, in order, seafood (pelagic and white fish), meat (red meat and poultry, occasionally game), dairy (cheeses), other, fungi, vegetables+herbs+leafy greans, pasta and cereals.
- The number of product categories increases.
- Norway has reported nearly in all years except for four since 2002. Most of the reports have been related to pelagic fish, but many different food categories have been reported.

13.13.5 Occurrence in reservoir animals (if relevant)

There is only passive surveillance of *Listeria* in animals in Norway. Positive samples are few, and mostly related to sheep. Some positive samples of feed and compost are found nearly every year.

13.13.6 Occurrence in food or water

There is no surveillance of fresh water or drinking water. However, a surveillance campaign of *Listeria* in sea, including sea water is currently on going. Although not considered a major risk for humans, sea water important for farmed fish.

13.13.7 Sources of infection in outbreaks

As described in earlier chapters, outbreaks of human listeriosis in Norway has been

- "Rakfisk" – 2018 – 13 people ill – no deaths
- Brie cheese, imported – 2018 – 3 people ill, deaths not known.
- "Rakfisk" – 2013 – 3 people ill – no deaths
- "Organic Camembert cheese» - 2007 – 19 people ill – 5 deaths
- Contaminated cold cuts slicer – 2005 – 3 people ill – no deaths
- Heat-treated meat toppings – 1992 – 8 people ill – no deaths

13.13.8 Sources of infection for sporadic cases

As described earlier, all food categories can cause sporadic cases. Until a few years ago, it was assumed that fish only caused sporadic cases, while meat and cheese caused outbreaks. Recent studies do not support this hypothesis. Based on the European BASELINE study in 2010-2012, ECDC, EFSA and ANSES performed a comparison of all isolates from humans and isolates from food. More than 10 clusters were found with isolates from both foods and patients, and the majority of clusters contained isolates from fish, while only some clusters from meat and cheese (ECDC et al., 2021). It should be noted that only the classical categories of ready-to-eat foods were included in the BASELINE study, which means that combined foods like mixed salads were not included.

13.13.9 Relative importance of different food sources

It should be noted that *Listeria* is a ubiquitous bacterium, which can survive in a variety of niches. It can therefore be present everywhere. However, its presence in high concentrations represent a larger risk for human illness than traces. The high-risk foods are therefore foods that are processed and stored in ways that do not eliminate *Listeria*, and/or allows its growth after recontamination.

Some categories are considered as high-risk foods (see VKM reports from 2018 and 2019 for further details).

- Ready-to-eat foods with a long shelf life, likely to be stored at abuse temperatures and with high growth potential (VKM et al., 2019; VKM et al., 2018). This category included rakfisk, cheeses, cold cuts, smoked fish, etc, but also foods with non-homogenous composition, where some parts represent a high growth potential for *Listeria*. Typical examples are "rullepølse" and mixed salads.

- Ready-to-eat foods that are prepared with stored ingredients or under poor hygienic conditions and then stored.
- Ready-to-eat foods packed in a modified atmosphere, but stored after opening the package (EFSA, Ricci, et al., 2018).
- Frozen food thawed at abuse temperature and/or stored for too long after thawing.
- Foods that are not intended as ready-to-eat foods but used as if they were so.

13.13.10 Risk factor identification

As *Listeria* can occur everywhere and can grow in foods, the concentration is as important as its presence. In most cases, contamination levels are low, at around 1 cfu/g (Skjerdal, Reitehaug, & Eckner, 2014) under good hygienic conditions. The risk factor is therefore mainly related to growth after processing. Examples are:

- Maturation of foods at temperatures that allows growth
- Abuse storage conditions, thawing conditions, etc., at all stages in the farm-to-fork chain. Lack of traceability increases the risk of growth.
- Undercooking of foods intended to be properly cooked
- Long storage of food leftovers, including storage after opening packages.
- Eating foods after "use by" date. *Listeria* has limited influence of the odour and appearance of food, and high concentrations are therefore not detected by sensory means.
- Incorrect use of "best before" and "use by" date labelling.
- Combinations of foods in new ways that result in niches occurring in the food where *Listeria* can grow.

13.13.11 Data gaps

Despite the extensive surveillance programmes for *Listeria* in foods, there are data gaps.

Until recently, it was assumed that cases were largely sporadic. Implementation of WGS demonstrated a link between cases and the impression is now that most cases are outbreak related. Furthermore, foods that have not previously been considered as high-risk foods for *Listeria* have been identified as sources for the outbreaks.

The outbreaks are often related to long farm-to-fork chains and cross contamination during processing in one step. It is a Food Business Operator responsibility to carry out internal controls and reporting of production-environment samples is not mandatory. Furthermore, the actual temperature conditions during distribution and storage are hard to measure. As abuse storage conditions are typical for high concentrations of *Listeria*, time-temperature conditions can be used to estimate the concentration.

New foods, in particular composite foods, have been included in the surveillance programmes only during the last few years. Positive samples have been found, even in products where this was not expected.

Unintended ready-to-eat foods have generally not been included in the active surveillance programmes but have been identified as sources in outbreaks; one example is frozen corn.

Listeria can be present everywhere, food producers make more complex products than earlier, and consumers, especially the elderly, store food at abuse conditions and use the food in unintended ways. All these factors may result in the major sources for *Listeria* being those foods that have been less investigated than classical ready-to-eat foods.

13.14 E. coli

13.14.1 Literature

PubMed searches November 2020:

(Norway[Title/Abstract]) AND (EHEC[Title/Abstract]) – 5 results

(Norway[Title/Abstract]) AND (STEC[Title/Abstract]) – 27 results

(Norway[Title/Abstract]) AND (VTEC[Title/Abstract]) – 2 results

(Norway[Title/Abstract]) AND (EAEC[Title/Abstract]) – 2 results

(Norway[Title/Abstract]) AND (EPEC[Title/Abstract]) – 6 results

(Norway[Title/Abstract]) AND (ETEC[Title/Abstract]) – 2 results

13.14.2 Surveillance data (animals and food)

There is no routine/yearly surveillance of VTEC in animals and food, but surveillance for VTEC was performed in cattle (2000 and 2003), sheep (2008), vegetable foodstuffs (2013), and minced meat (2018). The results are presented under the headings "Occurrence in reservoir animals" and "Occurrence in food or water", together with information on other screenings and investigations.

13.14.3 Rapid Alert System for Food and Feed (RASFF)

Several alerts were registered for EHEC in the Rapid Alert System for Food and Feed (RASFF) in the period from 2004 to 2019. The predominant categories were:

- Red meat: 352, since 2012 Argentina and Brazil were dominant sources
- Cheese: 74, mainly from France
- Game: 49, mainly from Europe, but also a few from Oceania and South Africa
- Sprouted seeds: 14 samples
- Leafy greens/other leaves: 9 samples

13.14.3.1 Data from programmes in Mattilsynet: Pathogenic **E. coli.**

Categories and numbers of samples tested, positive samples in parentheses below:

Red meat

2012: Uruguay (177,3), Swaziland (36,3), Namibia (51,0), Brazil (14,1), New Zealand (4,0), Argentina and Australia (1,0)

2017: Norway (308,2)

Table 13-7. Cheeses (numbers tested, positive samples)

Year/country	Pasteurized	Unpasteurized	Heat-treated
2014 France		1,0	
2015 France		1,0	
2016/France		24,4	
2016/Italy		2,0	
2016/Norway	1,0	49,15	8,0
2016/Switzerland		1,0	
2018/France		23,0	
2018/Italy		2,0	
2018/Norway		65,0	

13.14.4 Occurrence in reservoir animals

13.14.4.1 Bovines

The results of surveillance in 2003 (NVI, 2003) confirmed conclusions from earlier investigations that shigatoxin producing *E. coli* O157 were still rare in Norwegian cattle (Table 13-8) (Opheim, Hofshagen, Wasteson, Bruheim, & Kruse, 2003; Vold, Klungseth Johansen, Kruse, Skjerve, & Wasteson, 1998).

The results also showed that although the prevalence for some of the *E. coli* serogroups O26, O103, O111, O145 is high in Norwegian dairy cattle, the bacteria do not represent a significant human health hazard because the presence of the virulence factors shigatoxin and intimin is very low. This agrees well with the results of a similar study performed on samples from Norwegian beef cattle in 2002 (Opheim et al., 2003).

Table 13-8. Number of herds and cattle tested for *E. coli* O157/H7 during the time period 1998-2003

Year	Population	No. of herds sampled	No. of animals tested	No. of positive herds
1998	Dairy cattle	293	2,617	1
1999	Dairy cattle	281	2,497	0
2000	Beef cattle	165	1,425	0
2003	Dairy cattle	137	1,221	1

The results from a survey of zoonotic *E. coli* in cattle, which was carried out in 2014-2017, indicated a low occurrence of STEC of serogroups O26, O91, O103, O111, O121, O145 and O157 in Norwegian dairy herds (NVI, 2018a). Furthermore, the results indicated that there is a larger occurrence of aEPEC, in particular aEPEC O26 which was isolated from approximately 15% of the herds.

13.14.4.2 Sheep and lamb

A survey documented a very low occurrence of stx- and eae-positive strains of *E. coli* O26, O103:H2 and O157:H7 in sheep in Norway with < 1 % of the sheep flocks positive for these serogroups/-types. These results correspond well with the low number of reported human cases in Norway (Urdahl et al., 2008). There was no stx-positive and eae-positive *E. coli* O103:H25. For *E. coli* O26, O103:H2 and O103:H25 the survey showed higher numbers of stx-negative and eae-positive strains than of stx-positive and eae-positive strains.

E. coli with the same virulence genes, serotypes, biochemical characteristics and DNA profiles as those found in patients from an *E. coli* O103:H25 outbreak, were detected in sheep from 29 of 491 farms in Norway (Brandal et al., 2012).

13.14.5 Occurrence in food or water

13.14.5.1 Minced meat

The Norwegian Food Safety Authority commissioned a survey of STEC in Norwegian meat products. The samples were collected in 2017 with subsequent analyses in 2018. A total of 308 samples of minced meat were collected. The results indicate that the occurrence of STEC of the serogroups O91, O103, O111, O121, O145 and O157, is low, but such bacteria may occur. Atypical enteropathogenic *E. coli* (aEPEC) and *E. coli* without virulence factors belonging to the serogroups in question were also isolated (NVI, 2018b).

13.14.5.2 Cured mutton sausages

Cured mutton sausages caused the outbreak in 2006 (see below).

13.14.5.3 Bivalves

Only a few studies of Shiga toxin-producing *E. coli* (STEC) detection in bivalves and their harvesting areas have been reported. There are no outbreaks associated with STEC from bivalves described. A total of 269 samples of bivalves were screened for the presence of stx and eae genes, and markers for the serogroups O26, O103, O111, O145 and O157. The results suggest that the occurrence of STEC in Norwegian bivalves is low (Martin, Svanevik, Lunestad, Sekse, & Johannessen, 2019).

13.14.5.4 Vegetable foodstuffs

Selected produce types (salad leaves, strawberries, sprouts, mangetout, raspberries) both imported and domestic, were analysed for *E. coli.* Only in 8 of 194 samples were low levels detected. However, STEC was not detected (NVI, 2013a).

13.14.6 Sources of infection in outbreaks

13.14.6.1 Cured mutton sausages

An outbreak of *E. coli* O103:H25 in 2006 included 17 registered patients, including 10 children with HUS, was caused by cured mutton sausages (Schimmer et al., 2008).

13.14.6.2 Vegetables and herbs

Contaminated fenugreek seeds imported from Egypt and sprouted on a farm in Germany caused a major European outbreak of HUS with an EAEC O104 strain. Altogether 4,397 cases were diagnosed, but only one case was confirmed in Norway. However, the causative strain, O103:H25, which caused the Norwegian epidemic from cured mutton sausages in 2006 (Schimmer et al., 2008) resembled the 2011 German outbreak strain O104:H4, both in genome and Shiga toxin 2-encoding (Stx2) phage sequence. The nucleotide identity between the Stx2 phages from the Norwegian and German outbreak strains was 90% (L'Abée-Lund et al., 2012).

13.14.6.3 Imported chives

An outbreak of gastroenteritis, most likely caused by ETEC with possibly 110 cases, was caused by imported chives. An outbreak at a hotel (2012) involving more than 300 persons was also possibly caused by ETEC from imported chives (MacDonald, Møller, et al., 2015).

13.14.6.4 Contact with sheep and animals in general, unpasteurized milk and contaminated salad

The sources of some of the 12 national smaller outbreaks, mainly caused by EHEC, and involving children that developed HUS, were most often not identified, but possible contact with sheep and animals in general, unpasteurized milk, and contaminated salad were among the suspected sources. In two nursery outbreaks in Norway, pathogens isolated from children after farm visits matched those found in farm animals, implicating animal faeces as the source (Møller-Stray et al., 2012).

13.14.7 Sources of infection for sporadic cases

- Raw, rare, or undercooked beef, lamb or mutton products
- Unpasteurized milk and products thereof

- Foods contaminated from animal or human shedders, including unwashed raw vegetables, herbs, sprouts, fruits and berries
- Untreated contaminated water
- Cattle, sheep or human shedders

However, based on the information in the sections above the following risk factors might be added:

- Imported red meat in particular beef and game
- Unpasteurized cheeses
- Imported vegetables and herbs like fenugreek and chives

13.14.8 Relative importance of different food sources

Vegetable foodstuffs like herbs have dominated in recent outbreaks, but meat in the form of cured mutton sausages and raw meat (in, e.g., hamburgers) has been associated with EHEC outbreaks in previous years. For sporadic cases, it is often difficult to find the cause. Contact with ruminants might be a cause of unsolved sporadic cases also in Norway.

13.14.9 Risk factor identification

The general risk factors for EHEC and aEPEC (Kapperud, 2018) are:

- Consumption of raw, rare or undercooked beef, lamb or mutton products
- Food safety violation when cooking raw beef or lamb
- Consumption of unpasteurized milk and products thereof
- Eating other foods contaminated from animal or human shedders including unwashed raw vegetables, herbs, sprouts, fruits and berries
- Drinking untreated water
- Bathing in contaminated water
- Unsanitary contact with cattle, sheep or human shedders

However, based on the information in the sections above the following risk factors might be added:

- Eating imported red meat in particular beef and game
- Eating unpasteurized cheeses
- Eating imported vegetables and herbs like fenugreek and chives

The general risk factors for ETEC, EIEC, tEPEC (Kapperud, 2018) are the same as for *Shigella* spp.:

- Direct infection by faeces from human shedders
- Consumption of food or water contaminated from human shedders including unwashed raw vegetables, herbs, sprouts, fruits and berries
- Drinking untreated water

- Travel to endemic areas

13.14.10 Data gaps and research needs

Due to the shortage of Norwegian-produced beef, more and more beef is being imported from Central Europe and South America. Alerts in RASFF and results from "OK" programs show that VTEC occurs relatively often. VTEC was also detected in both imported and Norwegian-produced unpasteurized cheeses. Routine surveillance of VTEC in such products might give an even better overview.

ETEC, EIEC, and tEPEC have a human reservoir and are often connected to raw unwashed vegetables, herbs, sprouts, fruits and berries produced abroad. Accordingly, the effectiveness of import control of such products is crucial to which degree these agents represent a risk in foods in Norway.

13.15 *Campylobacter* spp.

13.15.1 Literature

Search string used for search in Pubmed:

(Norway[Title/Abstract]) AND (Campylobact*[Title/Abstract]) – 69 results

13.15.2 Surveillance and monitoring programmes

The surveillance programme for **Campylobacter** *spp. in broiler flocks in Norway*

In 2001, Norway implemented a surveillance programme for *Campylobacter* in broiler chickens. The surveillance is an integrated part of The Norwegian Action Plan Against *Campylobacter* in Broilers aiming at reducing human exposure to *Campylobacter* from chicken products. The action plan is updated regularly. Reports and plans from the current and previous years are available at https://www.vetinst.no/overvaking/campylobacter-fjorfe

In the years 2001 through 2008, all flocks slaughtered up to 50 days of age were examined for *Campylobacter* before slaughter. From 2009 onwards, only flocks processed in the period 1 May to 31 October are examined, as surveillance has detected very low prevalence in the other months.

Faecal samples are collected at the farm 4-7 days before the flocks are slaughtered, and the slaughterhouse is informed about which flocks have tested positive, enabling implementation of the following measures to minimize human exposure:

Carcasses from *Campylobacter*-positive flocks are heat treated or frozen for at least three weeks following slaughter, in order to reduce the potential for transmission to consumers.

Flocks with unknown status at the time of slaughter are sampled at the slaughterhouse and kept until results are available, alternatively the meat can be heat-treated or frozen.

The prevalence of *Campylobacter*-positive flocks has varied significantly since the Action Plan was launched. Over the past five years, the percentage has ranged from a minimum of 4.4% in 2015 to 7.7% in 2016. In 2019, 103 of 2018 flocks (5.1%) tested positive. The positive samples originated from 86 (17.2%) of the 500 farms included in the surveillance programme (Torp, Vigerust, Bergsjø, & Hofshagen, 2020).

Until 2008, all flocks were re-tested upon arrival at the slaughterhouse, to identify flocks infected during the days after the sample was taken on the farm, and thus uncover any positive flocks missed by the first sampling. In 2005, 31.8% (n = 42) of the positive flocks were detected at this stage, only. In 2006 this was reduced to 25.3% (n = 48), and in 2007 the corresponding figure was 24.5% (n = 58). Thus, approximately 1 in 4 of the infected flocks was sent directly to the market without being frozen or heat treated. Since re-testing at slaughter was discontinued in 2008, more recent data to calculate the number of *Campylobacter*-positive flocks sent to consumption without preventive actions being taken, are lacking. The average number of chickens in each flock has increased since 2001. Nevertheless, the data indicate that the number of broiler carcasses contaminated with *Campylobacter* at retail sale has been approximately halved due to measures implemented in the Action Plan.

13.15.3 Rapid Alert System for Food and Feed (RASFF)

In the period June 2004 to October 2020, the Rapid Alert System for Food and Feed (RASFF) received 183 notifications and alerts on food contaminated with *Campylobacter* (RASFF, 2020a) [1]. The majority (163) referred to poultry meat, poultry meat products, or prepared foods made from poultry offal, while 17 involved fruits, vegetables, herbs or spices, one incriminated rabbit meat from Argentina, one referred to butter produced in Spain, and one involved chilled pork from Spain. Only two of the notified poultry products originated from a country outside the EU (Brazil). Ten of the 17 reports on fruits, vegetables, herbs or spices involved products from the EU, five were from east Asia, and one each from Kenya and Egypt. In 2013, Norway forwarded one alert, a consignment of dill from Italy, the only notification where Norway was among the countries to which the product was distributed. Norway was not flagged as the country of origin in any of the notifications.

[1] The RASFF Portal was accessed 10 October 2020.

13.15.4 Surveys – prevalence studies

13.15.4.1 Broiler chickens older than 50 days

The Action Plan does not include surveillance of broilers older than 50 days at slaughter, which account for only a small proportion of all broilers consumed in Norway. These older chickens are reared under several different management systems, from conventional indoor

production to organic farming. Some of the flocks are free rang, while others are more or less sheltered from the outdoor environment.

A pilot study in 2018 on broiler flocks older than 50 days, showed that 43.3% of 104 flocks tested positive for *Campylobacter jejuni* when sampled during the period May through October (Torp & Bergsjø, 2019.). The age of the flocks ranged between 52 – 92 days at slaughter. The oldest flocks had the highest prevalence (87.5%); these were flocks that had access to the outdoor environment. The lowest prevalence (22.2%) was detected among younger flock without outdoor access. Although the number of samples is too low to justify definite conclusions, the results support suggestions that age and outdoor access are important risk factors for *Campylobacter* infection in broiler flocks.

13.15.4.2 Poultry products

During a one-year period in 2006-2007, the Veterinary Institute, examined 496 samples of fresh, non-frozen chicken and turkey products ready for marketing from five processing units (Johannessen, Opheim, Reitehaug, & Hofshagen, 2008.). In total, *Campylobacter* spp. was recovered from 39 (7.9%) of the samples. *Campylobacter* was isolated from 32 (8.5%) of 375 chicken products and from 7 of 121 turkey products (5.8%). The positive chicken products showed largely the same seasonal variation as is seen for chicken flocks, with a large majority of positive samples being found between June and September.

In the same study, the prevalence of *Campylobacter* in turkey flocks was investigated. The bacterium was detected in 20 (14.0%) of 143 flocks from 54 producers (1-8 flocks from each).

13.15.4.3 EFSA baseline survey of broiler batches and carcasses

In order to establish baseline and comparable values for all Member States, a European Union-wide survey was carried out at slaughterhouse level to determine the prevalence of *Campylobacter* in broiler batches and of *Campylobacter* and *Salmonella* on broiler carcasses (EFSA, 2010a). Throughout 2008, batches and carcasses were randomly selected from the broiler slaughterhouses within each Member State, plus Norway and Switzerland. At Community level the prevalence of *Campylobacter*-colonised broiler batches was 71.2% and that of *Campylobacter*-contaminated broiler carcasses was 75.8%. Member State prevalence varied from 2.0% to 100.0% and from 4.9% to 100.0%, for caecal contents and carcasses, respectively. In Norway, the prevalence was 3.2% for batches and 5.1% for carcasses; 97.8% of *Campylobacter*-positive carcasses contained below 10 cfu/g and none harboured above 10,000 cfu/g.

13.15.4.4 Imported fruits, berries, vegetables and herbs

In recent years, the Rapid Alert System for Food and Feed (RASFF) has received an increasing number of notifications and alerts on detection of pathogenic microbes in vegetables, fruits, berries, and herbs. In 2004 to 2020, RASFF recorded 183 reports on

Campylobacter in foods, of which 17 involved contaminated fresh produce, whereas poultry products comprised the majority (163 notification) (13.15.3). While only 2-3% of the total consumption of poultry and poultry products are imported (Animalia, 2020; Hjukse, 2020), a high proportion of vegetables, fruits and berries consumed in Norway are produced abroad, accounting for 27% of the economic value of all imported foods in the period 2014-2019 (SSB, 2020). In 2018, imported vegetables accounted for 54% of the total consumption, compared with 94% for fruits and berries (Hjukse, 2020). In 2019 the corresponding figures were 51% and 95%.

Although imported fresh and frozen produce have been the source of infection in an increasing number of disease outbreaks in Norway, *Campylobacter* has so far not been incriminated (Web-based Outbreak Alert System, Vesuv) (13.15.6). Fresh herbs, and green or leafy vegetables, are mainly imported from southern Europe. Some products are imported from tropical and sub-tropical regions where the endemic level of foodborne infections is high. However, the total import from such countries is modest but is probably increasing (VKM, 2008a).

In 2007, the Norwegian Food Safety Authority investigated the presence of *Salmonella* and *Campylobacter* spp. on imported fresh herbs and leafy vegetables originating from Thailand and Vietnam (NFSA, 2008). Of the 159 samples examined, none were positive for *Campylobacter*. *Salmonella* was detected in 15%.

In 2013, the Norwegian Food Safety Authority carried out an inspection project to assess the occurrence of pathogens in fresh, imported vegetables and herbs (NFSA, 2014). A total of 30 importers were inspected and 154 consignments were sampled. *Salmonella, Campylobacter* or *E. coli* were detected in 41 lots, 93% of which originated from countries outside the EU. *Campylobacter* was only isolated from one batch, a sample of dill from Italy.

13.15.5 Reservoir

In Norway, *Campylobacter* is frequently encountered in the intestines of many mammal and bird species, both wild and domesticated. The animals are usually healthy carriers.

13.15.5.1 Wild birds

Wild birds are probably the largest reservoir for *Campylobacter* in Norwegian ecosystems. Both *C. jejuni, C. coli* and *C. lari* have been isolated from several of species of wild birds, especially gulls and crows (Kapperud & Rosef, 1983; Willumsen & Hole, 1987). A study from 1980-1981 showed that 50 % of the seagulls at the Grønmo landfill in Oslo were carriers of such bacteria. Campylobacters were also found in 90% of the crows and 4% of the pigeons in Oslo (Kapperud & Rosef, 1983). Wild birds are effective spreaders of pathogens over long distances, for instance to vegetable crops, horticulture sites, pastures, feed, drinking water reservoirs and recreational waters.

13.15.5.2 Poultry

Poultry of all kinds are carriers of *Campylobacter*. Most of the strains isolated belong to *C. jejuni.* During the automated slaughtering process, the bacterium is easily transferred to the carcass surface. Less than 10 % of Norwegian broiler flocks are infected with *Campylobacter*, which is low compared with most other countries (EFSA, 2010a). The Norwegian Action Plan against *Campylobacter* in Broiler Chickens ensures a high percentage of carcasses from positive flocks are heat treated or frozen prior to sale in order to reduce transmission to consumers (13.15.2).

13.15.5.3 Cattle

Campylobacter is common in the intestinal contents of cattle. In a study of faecal samples from 804 dairy cows and beef cattle from 333 herds in the counties of Rogaland and Vest-Agder in 1999-2001, *C. jejuni* and *C. coli* were detected in 26% and 3% of the animals, respectively (Johnsen et al., 2006). However, the degree of contamination that occur during slaughter of large animal like cattle, pigs and sheep is usually lower than in the automated poultry processing. In addition, the bacterium dies on large carcasses when the surface dries during cold storage. In contrast poultry processing requires much water and the carcasses have a number of cavities that retain moisture which enhance survival of the bacterium (campylobacters are sensitive to drying) (Gondrosen, 1984). Thus, although the animal prevalence is fairly high, beef and other red meat play a lesser role as a source of infection than poultry products. However, faecal contamination of raw milk is a significant risk. Johnsen et al. (2006) found significant genetic similarity between human and bovine isolates, a finding which presumably mainly reflects infection from a common source.

13.15.5.4 Swine

Pigs are often healthy carriers of *C. coli*, while *C. jejuni* is less frequent. In a study from 1983, *C. coli* was isolated from all of 114 slaughter pigs from 19 herds in southern Norway, while *C. jejuni* was not detected (Rosef, Gondrosen, Kapperud, & Underdal, 1983). The bacteria were further found as surface contaminant on 56% of fresh pig carcasses.

Nesbakken et al. (2003) conducted a detailed study on *Campylobacter* contamination on 24 slaughter pigs at one slaughterhouse. Samples were taken from three lymphoid tissues, from several places throughout the intestinal tract and from five carcass surface sites. Campylobacters were detected in the gastrointestinal tract of all pigs. The bacteria were also frequently found in the tonsils (67%) and on carcass surfaces. The majority of the isolates belonged to *C. coli* (n = 155), followed by *C. lari* (n = 12), and *C. jejuni* (n = 6).

In 2008, Nesbakken et al. (2008) studied the effect of blast chilling on the prevalence of campylobacters on pig carcasses. *Campylobacter* spp. was isolated from 34 (56.7%) of 60 carcass samples before blast chilling. After this procedure, *Campylobacter* spp. was recovered from only one (1.7%) of the carcasses.

C. coli, the predominant *Campylobacter* species in pigs, is responsible for only a small proportion of all cases of human campylobacteriosis (see 12.15) and cold storage of pig carcasses results in drying of the surface, which is unfavourable for survival of campylobacters (see 13.15.5.3). Hence, the importance of pork products as a source of infection is less prominent than the animal prevalence would suggest. However, pork is by far the most common meat consumed in Norway and therefore represents a considerable opportunity for exposure (Animalia, 2020). In 2019, the annual net consumption of pork was calculated at 18.6 kg per capita compared to 13.3 for beef, 10.2 for poultry, and 3.1 for mutton.

13.15.5.5 Sheep

Campylobacter is not uncommon in sheep. In a study from the 1980s, *Campylobacter* was recovered in faecal samples from 16 (8.1%) of 197 sheep belonging to 5 herds (Rosef et al., 1983). Among the herds, the carriage rate varied from 0 to 30%. Sheep grazing on open pasture have contaminated drinking water and caused outbreaks (see 13.15.5).

13.15.5.6 Dogs and cats

Dogs and cats are not infrequently healthy carriers of *Campylobacter*. In a study from 1983, the bacterium was detected in stool samples from 22% of 147 dogs and from 12% of 85 cats, all of which were outpatient at the Norwegian School of Veterinary Science (Gondrosen, Knaevelsrud, & Dommarsnes, 1985). A more recent study from 2000-2001 included dogs and cats from six small animal clinics across the country (Sandberg, Bergsjø, Hofshagen, Skjerve, & Kruse, 2002). In stool samples from 595 dogs, *C. jejuni* was isolated from 20 (3%), *C. coli* in 5 (1%), while *C. upsaliensis* was found in 117 (20%). Among 332 cats examined, *C. jejuni* was found in 11 (3%), *C. coli* in 2 (1%), while *C. upsaliensis* was detected in samples from 42 (13%).

13.15.5.7 Other animals

The bacterium has only exceptionally been found in wild mammals, but its occurrence has not been thoroughly investigated. *Campylobacter* has been detected in flies caught in infected poultry flocks and pig herds in Norway, and flies can easily transfer the bacterium to broiler flocks and other domestic animals on the same or neighbouring farms, as well as to food and feed (Rosef & Kapperud, 1983).

13.15.5.8 Water and aquatic protozoa

Campylobacter can contaminate surface water sources from sewage, manure, pastures, birds, and from other wild-living and domestic animals. In Norway, contaminated drinking water has been the source of infection in several outbreaks of campylobacteriosis, sometimes with more than a thousand illnesses (see 13.15.6). In the doctoral dissertation of Ola Brennhovd, *Campylobacter* was detected regularly throughout the year in Norwegian

surface water sources, including those used for drinking water (Brennhovd, 1991; Brennhovd, Kapperud, & Langeland, 1992).

The low water temperatures in Norway throughout large parts of the year favour the survival of *Campylobacter*, and thus increase the possibility of waterborne outbreaks. In addition, the bacterium can persist intracellularly in aquatic amoebae, which further enhances survival.

13.15.6 Sources of infection in outbreaks

Since the Web-based Outbreak Alert System (Vesuv) was launched in 2005, and up to 15 October 2020, 66 outbreaks of campylobacteriosis with more than 5000 cases of illness have been reported, making *Campylobacter* the second most common causative agent of food- and waterborne disease outbreaks, following norovirus (see Appendix III). In five outbreaks, the infection was acquired abroad. As for the 61 domestic outbreaks, the suspected sources of infection were: chicken or chicken products, 11; turkey, 1; other poultry products, 2; drinking water, 4; raw milk, 1; contact with sheep, 1; beef or products thereof, 1; oyster, 1; other foods, 1; unknown/missing information, 38. However, the evidence supporting the suggestions regarding the source of infection varies considerably, from mere indirect assumption based on patients' reports of food to strong bacteriological or epidemiological documentation.

Major outbreaks are described in more detail on a NIPH website, which include a historical overview covering the years before 1999 (NIPH, 2019). Some of the outbreaks mentioned below occurred before Vesuv was launched:

13.15.6.1 Drinking water

Drinking water has been identified as the source of infection in several large outbreaks of campylobacteriosis. Since 1981, ten outbreaks in which more than 300 persons became ill have been reported, and in three of them the number of verified cases exceeded 1000. The source of contamination, to the extent this is known, have,s been seagulls, grazing sheep or cattle, and wild geese.

Waterborne outbreaks in Norway have been reviewed in two publications (Guzman-Herrador et al., 2016; Nygard, Gondrosen, & Lund, 2003): During 1988-2002, prior to implementation of Vesuv, a total of 72 waterborne outbreaks were recorded. *Campylobacter* was the cause in 26% (19/72) of the outbreaks, norovirus in 18% (13/72), while for 46% (33/72) the causal agent was unknown (Nygard et al., 2003). In the period 2003-2012, the Norwegian Institute of Public Health received 28 alerts on suspected or confirmed waterborne outbreaks. The most common agent was norovirus (7 outbreaks), followed by *Campylobacter* (5) and *Francisella tularensis* (5). Two outbreaks were caused by *Giardia* and one by *Cryptosporidium*. In three outbreaks, the agent was not identified (Guzman-Herrador et al., 2016).

13.15.6.2 Poultry

Poultry products were the suspected source in 14 domestic outbreaks notified to Vesuv in the period from 2005 to 15 October 2020 (see above). In addition, two such outbreaks were reported before Vesuv was launched (in 2000 and 2001, respectively; (NIPH, 2019)). Nine of these 16 outbreaks affected guests at restaurants or hotels, and in several of them the cause was probably not consumption of undercooked poultry products *per se*, but inadequate routines to prevent cross-contamination between raw poultry meat and other foods to be eaten without subsequent heat treatment. Four outbreaks occurred in private households. In nine of the 14 outbreaks, however, poultry was suspected as the source by indirect assumption based on food reports from the patients, without firm microbiological or epidemiological evidence.

Some outbreaks have afflicted workers in poultry slaughterhouses, and such outbreaks are probably under-communicated and under-reported.

13.15.6.3 Unpasteurized milk

Unpasteurized milk has been the source of infection in four known outbreaks; one affected student at an agricultural school, two occurred among children or students after farm visits, and one was traced to private raw milk sale.

13.15.6.4 Bicycle races

Five outbreaks occurred among participants in bicycle races, including Birkebeinerrittet, Mjøsa Rundt og Garborgrittet, which were arranged in areas with grazing animals or runoff from fields fertilized with manure. Cohort studies showed that the most likely cause was splashing of contaminated mud and water from the bicycle wheels.

13.15.6.5 Other sources

In 1998, participants at a Nordic sports event became ill with campylobacteriosis after eating crab meat in shell. The source of infection was identified by a retrospective cohort study. At the production plant, the crabs were boiled and then cooled outdoors before being opened and processed, and during this procedure they were probably contaminated by seagulls.

In 2007, 21 guests became ill after eating whole-grilled lamb at a barbecue. The reason was probably inadequate heat treatment or cross-contamination during cooking, because the chef used the same knife and cutting board for raw and heat-treated meat.

Ten kindergarten children became infected during a farm visit in 2009. The same strain of *Campylobacter jejuni* was found in the children as among lambs on the farm.

In 2019, imported raw oyster was the most probable source of infection in an outbreak among guests at a hotel where 13 cases of illness were detected.

13.15.7 Risk factors and sources of infection for sporadic cases

Since the early 1990s, four case-control studies have been conducted in Norway to identify risk factors and sources of infection for sporadic, domestically acquired campylobacteriosis and determine the relative importance of these factors (Hauge, 1996; Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natås, et al., 2003; Kapperud, Skjerve, Bean, Ostroff, & Lassen, 1992; MacDonald, White, et al., 2015). The principles for design, conduct and analysis of case-control studies, and how to interpret the results, are explained in Appendix III.

Four independent risk factors were identified in most studies, despite using different models and study designs in different parts of the country (ranked by importance):

1. Drinking untreated water (at home, at holiday cabins, or during outdoor activities)
2. Preparing raw chicken in the kitchen at home, or eating undercooked chicken
3. Eating at a barbecue outdoors
4. Having contact with reservoir animals or their faeces (dogs, cats, poultry, sheep or cattle)

13.15.7.1 Poultry consumption

Most case-control studies of sporadic campylobacteriosis, including those conducted in Norway, have identified consumption or preparation of poultry as important risk factors. In Norway, poultry consumption has increased steadily over the past decades (Animalia 2020), and raw refrigerated products became increasingly available towards the end of the last century; in previous years, a majority of the products were frozen. While frozen storage has been shown to reduce the number of viable campylobacters (see 12.15), the bacteria survive throughout the shelf life of fresh poultry products stored at refrigeration temperature in modified or normal atmospheres, although the proportion of viable bacteria is reduced. Increased consumption of fresh poultry may have contributed to the rising incidence of campylobacteriosis in Norway during the 1990s (12.15). People may become infected not only from exposure through consumption of undercooked poultry meat, but more importantly through cross-contamination of other food items and utensils during preparation (MacDonald, White, et al., 2015), a suggestion which is supported by the case-control studies and by outbreak data (see above). However, despite the interventions implemented in the Action Plan against *Campylobacter* in Broiler Chickens, which have substantially reduced human exposure, the incidence of domestically acquired campylobacteriosis has not decreased correspondingly but shows a slightly increasing trend (12.15).

13.15.7.2 *Consumption of untreated water*

Waterborne infection rivals poultry consumption as the most common transmission route, in contrast to the situation in most other European countries. While drinking untreated water achieved high population attributable fractions (PAF) in the Norwegian case-control studies, similar investigations in other countries have emphasized the predominant importance of

poultry products. This is not unexpected, since the prevalence of *Campylobacter* in poultry is comparatively low in Norway (EFSA, 2010a). In addition, Norwegian drinking water supplies largely use surface water sources, many of which are vulnerable to contamination. Moreover, many Norwegians drink undisinfected water directly from a surface source during outdoor activities, such as hiking or camping, and from wells at holiday cabins, because they feel confident that the water is clean. In the nationwide case-control study conducted in 2010-2011, drinking untreated water from a river, stream, or lake in nature, and having a household water-supply serving fewer than 20 households, were both identified as independent risk factors (MacDonald, White, et al., 2015). The cumulative PAF attributed to these exposures was ca. 25%, compared to 30% for chicken consumption. It is likely, however, that the importance of untreated water was underestimated in that study, since drinking untreated water at cabins, cottages or summer homes with wells, or other single-unit water supply systems, was not included in the questionnaire. In the study from 1999-2000, this exposure was reported by 68 percent of the cases who had consumed untreated water, thus contributing substantially to the high PAF obtained in that study (37%, calculated retrospectively) (Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natås, et al., 2003).

The importance of drinking water as a source of infection is supported by the large outbreaks attributed to this source and by the results reported by Sandberg et al. (2002). They used a statistical model to identify factors associated with increased and decreased risk for domestically acquired campylobacteriosis in 2000-2001 and found that treated drinking water was protective at the county level.

The significance of the waterborne route of transmission is further underscored by identification of untreated drinking water as a major risk factor for *Campylobacter* colonisation in Norwegian broiler flocks. An epidemiological study of broiler flocks in south-eastern Norway in 1993, concluded that disinfection of drinking water was the most critical measure in preventing *Campylobacter* infection among broilers in that area (population attributable fraction, 53%) (Kapperud et al., 1993). More recently, Borck Høg et al. (2016) conducted a risk factor survey comprising *Campylobacter* data from more than 5200 Danish and Norwegian conventional broiler flocks. Unique to Norway, the risk of colonisation increased when the drinking water provided in the broiler house came from surface sources or private bore holes instead of municipal water supply.

The waterborne route of transmission may be the common underlying pathway linking infection in humans, poultry, other domestic animals, and wild-living birds (Kapperud et al., 1993). Accordingly, surface waters may consitute the major reservoir pool from which *Campylobacter* is distributed to smaller cycling pools that are exchanging rapidly between mammalian and avian host species and between those species and their immediate environment. Therefore, detection of the same *Campylobacter* subtypes in a particular animal species as in humans is not necessarily due to a direct route of transmission and does not justify definitive conclusions about the relative importance of that animal as a proximate source of infection. It may as well reflect transmission from a common source or, more likely, indirect transmission via a different animal, food, or water, which is inserted as an

intermediary vehicle in the complex infection network (Appendix III). Although chicken or another domestic animal may be the ultimate origin of the bacterium, the proximate source of infection can be drinking water or fresh produce, which is contaminated from the animal in question (see 13.15.7.7).

13.15.7.3 *Red meat consumption*

While several meat-producing mammals are frequent carriers of *Campylobacter* in Norway, consumption of red meat products has only once been identified as a risk factor for campylobacteriosis; eating undercooked pork was independently related to illness in the study conducted between 1999 and 2000 (Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natås, et al., 2003). During the slaughtering process, carcasses may be contaminated as a result of intestinal spillage, but contamination is less common than it is in poultry processing, the level of contamination is relatively low, and the number of viable campylobacters is reduced during storage of the carcasses (see 13.15.5.4). The fact that undercooked pork was associated with disease in one study, despite the predominance of *C. coli* in pigs and the comparatively low contamination during slaughter, may be explained by the high frequency with which pork is consumed (see 13.15.5.4). In the nationwide study, eating undercooked meat was an independent risk. However, the type of meat consumed was not specified, and it is probable that consumption of undercooked poultry meat contributed significantly to the observed risk.

13.15.7.4 Contact with reservoir animals

Living in a household with a dog or cat has been associated with illness in most Norwegian studies of campylobacteriosis. The daily intimate contact between humans and their pets represents a significant risk of transmission. Although the animal prevalence is fairly low, even a modest prevalence constitutes a substantial overall exposure since the populations of dogs and cats are very large, and the number of persons at risk is correspondingly high. In one study (Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natås, et al., 2003), occupational exposure to farm animals, including poultry, sheep and cattle, was identified as an independent risk factor. Animal contact has been identified as the source of infection in several outbreaks of campylobacteriosis (see 13.15.6).

13.15.7.5 Barbecuing

Barbecuing, which was identified as a risk factor in most studies, provides many opportunities for undercooking, recontamination of cooked foods, and cross-contamination of other food items. One outbreak has been attributed to food safety violation at a barbecue where whole-grilled lamb was served (see 13.15.6).

13.15.7.6 *Raw milk consumption*

In one study, drinking unpasteurized milk was identified by the univariable analysis but did not attain statistical significance in the regression models, probably due to the low number of

cases and controls who reported this exposure (Kapperud, Espeland, Wahl, Walde, Herikstad, Gustavsen, Tveit, Natås, et al., 2003). The high prevalence of *Campylobacter* in dairy cows offer the potential for substantial contamination of raw milk. Unpasteurized milk has been the source of infection in numerous outbreaks abroad; faecal contamination from dairy cows is the most likely cause. In Norway, sale of raw milk is strictly regulated, and consumption is low. Nevertheless, four outbreaks of this type have been described (see 13.15.6).

13.15.7.7 Consumption of fresh produce

Consumption of fresh vegetable, fruits, berries or herbs was not identified as a significant risk factor in any of the case-control studies. Likewise, surveys of fresh produce have detected *Campylobacter* in only one sample and such products have never been identified as the source of infection in outbreaks of campylobacteriosis (see 13.15.6). In conclusion, there is no evidence suggesting that fresh produce *per se* constitute an important source of infection with *Campylobacter* in Norway. However, fresh produce may become cross-contaminated from raw poultry products during cooking and such food safety violation probably account for a considerable proportion of cases attributed to poultry consumption.

13.15.8 Conclusions

In conclusion, the majority of infections with *Campylobacter* in Norway is caused by: (1) consumption untreated water, at home, at holiday cabins, or during outdoor activities, (2) food safety violation during preparation of raw meat, especially poultry, including undercooking and cross-contamination of other food and utensils, and (3) unsanitary contact with reservoir animals, dogs in particular.

The results indicate that modification of water consumption habits, kitchen hygiene practices, including during barbecues, and animal contact patterns, offer the potential for substantial reduction of the burden of campylobacteriosis in Norway. The results support initiatives which encourage improvement of municipal drinking water quality, maintenance and reinforcement of the Action Plan against *Campylobacter* in Broiler Chicken, and continued restrictions on the sale of unpasteurized milk.

13.15.9 Data gaps and research needs

To understand the complex epidemiology of campylobacteriosis and guide prevention, further studies are needed to:

- identify the failures in kitchen hygiene practices and animal contact patterns sufficient to cause *Campylobacter*-infection,
- explore the ecology of *Campylobacter* in freshwater ecosystems, and
- identify factors responsible for the increasing incidence, including the potential emergence of new genetic subtypes.

13.16 Salmonella

13.16.1 Literature

PubMed search: (Norway[Title/Abstract]) AND (salmonell*[Title/Abstract]) - 104 hits

The present source attribution is limited to the large number of zoonotic serovars within *Salmonella enterica* subspecies I (*enterica*) that give rise to salmonellosis. The non-zoonotic serovars Typhi and Paratyphi, the causative agents of typhoid fever and paratyphoid fever, two diseases that are substantially different from salmonellosis, are not included. They are not endemic in Norway, the number of reported cases is very low, and the large majority is acquired abroad (0-3 cases infected in Norway, annually) (www.msis.no). Secondary transmission from travellers infected in a foreign country may occasionally occur. Any food or water source contaminated by a shedder poses a risk of infection.

13.16.2 Surveillance and monitoring programmes

The surveillance programmes for **Salmonella** *in live animals, eggs and meat*

In 1995, Norway implemented surveillance programmes for *Salmonella* in live animals, eggs and meat. The purpose is to provide reliable documentation of the prevalence of *Salmonella* in livestock populations and their food products, and to form a basis for preventing increased occurrence of *Salmonella* in Norway. The surveillance covers live animals (pigs, poultry and cattle) and fresh meat (pigs and cattle). Reports from the current and previous years, including the number of samples examined, are available at https://www.vetinst.no/overvaking/salmonella

The programmes are approved by the EU Commission, allowing Norway to require additional guarantees regarding *Salmonella* when importing live animals, feed and food products of animal origin from the European Union.

The *Salmonella* surveillance of live animals entails examination of faecal samples (including boot swabs) from swine and poultry, and lymph node samples from cattle and swine (at least five ileocaecal lymph nodes from each animal) and dust samples from pullets and rearing flocks. For poultry, all breeder flocks and commercial production flocks are sampled. The surveillance of fresh meat includes examination of swab samples from cattle and swine carcasses, and samples of red meat scraping from slaughterhouses and cold stores (Heier, Hopp, Mork, & Bergsjø, 2019).

The results show that the Norwegian cattle, swine and poultry populations are only sporadically infected with *Salmonella*. The estimated prevalence has been below 0.5% in the examined populations for all years since the surveillance programmes were commenced. In 2019, the estimated prevalence was below 0.1% in all populations surveyed. Likewise, the prevalence in fresh meat was lower than 0.1% (Heier et al., 2019).

13.16.3 RASFF notifications

As of 12 November 2020, the Rapid Alert System for Food and Feed (RASFF) had received 6715 notifications on food contaminated with *Salmonella* (RASFF, 2020b). In all, 355 notifications affected Norway. These notifications comprise all consignments distributed to Norway, whether notified by Norway or another country, and include consignments not distributed on the market because import was not authorised, the consignment was re-dispatched, returned to consignor, or for other reasons. Also included are four consignments originating from Norway. Norway issued 307 notifications (Table 13-9).

Table 13-9. Notifications on food contaminated with Salmonella, RASFF 1982-2020 [1]

Food category	No. of notifications		
	Total	Affecting Norway [2]	Issued by Norway
Poultry meat and poultry meat products	2557	48	45
Meat and meat products (other than poultry)	1119	147	
Nuts, nut products and seeds	800	20	
Herbs and spices	663	67	59
Fruits and vegetables	596	23	17
Eggs and egg products	158	5	3
Fish and fish products	131	10	9
Bivalve molluscs and products thereof	116		
Molluscs and products thereof	109	2	2
Crustaceans and products thereof	105	10	10
Milk and milk products	92	6	3
Cocoa and cocoa preparations, coffee and tea	44	2	1
Dietetic foods, food supplements, fortified foods	39	2	1
Cereals and bakery products	31		
Confectionary	30	2	1
Prepared dishes and snacks	30	4	3
Cephalopods and products thereof	24		
Soups, broths, sauces and condiments	9	1	
Gastropods (snails)	7		
Wild caught fish and products thereof	7	1	1
Food additives and flavourings	5	2	1
Farmed crustaceans and products thereof	4		
Fats and oils	4	1	1
Ices and desserts	3		
Natural mineral water	1		
Animal nutrition [4]	1		
Other food products / mixed	30	2	
Total	6715	355	307

[1] The RASFF Portal was accessed 12 November 2020.

[2] These notifications comprise all consignments distributed to Norway, whether notified by Norway or another country, and include consignments not distributed on the market. Also included are four consignments originating from Norway.

[3] Soybean meal incorrectly flagged as food.

Norway was flagged as the country of origin in four notifications:

- 2012: Pork meat and pork products manufactured in Norway with raw material from Belgium
- 2012: Smoked salmon from Greece with raw material from Norway via the Netherlands
- 2009: Reindeer meat ("reinskav") manufactured in Sweden with raw material from Norway
- 2006: Cured meat sausage manufactured in Norway (*S*. Kedougou in salami)

13.16.4 Surveys – prevalence studies

EFSA baseline survey of broiler batches and carcasses, 2008

In order to establish baseline and comparable values for all Member States, a European Union-wide survey was carried out at slaughterhouse level to determine the prevalence of *Campylobacter* in broiler batches and of *Campylobacter* and *Salmonella* on broiler carcasses (EFSA, 2010a). Throughout 2008, batches and carcasses were randomly selected from the broiler slaughterhouses within each Member State, plus Norway and Switzerland. *Salmonella* was detected on broiler carcasses in all participating countries with the exception of Denmark, Estonia, Finland and Luxembourg, and of the non-member state Norway. The EU prevalence of *Salmonella*-positive broiler carcasses was 15.6%. Member state prevalence varied widely, from a minimum of 0.0% to 26.6%. However, Hungary had an exceptionally high prevalence of 85.6%.

EFSA baseline survey on the prevalence of Salmonella *in holdings with breeding pigs, 2008*

This European Union-wide *Salmonella* baseline survey was conducted in 2008 in holdings with breeding pigs (EFSA, 2009). A total of 1,609 holdings housing and selling mainly breeding pigs (breeding holdings) and 3,508 holdings housing breeding pigs and selling mainly pigs for fattening or slaughter (production holdings) from 24 European Union Member States, plus Switzerland and Norway, were randomly selected and included in the survey. Sampling took place between January 2008 and December 2008. The European Union prevalence of *Salmonella*-positive breeding holdings was 28.7%, and prevalence varied from 0% to 64.0% among Member States. The European Union prevalence of *Salmonella*-positive production holdings was 33.3%, while the Member States' prevalence varied from 0% to 55.7%. Norway did not detect *Salmonella* in any of the holdings surveyed.

EFSA baseline study on the prevalence of Salmonella *in holdings of laying hen flocks, 2004-2005*

A baseline study was carried out to obtain comparable information on the prevalence of *Salmonella* in laying hen flocks in the EU Member States (EFSA, 2007). Norway also participated in the study on a voluntary basis. The sampling of the holdings took place between October 2004 and September 2005. A total of 5,310 holdings with validated results were included in the study analyses. *Salmonella* was detected in 30.8% of the laying hen holdings in the European Union; the prevalence ranged from 0% to 79.5%. Luxembourg, Sweden and Norway did not detect any *Salmonella* positive samples.

Surveys conducted by the Norwegian Food Safety Authority (NFSA)

Following several discoveries of *Salmonella* and *E. coli* in random samples of fresh herbs and leafy greens imported from South-East Asia in 2005-2006, the Norwegian Food Safety Authority directed a survey in early 2007 in order to investigate the occurrence of *Salmonella* and *Campylobacter* in fresh herbs and leafy green vegetables originating from Thailand and Vietnam (NFSA, 2008; VKM, 2008a). Of the 159 samples examined, none were positive for *Campylobacter*, while *Salmonella* was detected in 15%.

In 2013, the Norwegian Food Safety Authority carried out an inspection project to examine the occurrence of pathogens in fresh, imported vegetables and herbs (NFSA, 2014). A total of 30 importers were inspected and 154 consignments were sampled. *Salmonella*, *Campylobacter* or *E. coli* were detected in 41 lots, 93% of which originated from countries outside the EU. *Salmonella* was isolated from four consignments, from Laos (basil), Sri Lanka (spinach), Thailand (rice paddy herb), and Vietnam (horseradish). *Campylobacter* was only detected in one batch, a sample of dill from Italy.

During 2015 and 2016, the Norwegian Food Safety Authority performed a survey on imported fresh and frozen strawberries, raspberries, and blueberries (NFSA, 2017). The samples were analysed for selected bacteria, viruses and parasites. Of the 228 batches of berries examined, positive results were obtained in three batches (1.3 %). *E. coli* was detected in one batch of fresh strawberries from Spain and in one batch of blueberries from the Netherlands. *Giardia* was detected in one batch of fresh strawberries from Spain. *Salmonella*, *Cryptosporidium*, hepatitis A virus, or norovirus were not detected in any of the samples.

During 2017-2019, the Norwegian Food Safety Authority performed a survey on pathogens in green salads and fresh culinary herbs on the Norwegian market (NFSA, 2020b). A total of 426 samples of salad and 154 samples of fresh culinary herbs were analysed for *E. coli* as a hygiene indicator, and for the pathogenic microbes *Salmonella*, *Cryptosporidium*, norovirus and hepatitis A virus (HAV). Not all samples were analysed for *Cryptosporidium*, norovirus and HAV, however. *Salmonella*, *Cryptosporidium*, norovirus or HAV were not detected in any of the samples. Of the 575 samples analysed for *E. coli,* low numbers (<100 cfu/g) were detected in 57 samples while *E. coli* ≥100 cfu/g was detected in 36 samples. 13 of them had such high numbers of *E. coli* that the products were withdrawn from the market; 10 of these were imported culinary herbs from South-East Asia. The Norwegian Food Safety Authority recommends such products to be heat treated before consumption.

Other surveys

As part of a larger survey of microbial contamination of fruits and vegetables in Norway, four different sprouted seed products were analysed for bacterial and parasitic contaminants (n = 300 for bacterial analyses and from 17 to 171 for parasite analyses, depending on parasite) (L. J. Robertson et al., 2002). *E. coli* O157, *Salmonella, L. monocytogenes*, *Cyclospora* oocysts, *Ascaris* eggs and other helminth parasites were not detected in any of the sprout samples. Sprout irrigation water was also analysed for microbial contaminants. *E. coli* O157

and *L. monocytogenes* were not detected. Thermotolerant coliform bacteria (TCB) were isolated from approximately 40% of the water samples. *Salmonella* Reading was isolated from three samples of spent irrigation water on three consecutive days.

A total of 890 samples of fresh produce obtained from Norwegian markets were examined in order to assess the bacteriological quality of the products and their potential public health risk (Johannessen, Loncarevic, & Kruse, 2002)h. The samples comprised lettuce, pre-cut salads, growing herbs, parsley and dill, mushrooms and strawberries. The samples were analysed for the presence TCB, *Escherichia coli* O157, *Salmonella*, *Listeria monocytogenes*, *Staphylococcus* spp., and *Yersinia enterocolitica*. Neither *Salmonella* nor *E. coli* O157 were isolated.

13.16.5 Reservoir

The prevalence of *Salmonella* in Norwegian livestock is exceptionally low. The results from the Surveillance Programmes directed by the Norwegian Food Safety Authority show that less than 0.1% of several thousand samples examined annually contain *Salmonella* (Heier et al., 2019).

Nevertheless, *Salmonella* is sporadically detected in domestic animals and meat products. *S*. Typhimurium is the most common serovar isolated, often belonging to the same strains asfound among wild small birds (see below). Each time, the Norwegian Food Safety Authority or the producers have implemented measures to prevent further dissemination of the infection. Surveillance at the Norwegian Institute of Public Health shows that human illnesses have rarely been linked to such findings, with the exception of persons in close contact with the infected animals (Lindstedt et al., 2007; Lindstedt, Vardund, Aas, & Kapperud, 2004).

There are two known indigenous reservoirs for *Salmonella* in Norway that are significant for human infection: in wild-living birds, especially small passerines, and hedgehogs (Handeland et al., 2002; Heir et al., 2002; Kapperud, Stenwig, & Lassen, 1998; MacDonald et al., 2018; Refsum, Handeland, Baggesen, Holstad, & Kapperud, 2002; Refsum, Heir, Kapperud, Vardund, & Holstad, 2002). In both animal groups, there is a considerable prevalence of *S.* Typhimurium - the only serovar in subspecies I that is established at an endemic and enzootic level in Norway. Since bacteria isolated from each of these reservoirs are characterized by distinctive antigen patterns and DNA profiles, with clear host preferences, it is possible to estimate their relative importance by comparing the distribution of DNA profiles among bacterial isolates from animals and humans (Handeland et al., 2002; Heir et al., 2002; Kapperud, Stenwig, et al., 1998; Lindstedt et al., 2007; Lindstedt et al., 2004; MacDonald et al., 2018; Refsum, Heir, et al., 2002).

From 2004 through 2015, 34.2% (n = 354) of all *S*. Typhimurium cases acquired in Norway had a DNA profile linked to domestic reservoirs (MacDonald et al. 2018). Of these, 13.6% (n = 141) cases had the hedgehog DNA profiles and 20.6% (n = 213) cases exhibited DNA profiles associated with the avian reservoir.

13.16.5.1 The reservoir among small passerines

S. Typhimurium from the avian reservoir is responsible for between 20 and 50% annually of all human cases infected in Norway with this serovar. Case-patients appear nationwide, being detected in all counties. One striking feature is the predominance of infants and young children among the patients (Kapperud, Stenwig, et al., 1998; MacDonald et al., 2018). There is a distinct seasonality with accumulation of cases between the months January through April, when many people feed birds in their yards and gardens. At the same time of year, the endemic strains are regularly encountered as the aetiologic agent of fatal salmonellosis among wild passerine birds, suggesting an epidemiologic link between the avian and human cases (Refsum, 2003; Refsum, Heir, et al., 2002; Refsum, Vikøren, Handeland, Kapperud, & Holstad, 2003). The strains are sporadically recovered from other animals, including livestock, cats, dogs, pigeons, birds of prey, other bird species, and foxes (Handeland et al., 2008; Refsum, 2003). In 1987, a strain probably derived from this reservoir caused an extensive outbreak of salmonellosis in which contaminated chocolate bars produced in Norway were the sources of infection (Table 13-10).

13.16.5.2 The hedgehog reservoir

S. Typhimurium with the discrete phenotypic and genotypic characteristics associated with the hedgehog reservoir are isolated from 10-20% of all domestic human cases each year (Handeland et al., 2002; MacDonald et al., 2018; Refsum, 2003). The main incidence is in western Norway, where the disease afflicts all age groups, usually in the autumn months. These strains have caused several local outbreaks (Table 13-10).

13.16.5.3 Seagulls

Gulls are frequent carriers of *Salmonella*. A wide range of serovars have been detected (Kapperud & Rosef, 1983; Refsum, Heir, et al., 2002; Willumsen & Hole, 1987), with Typhimurium being the predominant serovar (28% of the isolates (Refsum, 2003). However, the genotypes found in gulls are different from those among passerines, and are rarely detected in human patients, suggesting that direct or indirect transmission from seagulls is unusual (Refsum, 2003; Refsum, Handeland, et al., 2002). Nevertheless, in 1999, an outbreak of *S.* Typhimurium infection occurred on Herøy in Møre og Romsdal County, where the source of infection was drinking water probably contaminated by seagulls (Refsum 2003).

13.16.5.4 Salmonella subspecies IIIb (diarizonae)

While *Salmonella enterica* subspecies I (*enterica*) has not been established in Norwegian livestock populations, a serovar from subspecies IIIb (*diarizonae*) is detected with fairly high prevalence from sheep herds in certain regions (Alvseike, 2001; Alvseike et al., 2004). Surveillance at the Norwegian Institute of Public Health shows that the bacterium only occasionally has caused disease in humans, mainly in persons with compromised immune

defence. The bacterium is an opportunist without significant human medical importance and is not considered a public health threat (VKM, 2008b).

13.16.5.5 Animal feed

Due to extensive monitoring and limited imports, the feed for Norwegian livestock has been virtually free of *Salmonella*. However, some serovar are sometimes detected in environmental samples from feed mills, including from gulls, notably fish feed plants (Tore Lunestad et al., 2007; VKM, 2006). However, the risk of *Salmonella* in fish feed being transmitted to the consumer via fish products is considered negligible (Nesse et al., 2005).

Table 13-10. Selected major outbreaks of salmonellosis acquired in Norway, NIPH 1982-2020

Year	Verified cases [1]	Serovar [2]	Source of infection
1982	126	Oranienburg	Black pepper, imported
1987	349	Typhimurium	Chocolate bars, produced in Norway
1987	14	Saintpaul	Almonds, imported
1989	60	Enteritidis	Oil-drilling platform; poultry, imported
1993	29	Enteritidis	Moussaka, hospital [3]
1996	28	Typhimurium	Hedgehogs
1997	8	Minnesota	Slimming product, imported
1999	54	Typhimurium	Drinking water
2000	30	Typhimurium	Hedgehogs
2001	23	Enteritidis	Cruise ship; eggs, imported
2001	40	Livingstone	Processed fish product, imported
2001	31	Typhimurium DT104	Halawa, imported
2002	44	Typhimurium	Hedgehogs
2004	78	Infantis	Cold-food, hospital [3]
2004	8	Uganda	Palestinian food, private import
2004	20	Thompson	Ruccola lettuce imported, multi-national
2004	15	Enteritidis	Chocolate cake, homemade [3]
2005	5	Typhimurium DT104	Minced meat, imported beef
2005	3	Typhimurium & Infantis	Salami, imported
2006	5	Typhimurium	Restaurant [3]
2006	52	Kedougou	Salami, produced in Norway
2007	19	Weltevreden & Senftenberg	Alfalfa sprouts, imported seeds
2007	38	Typhimurium	Catering food, imported
2007	4	Typhimurium	Cured sausage, imported, cruise ship
2007	10	Java [4]	Baby spinach, imported
2008	8	Java [4]	Ferry Oslo - Kiel
2008	10	Typhimurium	Minced meat with pork, Scandinavia
2010	20	Napoli & Poona	Unknown
2012	13	Mikawashima	Unknown
2013	26	Coeln	Mixed bagged salad, imported
2017	4	Agona	Unknown
2017	21	Typhimurium	Airport restaurant, Oslo [3]
2017-20	24	Enteritidis	Egg products, imported, multi-national
2018-19	56	Abgeni	Mixed dried fruits, imported
2021	22	Enteritidis	Minced meat, imported beef

[1] Laboratory verified cases. The actual number of cases is usually many times higher.

[2] Excluding Typhi, Paratyphi A, and Paratyphi B *sensu stricto*.

[3] Contamination from infected food handler suspected.

[4] Paratyphi B variant Java (previously named *Salmonella* Java).

In addition to the outbreaks presented in Table 13-10, there has been a large number of outbreaks among Norwegian tourists infected abroad. Also, several outbreaks have been

described in which foods served in businesses or institutions were contaminated by a food handler who had been abroad. The outbreak in 2001 caused by *S.* Infantis, and which occurred at a hospital in southern Norway, is probably an example of this. Previously, there were recurrent outbreaks of varying size on the oil installations in the North Sea and on the ferries between Norway and the continent. Most of those outbreaks were related to imported poultry products contaminated with *S*. Enteritidis. One example is the outbreak in 1989 in which employees at an offshore oil field were afflicted.

13.16.6 Risk factors and sources of infection for sporadic cases

Since the early 1990s, three case-control studies have been conducted in Norway to identify risk factors and sources of infection for sporadic, domestically acquired salmonellosis and determine the relative importance of these factors (Kapperud, Lassen, & Hasseltvedt, 1998; Kapperud, Stenwig, et al., 1998; MacDonald et al., 2018). The principles for design, conduct and analysis of case-control studies, and how to interpret the results, are explained in Appendix III.

1990-92: Risk factors associated with S. Typhimurium from the avian reservoir

In 1990-1992, a nationwide case-control study was conducted to investigate risk factors for domestically acquired infection with *S.* Typhimurium strains showing characteristics compatible with the passerine bird reservoir (Kapperud, Stenwig, et al., 1998). The following independent, preventable risk factors were identified in logistic regression analysis (estimates of attributable fractions are given in parentheses; figures indicate the relative importance of the factors):

- Using undisinfected drinking water (50%)
- Having contact with small birds or their droppings (21%)
- Eating snow, sand or dirt (21%)

Cases were also more likely than controls to report having antecedent or concurrent medical disorders.

The results documented that winter feeding of birds as well as activities linked to bird-feeding, including cleaning bird tables, removing bird droppings, handling dead birds, tending sick birds, and eating snow, sand or dirt under bird feeders, were significantly related to increased risk of human infection with strains of *S.* Typhimurium associated with the avian reservoir.

Wild birds may function as effective spreaders of pathogens by faecal contamination of the environment, including surface water. Hence, it is not surprising that using undisinfected drinking water was identified as an independent risk factor. Cases were more likely than controls to use untreated water from a small-scale private water supply in their primary residence, including from a well, borehole, or private waterwork serving few recipients. The high attributable fraction obtained is particularly striking considering that the cases and their controls were matched by geographic area, an approach which is prone to underestimate the

importance of drinking water, because people living in the same area are likely to have the same drinking water supply or to receive water from similar sources. The result is in accordance with case-control studies of campylobacteriosis and yersiniosis, in which untreated water figured as a prominent risk factor and underscores the importance of drinking water as a source of infection in Norway (Kapperud et al., 1992; Ostroff et al., 1994).

1993-1994: Risk factors associated with all non-typhoid serovars

In 1993-1994, a second nationwide case-control study was carried out, in which patients infected in Norway with any non-typhoid or non-paratyphoid serovar were enrolled (Kapperud, Lassen, et al., 1998). The study failed to demonstrate any statistically significant association between salmonellosis and consumption of domestically produced red meat, poultry or eggs. The only factor which remained independently associated with an increased risk in conditional logistic regression analysis, was consumption of poultry purchased abroad during day trips to neighbouring countries ("grensehandel"). In univariable analysis, the highest odds ratio was obtained for chicken bought in Denmark. A separate multivariable analysis of *S*. Typhimurium infections incriminated food from catering establishments and foreign travel among household members, in addition to poultry imported through cross-border trade. For other serovars, the numbers of cases were too low to enable meaningful analyses.

Many Norwegians visit other Scandinavian countries on day trips to buy cheap meat and other consumables. In 1990, imports of meat via such trade, accounted for 2.1% of wholesale consumption. In 2019, it had increased to 5.3%. For estimated real consumption, this category accounted for 2.5% of total meat consumption in 1990 and had increased to 6.6% in 2019 (Animalia, 2020). The finding parallels the results of a previous case-control study of sporadic *Campylobacter* infections in Norway, which found an association with poultry bought in Denmark or Sweden (Kapperud et al., 1992). However, the attributable fraction implies that cross-border trade would only account for a small part (10%) of the *Salmonella* problem. The majority of the cases may probably be explained by a variety of factors, the individual effects of which are too small to precipitate statistically significant risks, or by factors not included in the study questionnaire.

2010-2012: The largest nationwide study - all non-typhoid serovars

The largest case-control study, comprising 389 domestically acquired cases and 1500 control persons from all counties, was conducted in 2010-2012 (MacDonald et al., 2018). Eating snow, dirt, or sand or playing in a sandbox was the only exposure significantly associated with illness in the multivariable model. When stratified by serovar, this exposure was significant for Typhimurium but not for the other serovars. The result supports that indirect or environmental exposure remain sources of infection for salmonellosis in Norway, particularly for children. Neither direct contact with wild birds, hedgehogs, nor reptiles was associated with illness, but less than 1% of cases and controls reported such exposure.

In agreement with the preceding investigations, the study failed to demonstrate any statistically significant association between human salmonellosis and the consumption of domestically produced red meat, poultry or eggs. The results reinforce previous findings and indicate that the efforts invested to combat *Salmonella* in Norway during the past century have been successful. This conclusion is substantiated by surveillance data that have consistently documented an exceptionally low prevalence of *Salmonella* in Norwegian livestock and domestically produced meat (13.16.2 and 13.16.4). In contrast to many other European countries, close to 95% of the meat products sold at retail outlets are domestically produced (Animalia, 2020). Altogether, these factors, low domestic prevalence and limited import, are the major determinants accounting for the low incidence of salmonellosis acquired in Norway.

The lack of association with untreated water for all *Salmonella* serovars combined is in accordance with the suggestion that most serovars have so far failed to establish stable reservoirs in Norway, except certain subtypes within Typhimurium attributed to small birds and hedgehogs (13.16.5). However, no significant association with untreated drinking water was detected when Typhimurium was examined separately, in contrast to the results obtained in the early 1990s that incriminated small-scale private water supply as a prominent risk. One factor contributing to this apparent discrepancy is that the number of Norwegians who receive untreated water from such sources has decreased considerably since the 1990s.

Unlike the results obtained in the 1993-1994 study (Kapperud, Lassen, et al., 1998), consumption of poultry purchased abroad during day trips to Denmark or Sweden was not associated with salmonellosis. This may not be unexpected, since the prevalence of *Salmonella* in Danish poultry has been substantially reduced since the previous study (EFSA 2010). Accordingly, the EU Commission has granted Denmark similar status regarding *Salmonella* in poultry as Sweden, Finland, Norway, and Iceland.

13.16.7 Conclusions

Norway continues to have a comparatively low incidence of salmonellosis. Although the epidemiology of human salmonellosis in Norway shows close similarities to trends noted elsewhere in the industrialized world, several distinguishing features are evident. The high proportion of cases related to foreign travel, the relatively low level of indigenous infections, the low prevalence of the organism in the domestic food chain, and the lack of association with consumption of domestically produced meat and eggs, are all features which differ from the situation in most European countries (cited from MacDonald et al. 2018). There is evidence that indirect contact with domestic reservoirs, small birds and hedgehogs, through environmental exposure including drinking water, remains a source of infection with *S*. Typhimurium, particularly for children.

In the majority of outbreaks, the source of infection has been an imported food, including a wide range of food categories (Table 13-10). The progressive trend towards globalisation of the trade in food, feed and live animals represents a contemporary challenge to Norway's

favourable *Salmonella* status and predicates the need for renewed alertness and appropriate intersectoral actions.

13.16.8 Data gaps and research needs

Further studies are needed to:

- identify sources of infections, risk factors and any reservoirs for *Salmonella* serovars other than Typhimurium acquired in Norway, notably Enteritidis,
- identify factors responsible for the decreasing incidence of indigenous *S.* Typhimurium,
- calculate of the burden of disease.

13.17 *Shigella* spp.

13.17.1 Literature

PubMed search: (Norway[Title/Abstract]) AND (Shigell*[Title/Abstract]) – 22 results

13.17.2 Surveillance data (animals and food)

Surveillance and monitoring programmes are lacking for *Shigella.*

13.17.3 RASFF notifications

Only a few alerts (year, numbers in parenthesis) for *Shigella* were registered in the Rapid Alert System for Food and Feed (RASFF):

- *Cheese*: France (2002, 1)
- Cereals and dry legumes: Thailand (2007, 1)
- *Fresh pods, legumes and grain*: Denmark (2009, 1) and Kenya (2009, 1)
- *Fresh herbs*: Israel (2011, 1) and Netherlands (2011, 1)

13.17.4 Occurrence in reservoir animals (if relevant)

Humans are the only reservoir.

13.17.5 Occurrence in food or water

Faecal-oral contact or via contaminated water or food, such as imported salads and herbs, are the main routes of infection. Food may be contaminated through handling by infectious persons or by being in contact with contaminated water.

The bacteria usually survive no longer than a few days in food, but in high-fat products and water, survival has been demonstrated for up to 100 days. The bacteria can multiply at temperatures above 6 ° C in some foods.

13.17.6 Sources of infection in outbreaks

2011: The same strain of *S. sonnei* was detected in a total of 46 people who had eaten fresh basil imported from Israel (Guzman-Herrador et al., 2013). Also in 2011: Epidemiological studies showed that those who had eaten from a salad buffet became ill. However, it was not possible to identify which ingredient in the salad buffet was contaminated.

2009: Sugar snap peas imported from Kenya (Heier et al., 2009).

1994: Epidemiological studies showed that iceberg lettuce imported from Spain was the likely source of a European outbreak, including Norway (Kapperud et al., 1995).

13.17.7 Sources of infection for sporadic cases

- Faeces from human shedders
- Food or water contaminated by human shedders, including unwashed raw vegetables, herbs, sprouts, fruits and berries

13.17.8 Relative importance of different food sources

Imported foods, such as imported salads and herbs, seem to have the highest relevance for consumers in Norway.

13.17.9 Risk factor identification

The general risk factors (the same ones as for ETEC, EIEC, tEPEC) (Kapperud, 2018) are:

- Direct infection by faeces from human shedders
- Consumption of food or water contaminated from human shedders Including unwashed raw vegetables, herbs, sprouts, fruits and berries
- Travel to endemic areas

Based on the information in the sections above the following risk factors might be added: Eating imported sugar snap peas, imported fresh basil, and imported iceberg lettuce.

13.17.10 Data gaps and research needs

Shigella spp. have a human reservoir and are often connected to raw unwashed vegetables, herbs, sprouts, fruits and berries produced abroad. Accordingly, the effectiveness of import control of such products is crucial regarding the extent to which these agents represent a risk in foods in Norway.

13.18 *Vibrio* spp.

13.18.1 Literature

Search string used for search in Pubmed:

(((Vibrio sp - non cholerae,) AND (Clinical disease,)) AND (Source attribution)) AND (Food) 0 results

((Vibrio sp - non cholerae,) AND (Clinical disease,)) AND (Source attribution)) 0 results

(Vibrio sp - non cholerae,) AND (Clinical disease,). 4 results

13.18.2 Surveillance and monitoring programmes

13.18.2.1 Status reports

Control programmes aimed at investigating oysters and other seafood for *Vibrio* spp. are being established in Norway (NIFES, 2020). Reporting of *Vibrio* spp. infections other than *V. cholerae* in humans was only made compulsory in Norway in June 2019 (MSIS, 2021). Thus, the availability of official information on this topic is limited.

13.18.3 Reservoir of *Vibrio* spp. in Scandinavian coastal areas

More than 140 different *Vibrio* species have been detected, and several species have been detected both in shellfish and fish. However, very few *Vibrio* species (N=12) have been shown to result in disease in humans (McLaughlin et al., 2005; Newton et al., 2012; Newton et al., 2014; Slayton et al., 2014). Control systems for the detection of *Vibrio* in seawater and in seafood will soon be established in Norway (NIFES, 2020).

ECDC has supported a systematic survey of seawater for the presence of *Vibrio* spp in the Baltic Sea since 2018 (Levy, 2018). As human pathogenic *Vibrio* spp are found in variable concentrations in raw oysters (McLaughlin et al., 2005; Newton et al., 2012; Newton et al., 2014; Slayton et al., 2014) investigations into possible consequences of increased seawater temperatures noted in Northern Europe (Levy, 2018; Martinez-Urtaza et al., 2013) are of relevance.

As for the influence of various pathogens on the cultivation of shellfish, EFSA has been concerned about the importance of the influence of various pathogens including *Vibrio* spp. on the mortality of oysters in cultivation. However, the *Vibrio* spp. in focus do not belong to the subset that cause disease in humans (CDC, 2019a).

13.18.4 Sources of foodborne infection in outbreaks

In general bathing and swimming with an exposed open wound in *Vibrio*-contaminated seawater is the usual port of *Vibrio* infection in a Norwegian setting (MSIS, 2021), particularly affecting individuals suffering from a downregulated immune system (McLaughlin et al., 2005; Newton et al., 2012; Newton et al., 2014; Slayton et al., 2014).

Regarding, eating contaminated shellfish, ingestion of contaminated oysters is the most common route of infection for food-based infection with *Vibrio* spp. (Bisharat et al., 1999; Daniels et al., 2000). Several reports are available from areas where the seawater temperature is higher than in Scandinavia (Banatvala et al., 1997; Desenclos, Klontz, Wolfe, & Hoecheri, 1991; Klonz et al., 1988). *V. vulnificus* is responsible for over 95% of seafood-related deaths in the United States and carries the highest fatality rate of any food-borne pathogen (14). No scientific report is available from a Norwegian setting, except comments on reported infections (MSIS, 2021).

Other sources

Vibrio spp. have also been detected in fish, particularly on the gills, as part of the local flora on fish exposed to seawater with a high content of *Vibrio* spp.

13.18.5 Risk factors

The following three risk factors could be identified from the studies/reports listed above (ranked by importance):

- Eating raw oysters
- Preparing raw shellfish in the kitchen
- Having contact with shellfish or fish in particular in areas where the seawater is brackish and increased temperature.

13.18.6 Data gaps and research needs

To understand the complex epidemiology of *Vibrio* infections in a Scandinavian setting and to enable guidance in prevention, further studies are needed into:

The ecology of *Vibrio* spp. in salt/brackish water ecosystems in Scandinavia/Norway.

The identification of possible failures in hygiene practices and contact patterns sufficient to cause transmission of *Vibrio* spp. infections in a Scandinavian (or, better, Norwegian) setting.

Identification of factors responsible for the increasing incidence of *Vibrio* cases in Scandinavia.

The potential emergence of new genetic subtypes among the prevalent species of *Vibrio* spp. that might provoke foodborne clinical illness in Norway.

13.19 Yersinia enterocolitica

13.19.1 Literature

PubMed search: Search: (Norway[Title/Abstract]) AND (Yersin*[Title/Abstract]) – 55 results

13.19.2 Surveillance data (animals and foods) and monitoring programmes

Regular Norwegian surveillance and monitoring programmes are lacking for *Y. enterocolitica.* 152 samples of minced pork meat were analysed in 2019.

13.19.3 RASFF notifications

Only a few alerts (year, numbers in parenthesis) for *Yersinia* were registered in the Rapid Alert System for Food and Feed (RASFF):

Imported meat

- Red meat: Germany (2004, 1), UK (2008, 1) and Spain (2013, 1)
- Poultry: Germany (2011, 1)

Imported fish product

- Thailand (2006, 1)

Imported vegetables and herbs

- Leafy greens: Italy (2011, 1; 2019, 1) and UK (2019, 1)

13.19.4 Occurrence in reservoir animals

13.19.4.1 Pigs and pork

Y. enterocolitica is one of a few zoonotic bacteria that have a stable reservoir within the domestic animal population in Norway. The pig is the only animal consumed by man, that regularly harbours the pathogenic serovars O:3 and O:9. In addition to being faecal commensals, these serovars inhabit the oral cavity of swine, especially the tongue and tonsils. As a result of present slaughter techniques, they are also encountered as surface contaminants on freshly slaughtered pig carcasses (Nesbakken, Nerbrink, Røtterud, & Borch, 1994).

In Norway, a decline in human cases of yersiniosis has been recorded since the middle of the 1990s (msis.no). This decline has been attributed to implementation of improved

slaughtering methods, including enclosure of the anus into a plastic bag after rectum-loosening (Nesbakken, 2015).

Because *Y. enterocolitica* is able to propagate at refrigeration temperature, avoidance of cross-contamination in the kitchen and of heat-treated products is particularly necessary.

13.19.5 Pets

Pets may occasionally be faecal carriers, and raw pork might be an important source of *Y. enterocolitica* O:3 infections in dogs and cats. These animals might be vehicles for infections in humans (Fredriksson-Ahomaa, Korte, & Korkeala, 2001) but have not been identified as risk factors in case-control studies (Ostroff et al., 1994; Tauxe et al., 1987).

13.19.6 Occurrence in food and water

13.19.6.1 Pork

Pathogenic *Y. enterocolitica* have only infrequently been recovered from pork products at the stage of retail sale. This might be explained by the lack of appropriate selective methodology for isolation of pathogenic strains. Studies using DNA-based detection methods, including colony hybridization (Nesbakken, Kapperud, Dommarsnes, Skurnik, & Hornes, 1991) and PCR (Johannessen, Kapperud, & Kruse, 2000) have indicated that such strains are more common in pork products than previously documented in Norway.

13.19.6.2 Leafy greens

In recent years imported leafy greens have played a major role in outbreaks in Norway. The three largest outbreaks have potentially been caused by mixed salads from Italy.

13.19.6.3 Drinking water

Yersinia spp. in three surface water sources in Norway which represented different levels of pollution and eutrophication, have been investigated. Samples were collected every fortnight during a 14-month period. In addition, samples from 100 private wells were examined for campylobacters only. *Yersinia* spp. were isolated from four (4.2%) of the samples. All four *Yersinia* isolates were non-pathogenic variants (Brennhovd et al., 1992).

13.19.7 Sources of infection in outbreaks

13.19.7.1 Leafy greens

Y. enterocolitica has been a cause of several food and waterborne outbreaks recorded in Norway. Since 2005, 9 outbreaks with around 202 persons recorded ill have been reported to VESUV. In 2018, 2014 and 2011 outbreaks caused by *Y. enterocolitica* serotype O:9 in

imported mixed salad were reported (MacDonald et al., 2011). A total of 133 patients were confirmed in the 2014 outbreak, and 117 of the infected persons were associated with four different military camps.

13.19.7.2 Pork

Even smaller outbreaks, in 2013 and 2006 from brawn made from pork were caused by serotype O:9 (Grahek-Ogden et al., 2007). Brawn made from pork was also involved in small 2006 and 2000 outbreaks caused by serotype O:3.

13.19.8 Sources of infection for sporadic cases

13.19.8.1 Pork

Epidemiological investigations have supported the role of pork as a vehicle for *Y. enterocolitica*. Case-control studies of sporadic cases conducted in Belgium (Tauxe et al., 1987) and Norway (Ostroff et al., 1994) have identified consumption of pork as an important risk factor for infection.

13.19.8.2 Drinking water

Consumption of untreated drinking water was also identified as a risk factor for infection with serovar O:3 in a case-control study conducted in Norway (Ostroff et al., 1994).

13.19.9 Relative importance of different food sources

In recent years imported mixed salads/leafy greens from Italy have played the most important role in Norwegian foodborne outbreaks caused by *Y. enterocolitica* while pork probably still plays a dominant role in sporadic cases.

13.19.10 Risk factor identification

- Consumption of raw, rare or undercooked pork products
- Food safety violation when preparing raw pork (cross contamination)
- Eating other foods contaminated from porcine or human shedders
- Drinking untreated water
- Unsanitary contact with pigs
- Consumption of mixed salads containing leafy greens

13.19.11 Data gaps and research needs

The lack of recent case-control studies and baseline studies for *Y. enterocolitica* in food means that there is greater uncertainty concerning source attribution now than about 30 years ago when the previous studies were conducted. The Norwegian Food Safety

Authority's sampling is also reduced, and the budget is tied to what the EU requires of sampling, which often does not reflect what is needed at national level.

Outbreaks of yersiniosis in recent years have mainly been caused by serotype O:9 and not O:3 in Norway. Some pig herds (even at least one SPF herd) seem to be carriers of serotype O:9 at the expense of O:3? What has happened and why?

14 Appendix III - Supplementary information on criteria for risk ranking and exposure assessment

The present risk assessment consisted of two steps:

(1) risk ranking of 20 selected pathogens with respect to the incidence and severity of the diseases consequential to the pathogens, and

(2) a source attribution process aimed at identifying pathogen-food combinations that may pose a risk to human health.

The procedure and methods employed, and the results obtained, are described in detail in the previous chapters of this report, and the internal validity and reliability of the results are discussed in chapter 9. The present appendix provides supplementary information, which may serve to elucidate and elaborate some of the most pivotal steps in the assessment.

14.1 Risk ranking of food- and waterborne pathogens

The risk ranking was performed using six criteria, of which one, number of food and waterborne illness (C1), poses considerable challenges. This section provides a detailed description of the data sources used, the quality and reliability of these sources, and the assessments performed to estimate the number of illnesses attributable to food- and waterborne transmission.

14.1.1 Number of food- and waterborne illnesses

For each pathogen, the total number of persons infected in Norway was estimated using information from the following sources:

1. Norwegian Surveillance System for Communicable diseases (MSIS)
2. Web-based Outbreak Alert System (Vesuv)
3. Norwegian Syndromic Surveillance System (NorSySS, Sykdomspulsen)
4. National and international scientific articles and reports

Data from the surveillance system (MSIS) were adjusted to correct for underestimation due to under-reporting and under-ascertainment. This was pursued by using the information from the sources 2-4 listed above. For most diseases, only rough estimates for the number of illnesses were attainable. Nevertheless, we believe this is sufficient to score the diseases on a semi-quantitative scale in the multicriteria-based approach used in this report.

In order for an illness to be captured by surveillance, it is a prerequisite that

- the patient seeks medical attention,
- the physician takes a sample to determine an aetiologic diagnosis,
- the laboratory receiving the sample detects a pathogen indicating a notifiable disease, and
- the laboratory and the physician report the case to MSIS.

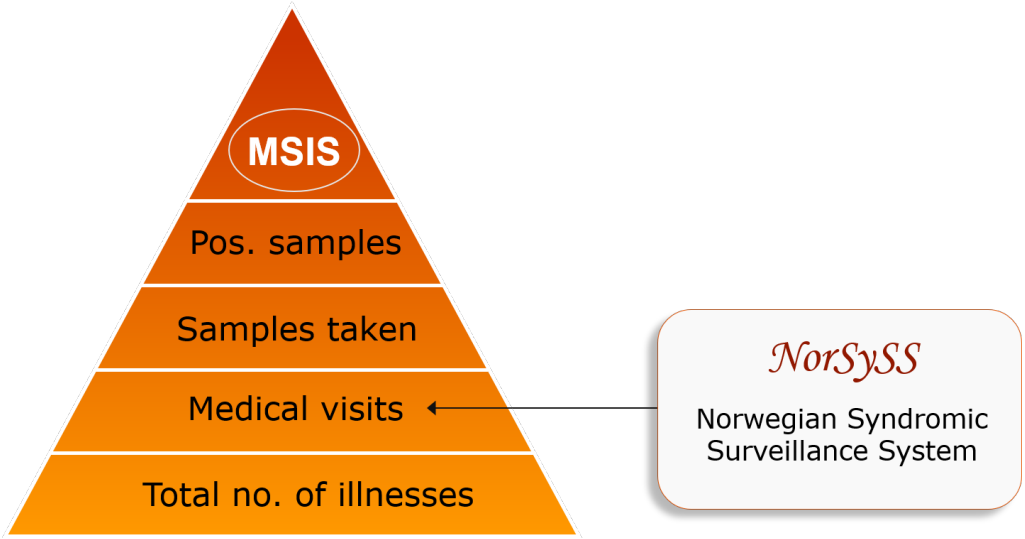

Figure 14-1. The surveillance pyramid. The number of cases reported to surveillance (MSIS) is only the tip of the iceberg. The syndrome-based surveillance system (NorSySS) monitors the number of consultations in the primary health care.

There is considerable uncertainty about the number of patients who are not detected by surveillance because they do not seek healthcare. Likewise, the proportion of patients who do visit a doctor, but are not tested to determine an etiological diagnosis, is unknown. Both parameters vary primarily with the perceived severity of the disease, but also depend on the patient's overall health status, age, and perhaps with gender and travel history. Moreover, the doctors' decision to take a sample relies essentially on whether there are clinical or epidemiological reasons to establish an aetiologic diagnosis.

Once a sample has been submitted, the laboratory's ability to detect an etiological agent is determined by the panel of diagnostic methods implemented and which methods are used routinely. At Norway's medical microbiological laboratories, all faecal samples from patients with gastroenteritis submitted for microbiological analysis are routinely examined for *Campylobacter, Salmonella, Yersinia*, enteric *E. coli, Shigella* and *Vibrio*. Previously, enteric viruses and parasites were investigated only if clinical or epidemiological incentives were

present, and the doctors had to request such analyses explicitly. However, implementation of PCR-based methods has allowed these pathogens to be included in the routine panel at an increasing number of laboratories.

Financial barriers to attending healthcare and taking samples are not considered a significant issue in Norway, since the costs of visiting doctors and collecting and analysing samples are largely covered by the national social security system.

Among the 20 pathogens included in this report, seven are the causative agents of diseases that are not notifiable to the surveillance system at all (e.g., norovirus). Hence, the most important basis for estimating their incidence is lacking. However, some of the diseases have been subject to extensive research projects in which incidence or prevalence were determined directly (e.g., toxoplasmosis) or where these parameters can be estimated indirectly using the results obtained. Many of them are not infrequently the cause of disease outbreaks reported to Vesuv (e.g. *S. aureus*, *Cl. perfringens*, *B. cereus*, norovirus). Thus, the frequency of outbreaks and the number of people afflicted can be used as a provisional indication of how common the diseases are.

14.1.2 Outbreaks of food- and waterborne illness

Most outbreaks are small, and only a small fraction is detected and notified to Vesuv. Like MSIS, Vesuv records only the tip of an iceberg. The degree of under-reporting varies considerably depending on the severity of the disease, the size of the outbreak, whether sensitive diagnostic methods have been implemented, and who are afflicted. The probability of detecting an outbreak is greatest for the following categories:

- Outbreaks of very severe illness (e.g. HUS or botulism)
- Large outbreaks (e.g., waterborne)
- Outbreaks in which patients become ill almost at the same time, due to short incubation period (e.g. foodborne intoxications)
- Outbreaks afflicting a small, closed population (e.g. an institution, a family, or participants at a meeting)
- Outbreaks affecting children
- Outbreaks of diseases for which sensitive diagnostic and subtyping methods have been implemented.

Consequently, the reported outbreaks are not necessarily representative.

Information from outbreak investigations may provide an indication of the patients' propensity to seek medical attention and the physicians' sampling practices. It notable, however, that outbreak data are inclined to overestimate these parameters due to increased awareness among both the public and physicians in an outbreak situation.

During an outbreak of campylobacteriosis in a small town (Røros, 2007), it was estimated that approx. 200 (13.3%) of at least 1500 patients consulted a doctor, and only 36 (2.4%) were sampled, despite substantial public and medical awareness. In an outbreak after a

bicycle race (Birkerbeinerrittet, 2009, campylobacteriosis and cryptosporidiosis), an interview survey among the participants revealed that 1873 became ill, 167 (8.9%) visited a doctor, and 41 (2.2%) were sampled. The outbreak received considerable attention among the bikers through social media. For sporadic cases of diarrhoeal disease, one would expect a much lower proportion of patients to seek medical attention and to be tested.

In 1999–2000, the Norwegian Institute of Public Health (NIPH) conducted a one-year, nationwide retrospective population-based survey to estimate the incidence of acute gastroenteritis (Kuusi, Aavitsland, Gondrosen, & Kapperud, 2003). The incidence was 1.2 per person-year among the responders. Of the 171 cases detected, 29 (17%) consulted a physician, 13 (8%) reported that a stool sample was taken, and 7 (4%) were admitted to hospital. These figures are most probably overestimates, since the response rate was modest (61%) and persons with milder symptoms may be over-represented among the non-responders. The hospitalization rate is obviously far too high since it would result in 220 000 admissions to hospital due to acute gastroenteritis annually.

14.1.3 Number of illnesses attributable to food- and waterborne transmission

Many food- and waterborne illnesses can be transmitted in several different ways:

- by direct contact with infectious animals or persons, their faeces, urine, vomiting or secretions,
- indirectly via vehicles (food and beverages of animal or vegetable origin, other animal products, objects and water), or
- indirectly via vectors (insects and ticks; e.g. tularemia).

The proportion of illnesses attributable to food- and waterborne transmission varies between diseases, and there are major differences between countries in the relative importance of different sources of infection. In Norway, a series of analytical epidemiological studies of food- and waterborne zoonoses have been undertaken to identify preventable risk factors and estimate the relative importance of these factors. The results make it possible to estimate the proportion of illnesses caused by different foods, drinking water, contact with reservoir animals, etc. using population attributable fractions (PAFs) (see 14.3.2). However, it is important to note that the percentages calculated in this way indicate the relative importance of the factors, not the absolute ones, because most studies are matched case-control studies, not cohorts. Moreover, the majority of the investigation was carried out several decades ago.

There is a general impression from these studies that waterborne transmission is more important in Norway than in most other European countries, a conclusion supported by the comparatively high number of large waterborne outbreaks. The widespread use of surface water supplies as drinking water is the most likely explanation. In addition, many Norwegians drink undisinfected water directly from a surface source during outdoor activities like hiking or camping, and from wells at holiday cabins.

For most diseases in this report, no such studies have been performed in Norway. To the extent that foreign publications are taken into consideration, they are mainly selected from Scandinavia or Northern Europe, which are believed to be reasonably representative of the Norwegian conditions. Estimates of the proportion of illnesses attributable to food and water transmission are therefore based on a rough best-guess assessment.

14.2 Description of the data sources

14.2.1 Norwegian Surveillance System for Commun,icable diseases (MSIS)

MSIS is the national surveillance system for communicable diseases in the Norwegian population. All doctors and medical microbiological laboratories have a statutory obligation to report each case of a number of notifiable diseases. MSIS conducts continuous and systematic collection, compilation, analysis, interpretation and reporting of information on the incidence of the diseases.

The NIPH disseminates MSIS statistics by year in annual reports, and via customizable tables from the MSIS online Statistics Bank. Tables can be downloaded by disease, month and year of diagnosis, age, county, and place of infection (in Norway, abroad, or unknown).

The present report is confined- to persons infected in Norway. Unfortunately, information on place of infection is lacking for a considerable proportion of the cases (5-10%), even after reminders to the doctors requesting data on the patients travel history prior to onset of the symptoms.

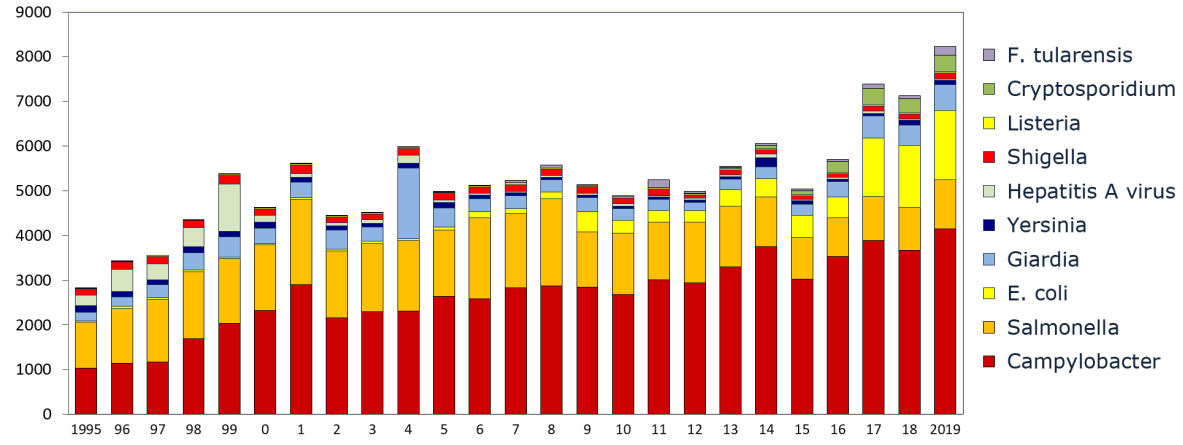

Figure 14-2. Number of notified cases infected in Norway caused by 10 selected pathogens, MSIS 1995-2019

14.2.2 Web-based Outbreak Alert System (Vesuv)

The Norwegian Institute of Public Health has established a web-based outbreak rapid alert system (Vesuv), which is used for mandatory outbreak alerts from municipal medical officers, healthcare institutions, and food safety authorities. Suspected and confirmed outbreaks of infectious diseases should be notified immediately to the NIPH through Vesuv. It is also possible to submit alerts via telephone or email, but it is required that Vesuv be notified as soon as possible.

All outbreaks are compiled in a single database containing information on, among other things, causal agents (if known), the number of registered illnesses, the expected source of infection (for example, which food product) and where the outbreak occurred. The NIPH publishes Vesuv statistics in annual reports.

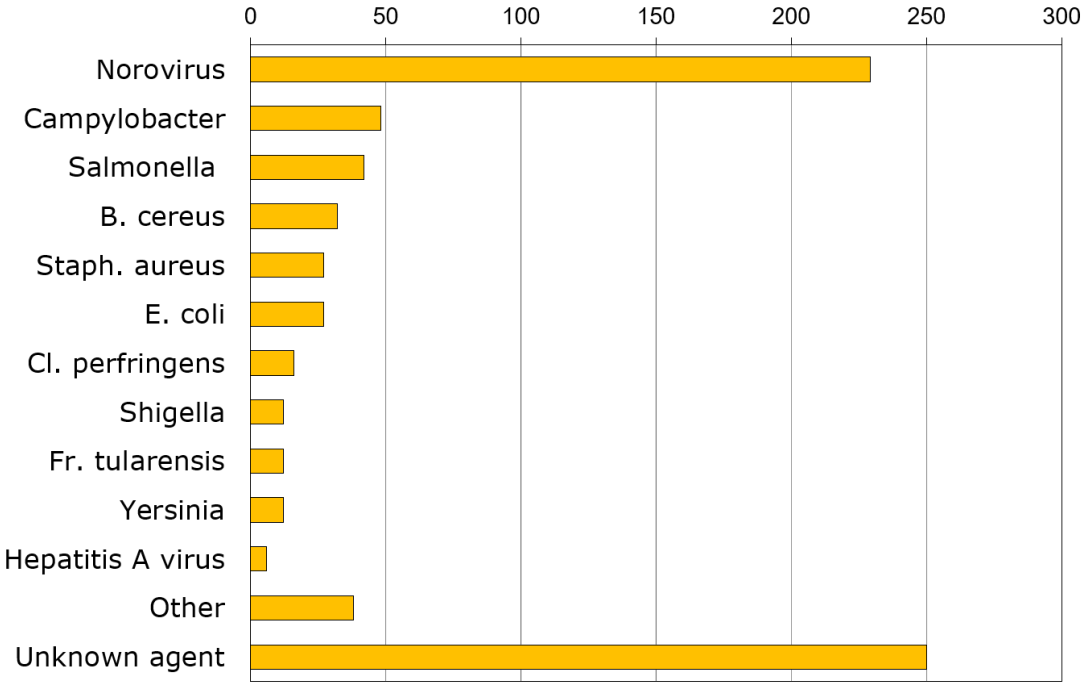

Figure 14-3. Number of reported outbreaks by causative agent, Vesuv 2006-2019

14.2.3 Norwegian Syndromic Surveillance System (NorSySS, Sykdomspulsen)

NorSySS is a syndrome-based surveillance system that monitors the number of consultations in the primary health care due to presumed infectious diseases. The reported diagnoses are preliminary and are based on the clinical symptoms the patients present at their first medical contact, since the etiological diagnosis is usually unknown at this stage. NorSySS provides the number of both telephone and face to face consultations at the general practitioners (GPs) and other primary care facilities within a given period. NorSySS enable detection of trends and possible disease outbreaks that are causing more people to seek medical attention. NorSySS does not provide the exact number of infected people since some

patients will contact their GP several times with the same diagnosis, while others may not seek medical attention at all. Data on the number of recorded cases by counties and age groups are updated every month on the NorSySS website.

14.2.3.1 Gastrointestinal infections

NorSySS includes approximately 80 diagnosis codes, all of which represent symptoms of infectious diseases. Gastrointestinal infections are covered by three codes: D11-Diarrhoea, D70-Gastrointestinal infection and D73-Gastroenteritis, presumed infection. Which codes the doctors choose is not based on specified criteria but is probably quite arbitrary. The number of consultations assigned to these codes has increased somewhat since 2006, but has remained stable over recent years, with over 200,000 consultations per year. For D73-Gastroenteritis, presumed infection, the annual number of consultations varies from 70,000 to 90,000.

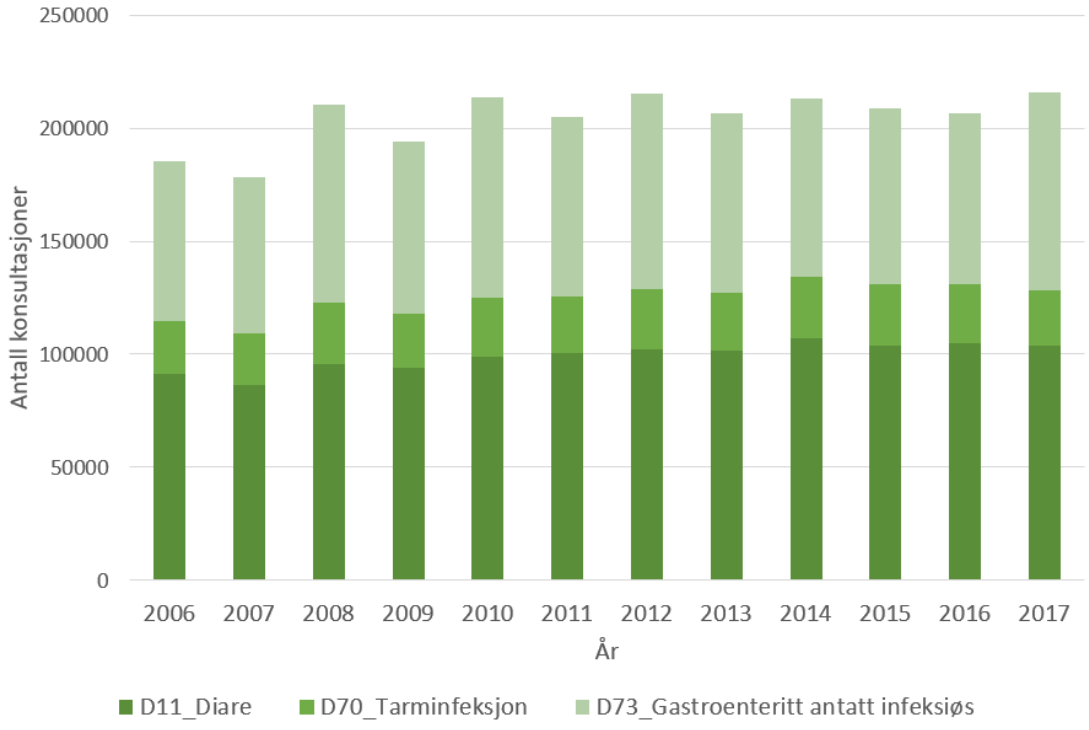

Figure 14-4. Number of consultations for gastroenteritis, NorSySS 2006 – 2017

14.3 Source attribution

For each pathogen, identification of key foods of concern in Norway was obtained from the following sources:

- Surveillance and monitoring programmes under the auspices of the Norwegian Food Safety Authority (NFSA)
- National surveys (i.e. prevalence studies)

- Baseline surveys conducted by the European Food Safety Authority (EFSA), in which Norway was included
- Rapid Alert System for Food and Feed (RASFF)
- Outbreak investigations in which the source of infection was identified (Vesuv)
- Analytic epidemiological investigations aimed at identification of sources of infection and risk factors for sporadic cases of disease
- Previous risk assessments and opinions from Norwegian Scientific Committee on Food and Environment (NSCFE)
- Information on food consumption patterns in the Norwegian population, and food imports

When Norwegian data were sparse or absent, information was obtained from:

- Risk assessment and opinions published by EFSA
- Data from other countries, preferably with comparable epidemiological situation
- Data from reference laboratories and outbreak investigations in other countries when source and risk factors are relevant for Norway

Hence, both microbiological and epidemiological results were implemented in the source attribution process. These methods represent two different research strategies, both of which have their advantages and limitations, as discussed in detail in the online Guidelines for Investigation of Food and Waterborne Outbreaks provided by the NIPH (Norwegian version (Utbruddsveilederen): https://www.fhi.no/nettpub/utbruddsveilederen/).

Microbiological source attribution consists of detection and characterization of pathogens in the food chain, followed by comparison of isolates from suspected sources and infected patients, sometimes facilitated by implementing advanced genotyping and mathematical model building. Microbiological methods also include examination of virulence factors, as well as the pathogens' ability to survive, grow and spread at various stages in the production and distribution chain. Microbiological source attribution is therefore an easily understandable and appealing principle. Nevertheless, microbiology is not always sufficient, as emphasized in 14.3.1, below.

Analytic epidemiological methods, in turn, are based on interviews with patients who have recently been ill, and with healthy control persons enrolled from the study population. These two groups are compared using statistical multivariable analyses to uncover significant differences in their past consumptions and other exposures in the incubation period prior to the patients' illness onset. This approach enables identification of independent risk factors and the corresponding sources of infection. The risk associated with each factor is computed, and their relative impact is estimated by calculation of population attributable fraction.

There is a general impression that knowledge about and acceptance of analytical epidemiology is not always complete. Since such studies have been implemented for several

of the diseases included in this assessment, it may be appropriate to explain in more detail what this approach entails. Section 14.3.2 therefore describe the purpose of analytical epidemiology and clarifies its delimitation against microbiological methods. The basic principles of design, conducting, analysis and interpretation are also explained.

14.3.1 Microbiological source attribution

In Norway, considerable amounts of work have been invested to investigate the prevalence, growth and survival of pathogens at various stages in the food chain. These efforts include specific research, as well as surveillance and monitoring programmes, and prevalence surveys, under the auspices of the Norwegian Food Safety Authority. Although the investigations have identified several possible sources of infection, they are not sufficient to determine the relative or absolute contribution of the various sources to the total number of illnesses in the population. The reason for this is:

- Not all possible sources have been examined. Although a pathogen has been detected in a number of animals and foods, the agent may, nonetheless, be found in other sources, which may be even more, or equally, important as those investigated.
- The occurrence in the food chain may be underestimated or overlooked due to insufficient or labour-intensive detection methods with suboptimal sensitivity or specificity. For some pathogens, effective methods are lacking or have not yet been implemented. Moreover, the agent may be present in a number too low to be detectable with current methods, but nevertheless sufficient to cause disease.
- Putative pathogens isolated from foods or animals may belong to species-adapted subtypes, which differ from those capable of causing disease. Although the same subtypes are detected in animals or foods as in patients, they may lack the necessary pathogenic properties. For some agents, it is still disputed which factors, or combination of factors, are responsible for virulence.
- The prevalence of a pathogen in food-producing animals or a food source does not reflect directly the importance of that reservoir as a cause of disease:
    - Occurrence of the same pathogen or its subtypes in a particular animal species as in humans is not necessarily due to a direct route of transmission and does not justify definitive conclusions about the relative importance of that animal species as an ultimate source of infection. In general, the of similar subtype patterns in humans and reservoir animals may reflect transmission from a common source or, more likely, indirect transmission via a different animal, food, or water, which is inserted as an intermediary vehicle in the infection chain. Consequently, quantitative microbiological source attributions are vulnerable to confounding bias resulting in overestimation of causal relationships.

      For example, the presence of the same *Campylobacter* genotypes in poultry and humans may partly be due to the fact that both are receptive to infection from the same sources, most notably drinking water, which in turn is susceptible to contamination from a variety of mammals and birds.

- Pathogens are rarely associated with only one unique source. This applies to their subtypes as well, although source-specific subtypes do occur. Therefore, unless prevalence in other sources is being investigated, conclusions regarding the relative importance of a particular source of infection, based on subtyping data, are unwarranted.
- Correlation is not causation: Time series analysis showing that the incidence of infection in correlation between incidence of infection in humans and an animal species increase and decline in parallel, does not necessarily prove a causal relation, since both host species may be susceptible to simultaneous variations in the same environmental reservoir, whether directly or via intermediary vehicles (e.g., water).
- During the production chain, a pathogen can be introduced, be re-introduced, multiply, be killed, decimated, reduced in number, or sub-lethally injured, depending on the product and pathogen in question, and how the food item or its ingredients are processed, stored, distributed, and cooked. Thus, the prevalence of a pathogen at an early stage of the production chain rarely result in an equal level of that pathogens in the final product.
- The consumption amount of a particular food in the population, and the number of persons who prepare and eat the food in a way that render them susceptible to infection, are decisive factors in determining the number and proportion of illnesses ascribable to the food concerned.

Consequently, knowledge about the presence of pathogens in the food chain is not sufficient to draw safe conclusions regarding the significance of the product examined compared to other possible sources (relative importance), or what proportion of illnesses the food source is responsible for (absolute importance). To address these issues, a series of analytic-epidemiological studies of food- and waterborne zoonoses acquired in Norway have been conducted, in order to identify the most important preventable risk factors for sporadic cases of disease and the corresponding proximate sources of infection, and estimate the relative significance of these factors.

14.3.2 Analytical epidemiology

For each disease, the significance of a particular food as a source of infection is determined by two parameters: the probability of becoming ill when eating the food (the risk associated with consumption) and the frequency of its consumption in the population. The most effective and direct approach for determining such factors is analytic-epidemiological studies, which entail interviews with patients who have recently been ill with the disease concerned, and with healthy control persons enrolled from the general population as a basis for comparison (e.g., case-control studies). In this way, the significance of several exposures can be investigated in the same study using statistical multivariate analyses. Hence, the risk factors identified are independently related to disease; their effects cannot be explained by co-variation with other factors, since confounders are controlled by the multivariate analyses, usually in the form of logistic regression.

Although analytic-epidemiological studies aim at identification of risk factors, the risk factor is explicitly related to a corresponding source of infection. For instance, if drinking untreated water from a private well or eating undercooked pork are identified as risk factors, it follows logically that water and pork are the proximate sources of infection, respectively.

The risk factor provides important additional information that cannot be deduced from knowledge about source of infection. Unlike studies of prevalence, growth and survival in the food chain, or quantitative microbial source attribution studies, the results from analytical epidemiology can be converted directly into preventive actions because such studies identify preventable risk factors (what people do - or don't do - to get sick), for instance consumption of an undercooked meat product, insufficient kitchen hygiene practices, cleaning the cat litter tray, living in a household with a dog, or drinking untreated water directly from a surface source during outdoor activities. Such information enables implementation of targeted control and prevention measures and contributes to risk management decisions.

In analytic-epidemiological studies, estimation of two variables is pursued: the size of the risk (the risk estimate) and the exposure frequency (the frequency with which the food is consumed in the population). No separate studies are required to determine the size and frequency of consumption; it is embedded in the analytical epidemiological process in which consumption in the general population is assessed through interviews with control persons randomly enrolled, preferably from a population registry.

The risk estimate and exposure frequency can be combined by calculating population attributable fractions (PAF), the proportion of total illnesses in the study population attributable to each exposure, a parameter that quantify the relative importance of risk factors and their corresponding sources of infection. PAF is the proportional reduction in population disease that would occur if exposure to a risk factor was eliminated. Thus, one can decide which causes deserve priority in terms of control and preventive efforts, and which can be downgraded.

If a biologically or technologically plausible factor does not reach statistical significance, one may be misled to believe the importance of that factor is scientifically disproved, which is not necessarily the case. The explanation may rather be that the risk is not very high, the exposure is rare, or both. It may be necessary to repeat the study with a larger number of patients to uncover other, less-important factors.

14.4 Video podcasts

An overview of incidences, reservoirs, sources of infection and risk factors for food- and waterborne diseases in Norway is presented in a series of podcast videos (in Norwegian):

- Food- and waterborne diseases: Introduction https://vimeo.com/445566839/78b362b54b
- Incidence of illnesses – MSIS https://vimeo.com/445568147/fbbdf92f7f
- Incidence of outbreaks – VESUV https://vimeo.com/445568140/507d54827a

Final 09.06.2021

- Impact of the diseases https://vimeo.com/445568142/232f1f5827
- Reservoirs, sources of infection and risk factors https://vimeo.com/445568144/5dc2b86e5e
- Challenges and conclusions https://vimeo.com/445566840/63d16556a8

PDF-file with all slides from the videos:

Food- and waterborne diseases

15 Appendix IV

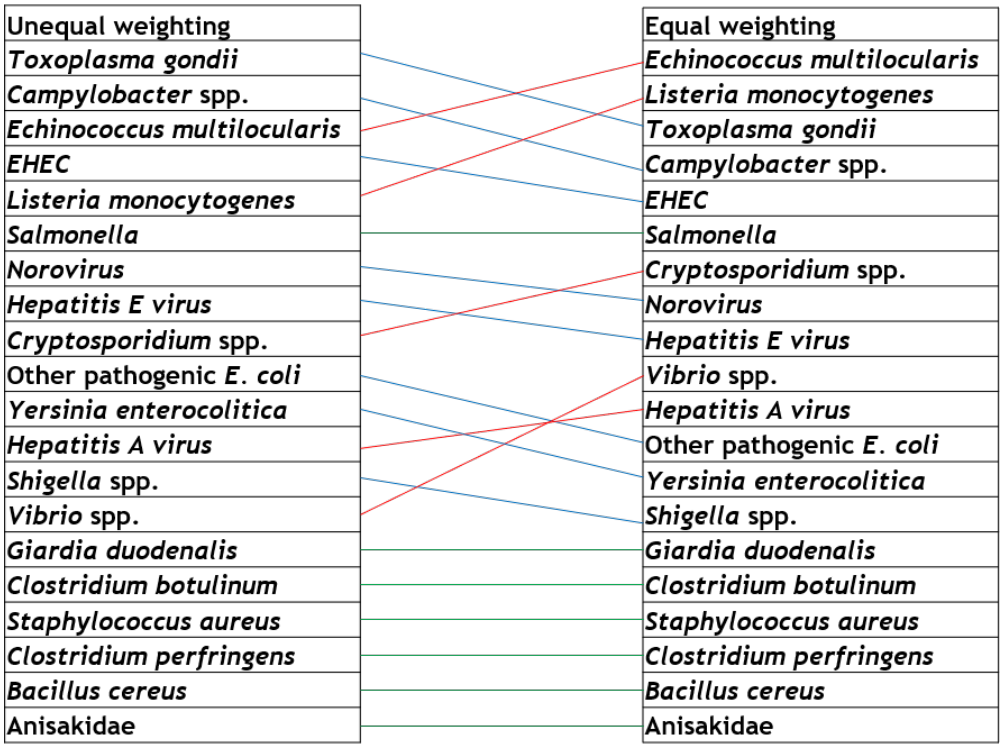

Figure 15-1. The difference in risk ranking using unequal weighting as described in chapter 5 and equal ranking (0.25) for all criteria. Green lines indicate pathogens with the same ranking regardless of weighting, blue lines show pathogens with a lower ranking if equal weighting is used, and red lines shows pathogens with increased ranking if equal weights are used.