Risk from Listeria monocytogenes in ready to eat smoked fish: Hazard characterisation

L. monocytogenes is a human foodborne pathogen, with infection by *L. monocytogenes* known as listeriosis. Foodborne listeriosis is a relatively rare illness in comparison to other foodborne diseases (see Table 3); however, the outcomes of illness can be serious with high fatality rates reported (PHE, 2018; PHS, 2020). Listeriosis mainly affects vulnerable groups such as immunosuppressed people, infants and pregnant women (and their unborn children). Levels of miscarriage are around 30%, but a *L. monocytogenes* infection can be asymptomatic in the pregnant person.

Table 3. Listeriosis cases in UK, 2018-2020 (personal communications with Epidemiology in Foodborne Infections Group "Report of Annual Human Infection Data for 2020")

Nation	Case/rate	2018	2019	2020
England	Cases	151	142	116
England	Rate	0.27	0.25	0.21
Wales	Cases	6	3	7
Wales	Rate	0.19	0.10	0.21
Scotland	Cases	12	6	13
Scotland	Rate	0.22	0.11	0.24
Northern Ireland	Cases	3	5	6
Northern Ireland	Rate	0.16	0.26	0.32
United Kingdom	Total cases	172	156	142
United Kingdom	Rate	0.26	0.23	0.21

*per 100,000 population. Population data are ONS mid-year estimates.

Disease characterisation

Various clinical manifestations are associated with *L. monocytogenes* infection, and these can be grouped in two categories: invasive and non-invasive listeriosis. Non-invasive listeriosis typically occurs in immunocompetent individuals, it has been observed during outbreaks where the majority of cases develop symptoms of gastroenteritis, such as diarrhoea, fever and headache, after a short period of incubation, as described by Aureli et al. (2000). Non-invasive listeriosis has not been well-studied as the clinical presentations do not typically warrant medical intervention and are therefore not identified as testing is unlikely to take place. Additionally, it is difficult to culture *Listeria* in stool samples, which may limit the detection of non-invasive listeriosis. There is no data available to define the number or proportion of cases of non-invasive listeriosis that occur in the populations considered vulnerable in this risk assessment, however, there is some evidence of vulnerable individuals being identified in investigations into outbreaks of non-invasive listeriosis, for example over 65 year olds in Dalton et al., 1997. Non-invasive listeriosis is typically self-limiting and symptoms only last a few days (Aureli et al., 2000). According to Warriner and Namvar non-invasive listeriosis is associated with an intake of high levels of *L. monocytogenes* (>1000 CFU/g) (Warriner and Namvar, 2009), which is also supported by assessment carried out by EFSA (EFSA, 2018) and this may reflect the suspected under reporting of non-invasive listeriosis in immunocompetent individuals who are unlikely to seek medical support.

Invasive listeriosis typically occurs in vulnerable or immunocompromised individuals. The symptoms of invasive listeriosis are severe, and include fever, myalgia (muscle pain), septicaemia, and meningitis. The incubation period is usually one to two weeks but can vary from between a few days to 90 days (WHO, 2018; Johnsen et al., 2010). The long incubation period creates difficulty in identifying the food vehicle responsible for infection, although the adoption of whole genome sequencing has improved the ability to link individual cases to outbreaks, which had previously been more challenging. Anyone can become ill from *L. monocytogenes* infection, but those aged over 65, pregnant women, unborn and new-born babies and otherwise immunocompromised persons can be considered higher-risk groups as they are more likely to acquire listeriosis from *L. monocytogenes* contaminated food, and subsequently this infection is more likely to be invasive compared to the immunocompetent population (see section 3.2). The case fatality rate of invasive listeriosis is high, ranging from 20 - 30% (Mead et al., 1999; PHE, 2017, 2018, 2021). Pregnant women infected with *L. monocytogenes* can experience miscarriage, stillbirth and premature birth which, while not typically fatal for the mother, can be fatal for the foetus or baby (Pezdirc et al., 2012).

Presentation of Listeriosis

L. monocytogenes is a cause of acute, self-limited, febrile gastroenteritis in immunocompetent persons. Invasive listeriosis causes severe acute (and sometimes fatal) illness, and post-listeriosis sequelae such as neurological symptoms can persist chronically (Drevets and Bronze, 2008). In addition, there are findings that some *L. monocytogenes* are able to colonise and persist in the gallbladder, which suggests the occurrence of long-term and chronic infections and demonstrates the ability of pathogenic Listeria spp. to survive within the various microenvironments of the gastrointestinal tract for a long period (Gahan and Hill, 2005). Although rare, *L. monocytogenes* infections can also affect bone, joints and sites in the chest which could develop into chronic disease (Bader, Al-Tarawneh and Myers, 2016).

We could not find a recent estimation of the underreporting of listeriosis cases in the UK, but Adak et al. (2002) put a factor of two for the number of cases and those not reported. It is also noted that *L. monocytogenes* is a schedule 2 causative agent which it is mandatory to report (Adak, Long and O'Brien, 2002). This should mean that any detected cases are reported, and that only undetected cases are likely to remain unreported.

Infective Dose

Quantitative assessments indicate that among immunocompetent adults, exposure to high doses of *L. monocytogenes* in foods is required to cause febrile gastroenteritis. Additionally, EFSA modelling suggests that 90% of invasive listeriosis cases are caused by ingestion of RTE foods containing > 2000 CFU/g (EFSA, 2018). Levels under 100 CFU/g in food at point of consumption (for example the legal limit at the end of shelf life) are regarded as safe, meaning that people consuming foods with low levels of *L. monocytogenes* have an extremely low risk of contracting listeriosis (EFSA, 2013, 2014, 2018). Nevertheless, as with all disease-causing microorganisms, there is no threshold below which there is a true “zero” risk for human illness. Epidemiological data has indicated that doses as low as 8 CFU/g of *L. monocytogenes* can cause listeriosis (Pouillot et al., 2016), although it is recognised that further data is required to further inform understanding of infective dose and probability of infection in vulnerable populations (Farber et al., 2021). In ready-to-eat (RTE) products intended for infants and for special medical purposes, there must be absence of *L. monocytogenes* in samples of 25g throughout shelf-life (EFSA, 2018). In other RTE foods that can support the growth of *L. monocytogenes* (including smoked fish) the bacterium must not be present in 25 g of sample when leaving the production plant, or the business must demonstrate that the product will not exceed the limit of 100 CFU/g throughout its shelf life.

Dose-response data from human volunteer studies with L. monocytogenes or from volunteer studies with a surrogate pathogen do not exist. In 2018, EFSA conducted a risk assessment on “ *Listeria monocytogenes* contamination in RTE food and the risk for human health”. This risk assessment states that the average probability of a single *L. monocytogenes* CFU to cause illness in a specific host (the r value), reflects the strain virulence and host susceptibility, and ranges three orders of magnitude, from the least (for example under 65 years old without underlying condition) to the most susceptible (for example immunocompromised) populations. Reported r values for specific outbreaks with highly susceptible populations increased the range by another five orders of magnitude. Thus, the probability of a single bacterium to cause illness may range 100 million times depending on variability in host susceptibility and *L. monocytogenes* virulence (EFSA, 2018). It is recognised that uncertainty in most dose-response models results from a lack of data on the impact on highly susceptible populations from low level exposure (Farber et al., 2021). As a result, there is no single value for infectious dose. In earlier dose response modelling work, Pouillot et al. (2015) reviewed available literature and estimated that the relative risk of invasive listeriosis for pregnant women was 100 times higher than for non-pregnant women, and that relative risk levels more than 1000 times higher than that for the <65 year old general population have been reported for individuals with chronic lymphocytic leukaemia (Pouillot et al., 2015). This data is broadly similar to that reported in section 1.3 from previous risk assessments, but it does indicate the uncertainty in the understanding of infectious dose. For example, Pouillot et al. (2009) reported that the mean risk of contracting invasive listeriosis for susceptible (immunocompromised) individuals is x 54, but Pouillot et al. (2015) reported a risk level of more than x 1000 for a specific medical condition. Similarly, the WHO technical report on *L. monocytogenes i*n ready-to-eat foods calculated susceptibilities ranging from x 7.5 to x 2,500 for different vulnerable groups compared to the reference population of under 65 years in age with no other medical conditions (WHO, 2004).

Previous outbreaks

To identify outbreaks associated with *L. monocytogenes* and smoked fish, a literature search was performed. Pubmed and Scopus were searched using the search terms “listeri* AND outbreak AND ("smoked fish" OR "smoked salmon" OR "smoked trout" OR "smoked mackerel" OR kipper)” with no restriction on language or date of publication. Google scholar was also searched, reviewing the first 100 hits sorted on relevance. Public health websites from the CDC, EFSA and

the four UK nations were also searched.

A total of eight outbreaks were identified from the literature search (Table 4). Case numbers ranged from 4 cases up to 27 cases. In the 6 outbreaks that provided sufficient detail on the types of cases, vulnerable groups were a majority of the cases in 5 of them. Where it was specified, all the outbreaks were due to cold-smoked fish products.

Table 4. Outbreaks associated with *L. monocytogenes* contamination of smoked fish

Years/location	Number of cases (deaths)	Vulnerable groups affected	Product	References
August 1994 to June 1995 Sweden	9 (1)	5 elderly 3 pregnancy 1 clinically vulnerable	Cold smoked gravad rainbow trout	Ericsson, 1997, Tham et al., 2000
1997 Finland	5 (0)	1 pregnancy All cases from known risk group	Cold smoked halibut and trout	Miettinen et al., 1999, Nakari et al., 2014
May 2013 to September 2015 Denmark	10 (3)	1 pregnancy All cases from known risk group	Cold smoked halibut and trout	Gillesberg Lassen et al., 2016
June 2013 to September 2015 Denmark	10 (4)	All cases from known risk group	Cold smoked salmon	Gillesberg Lassen et al., 2016
2013 to 2015 Sweden	27 (NA*)	NA	Gravad and smoked fish	Lopez-Valladares Danielsson-Tham and Tham, 2018

Years/location	Number of cases (deaths)	Vulnerable groups affected	Product	References
July 2014 to February 2019 EU	22 (5)	Median age of outbreak cases 76 years, interquartile range 64 to 83	Cold smoked or gravad salmon and cold smoked trout	EFSA and ECDC, 2019
October 2015 to May 2018 EU	12 (4)	9 elderly	Cold smoked salmon	Schjørring et al., 2017; EFSA and ECDC, 2018
2020 UK	4 (2)	3 clinically vulnerable 1 pregnancy	Smoked salmon^	EFSA, 2020, UKHSA personal communication

* NA details not provided in reference

^ Further details on smoking process unavailable

Given the low case numbers and the extended incubation period, historically it has been difficult to identify *L. monocytogenes* outbreaks. This was highlighted by a recent paper which made use of sequencing data from German clinical and food isolates to link cases to food exposures (Lachmann et al., 2022). This analysis retrospectively identified 22 outbreaks in Germany attributed to *L. monocytogenes* in smoked fish between 2010 and 2021. These outbreaks were associated with 228 cases, with a median age of 78 years, and involved 50 deaths, of which 17 were confirmed to have died from listeriosis. The results estimated that 27% of all listeriosis cases in Germany between 2018 and 2020 were likely due to *L. monocytogenes* contamination of smoked or gravad salmon products (Lachmann et al., 2022).

UK Food Safety Incidents involving *L. monocytogenes* and Smoked Fish

A food safety incident is defined as any event where, based on the information available, there are concerns about confirmed or suspected risks to the safety, quality, or integrity of food and/or feed that could require intervention to protect consumers' interests (FSA, 2021). Incidents are usually notified to FSA or FSS if they concern a serious localised food hazard, if they are likely to affect a vulnerable population or if the food is distributed in an area encompassing more than one Local Authority/Local Council; it does not necessarily mean a clinical case of foodborne illness was associated with the incident. Microbiological incidents recorded by the FSA and FSS for the time period of 2015 – 2019 were investigated for those relating to *L. monocytogenes* in smoked fish. Out of 1,734 incidents, 18 were due to *L. monocytogenes* in smoked fish, meaning 1.0% of all incidents in this time period could be attributed to this specific pathogen and food product

combination (Table 5). All recorded incidents in Table 5 involved smoked salmon as opposed to other types of smoked fish.

Table 5. Incidents reported to the Food Standards Agency and Food Standards Scotland involving L. monocytogenes in smoked fish, 2015 - 2019

Year	Microbiological incidents	*L. monocytogenes* incidents	*L. monocytogenes* and smoked fish incidents
2015	290	29	1
2016	302	34	6
2017	380	49	2
2018	358	39	6
2019	381	63	3

Due to changes in recording and accessing incidents data, data for the years 2020-2022 was extracted differently than for previous years. Table 6 provides the number of *L. monocytogenes* in smoked fish incidents recorded by the FSA and the FSS for these years.

The number of food incidents per year in the UK ranged from 1 to 6. In all but one instance where the fish species was recorded, smoked salmon was the source of *L. monocytogenes* contamination.

Table 6. Incidents reported to the Food Standards Agency and Food Standards Scotland involving *L. monocytogenes* in smoked fish, 2020 - March 2022

Year	*L. monocytogenes* and smoked fish incidents
2020	4 (2 salmon, 2 species not defined)
2021	6 (4 salmon, 1 smoked salmon pâté, 1 speciies not defined)
2022	4 (3 salmon, 1 trout)

UK Listeriosis cases associated with Smoked fish

This section was provided by the UKHSA from their records relating to listeriosis, and therefore an incident in this section refers to cases or outbreaks of listeriosis.

All cases of listeriosis reported in England are requested to complete a food history questionnaire, asking about food exposures in the 30 days prior to illness onset (UK Health Security Agency). This questionnaire includes questions around smoked fish consumption and location of purchase. Where *L. monocytogenes* from multiple cases match by analysis of WGS results, food exposures can be compared to identify similarities between cases, which allows potential vehicles of interest to be further investigated to uncover the source of the outbreak. However, the most common way to initially identify likely food sources is by the unrelated examination of foods as part of Local Authority routine food inspections and the matching by WGS analysis of food or environmental *L. monocytogenes* to those from cases of human listeriosis, sometimes several years apart. Due to the sensitivity and specificity of analysis of WGS data, where there is a match to a non-human isolate, food exposure information and traceback can identify a likely source of contamination, even in instances where there is only one case.

As of 11 March 2022, data from investigations into outbreaks and single cases matching food isolates identified by WGS in UKHSA have identified a total of seven incidents that have been linked to smoked fish from 2015 - 2022 through microbiology and epidemiological evidence (see Table 7). Between 2015 - 2019, there were an additional three incidents, leading to 5 cases and 3 deaths, that were potentially linked to smoked salmon by microbiology (WGS) without corroborating epidemiological or food chain traceback data.

From 2015-2019, there were 3 incidents involving a total of 3 cases, with one case each linked to smoked fish via microbiological and epidemiological evidence. From 2020-March 2022 there were 4 incidents involving a total of 16 cases. Despite covering less than half of the same time period, the 2020-2022 period resulted in 5 reported deaths and 2 pregnancy-associated cases, compared to 1 death and 1 pregnancy associated case in 2015-2019. This suggests an increase in the number of cases associated with smoked fish consumption, number of deaths and number of pregnancy-associated cases in 2020- March 2022 as compared to 2015-2019, but it is not known if there were any differences in consumption volumes or frequency in the population between these two time periods. However, this pattern is not represented as strongly in the FSA/FSS food incident data.

Table 7. Summary of *L. monocytogenes* incidents and cases from 2015-2019 and from 2020-present with microbiological and epidemiological evidence implicating smoked fish as the vehicle of infection

Year period	Incidents	Cases	Size of incidents (average range)	Deaths	Pregnancy associated cases	Fish species/products
2015 to 2019	3	3	1 (1 case each)	1	1	1 smoked salmon, 1 salmon pâté, 1 smoked mackerel
2020 to March 2022	4*	16	4 (1 to 10)	5	2	4 smoked salmon^

*Includes the ongoing national outbreak of *L. monocytogenes* related to smoked fish. Data correct to March 2022.

^Four independent incidents, involving 4 different suppliers of smoked fish.