A systematic review of Bacterial foodborne outbreaks related to red meat and meat products

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17 Abstract

Our investigation focused on foodborne outbreaks related to meat and meat products, published in peer-reviewed journals in the 18 period 1980 – 2015. Most of the outbreaks, investigated in this study, were caused by Escherichia coli and Salmonella, causing 33 19 and 21 outbreaks respectively, mostly in Europe and the United States. In the *E. coli* outbreaks, the total number of reported cases 20 was 1966, of which 1543 were laboratory confirmed. The number of cases requiring hospitalization was 476, of whom 233 cases had 21 a hemolytic-uraemic syndrome (HUS), and the reported deaths were 32. All of the E. coli outbreaks, except four, were caused by 22 serovar O157:H7. The other four outbreaks were caused by the following serovars: O111:H8, O26:H11, O111, and O103:H25. Fresh 23 processed meat products were the category most frequently implicated. In the Salmonella outbreaks the total number of all reported 24 cases were 2279, of whom 1891 were laboratory confirmed. The number of reported cases requiring hospitalization was 94, and 25 seven were reported dead. Regarding Salmonella, eight serovars caused those outbreaks. The most common serovar causing 26 Salmonella-related outbreaks was S. Typhimurium. The food category most frequently implicated in those outbreaks was raw cured 27 fermented sausages. Other organisms linked to meat-associated outbreaks, but less frequently reported, were Staphylococcus 28 aureus, Bacillus cereus, Clostridium perfringens, Clostridium botulinum, and Listeria monocytogenes. Issues of the burden of 29 outbreaks, the challenges of comparing global outbreaks, food attribution and how the meat industry works to meet consumer 30 demands while maintaining food safety are discussed. 31

32 Introduction

Though there has been much progress in food safety measures, foodborne diseases still pose significant public health challenges. Non-typhoid salmonellosis saw a surge in the 1980'ies, *Escherichia coli* (*E. coli*) O157:H7 was first identified as a pathogen in 1982, and in the last 30 years a number of infectious agents have been either newly described or newly associated with foodborne transmission (Riley, Remis et al. 1983, Tauxe 1997). Along with new pathogens, an array of new food vehicles have been implicated in recent years, and many emerging zoonotic pathogens have become increasingly resistant to antimicrobial agents (Tauxe 1997).

Our investigation of foodborne outbreaks related to meat products is confined to the period 1980 – 2015 and is limited to bacterial foodborne pathogens, as most detected and reported outbreaks are caused by bacterial agents. Though bacterial food-borne agents and their diseases have been well studied in past years and reported cases are on a downward trend, the disease burden remains substantial and throughout the 1990'ies until today three primary foodborne bacterial agents, i.e., *Salmonella, Campylobacter* and *E. coli*, have persisted (Newell, Koopmans et al. 2010).

Reports of outbreak investigations provide the most comprehensive data for determining the foods responsible for illnesses (Batz, Doyle et al. 2005), but of course only represent a fraction of the real occurrence. However, attributing all illnesses to specific foods is challenging, as most agents are transmitted through a wide range of foods and linking them to a particular food is rarely possible except during an outbreak (Painter, Hoekstra et al. 2013). One general method for attribution of the human disease burden of foodborne infections to specific sources is the "microbiological approach", which involves isolation of the pathogen from the source and from ill humans (Pires, Evers et al. 2009).

Raw cured fermented sausages are foods whose safety is based on the addition of salt and nitrite, drying, low pH and water activity
 (a_w), competition from starter cultures, pre-treatment of the meat, addition of antimicrobials, fermentation temperature and storage

conditions (Bacus 1997, Riordan, Duffy et al. 1998, Heir, Holck et al. 2010, Holck, Axelsson et al. 2011). The recognition of dry fermented sausages as a potential threat to food safety has led some countries to introduce regulations to minimize the risks (Heir, Holck et al. 2010). Yet, several recent reports highlight the significance of fermented meats as a source of outbreaks (Moore 2004). The food industry is challenged by public health authorities to reduce salt (Na⁺) content in their products. The question then arising is what is a "safe" reduced salt level. The meat industry has gradually responded to authorities' recommendations, and it is of interest whether outbreaks have been more often linked to low salt products or if there is any indication of more frequent outbreaks in this type of products.

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The aims of this study were to review global outbreaks where red meat and meat products were incriminated as a source for outbreaks and their main clinical consequences involved, and thus poultry was not included. In particular, we wanted to illustrate different risks posed from raw cured fermented meats and other main product categories, to better understand causes and to detect epidemiological trends in pathogens and meat products implicated.

63 Materials and methods

64 Literature search

The primary literature search was undertaken using the Advanced Search Builder provided by PubMed (<u>www.ncbi.nlm.nih.gov/pubmed</u>), Web of Science[™] by Thomson Reuters (<u>http://apps.webofknowledge.com</u>) and Google Scholar (<u>https://scholar.google.no/?hl=no</u>).

Search settings in Web of Science were "All years" and language "Auto-select". The following search terms were used in Web of 68 Science: Web of Science search, "Language all, years 1980 – 2015: meat, fermented, outbreaks". In total, 77 manuscripts were 69 obtained. PubMed searches resulted in 78 hits, using the above filters, and the following search details:(("meat"[MeSH Terms] OR 70 "meat"[All Fields]) AND fermented[All Fields] AND ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "outbreaks"[All 71 Fields] OR "disease outbreaks"[MeSH Terms] OR ("disease"[All Fields] AND "outbreaks"[All Fields]) OR "disease outbreaks"[All 72 Fields])) AND ("1985/01/01"[PDAT] : "2015/12/31"[PDAT]). The search was conducted in October 2015, and a final search and update 73 were conducted in July 2016. Selected manuscripts were then checked for other relevant references not obtained from direct 74 searches. For the purposes of this study, we defined a foodborne disease outbreak as the occurrence of two or more similar illnesses 75 resulting from the ingestion of a common food. Bacterial food-borne outbreaks that were included were those that were published in 76 peer-reviewed journals between January 1, 1980 and December 31, 2015 and were confirmed by laboratory diagnosis. 77

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79 Inclusion criteria

In the screening process, we first reviewed titles to check if selected articles were appropriate. Then all abstracts were screened, and if abstracts were relevant, we checked the full-text article considering the following inclusion criteria: (i) At least two of the cases were laboratory confirmed; (ii) The incriminated food was given, (iii) Sufficient data was given on the cases. Exclusion criteria were the following criteria: (i) No sufficient data are given to compare the results and ii) outbreaks due to poultry meats were also excluded. Out of the 78 PubMed search results, 28 were further screened and 11 results were included in the study. Using the Web of Science search, out of the 77 results, 13 were further screened and 6 were included. Using the Google Scholar, yielded 39 results that were further screened and 17 of those met the study criteria. Further outbreak studies were screened from the related references. Duplicates were checked for year and characteristics of outbreaks and excluded from the study.

The outbreak details of all papers meeting our inclusion/ exclusion criteria for etiology and food vehicle were entered into an Excel sheet and checked by two of the authors, before data analysis. Thus, we included all outbreaks reported in peer reviewed publications from 1980-2015, caused by any bacterial enteric pathogen, in which the implicated food item included beef, lamb, pork and meat products thereof.

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93 Entities and variables

We recorded variables from the entities Outbreak, Cases and Incriminated products. Our database included (i) **Outbreak**, with variables: Year outbreak, Incriminated meat product, Main reason, Pathogen, Serovar, Country, State, International, Age Minimum, Age Median, Age Mean and Age maximum; (ii) **Cases**, with variables Diarrhoea, Bloody diarrhea, HUS, Neurological, thrombotic thrombocytopenic purpura (TTP), Bacteremia/Septicemia, Nausea-vomiting, Abortion, Allergy, Hospitalization, and Death; and (iii) **Incriminated product**, with variables Heat treatment, Salt content, nitrate/nitrite content, a_w, pH, casings, drying, starter culture and fat content. 100 Meat categories

The meat products linked to outbreaks of disease were classified into the following four categories, as defined in Annex I of Regulation
 (EC) No 853/2004 (EU Commission 2004):

103 1. Fresh processed meat products: Hamburgers, barbecue meat and fresh sausages were included in this category.

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Salted dried meat products: Whole muscle cuts, like ham and bacon, treated with dry salt or a curing solution (pickling), dry cured, smoked and/or seasoned. Shoulders and legs of pork are the pieces most commonly cured. Examples of this type of
 products are dry-cured ham, cecina, jerky, and fenalår. In the European Union legislation, they are known as meat products.

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Raw cured fermented sausages: The meat can come from beef, veal, pork, lamb, or a combination of these species. Some sausages are made from meat that is cured and smoked before it is minced; most sausages are formed first (mincing, salting), and then cured, smoked, or treated by a combination of these processes. Production of dry and semi-dry sausages requires carefully controlled fermentation and drying. There is a variety of this kind of products including chorizo and salami. The legislation describes those as meat products.

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Cooked meat products: Cooked ham, frankfurters, bologna, etc. are typical products included in this category. Products such as
 mortadella, bologna, frankfurters and many loaf types of luncheon meat are made from finely ground meat emulsions. Some
 cooked sausages are made from meat that is cured, smoked or cooked before it is ground; other sausages are formed first, and
 then cured, smoked, cooked (in another category) or treated by a combination of these processes.

119 Data analysis

The Excel[®] database of meat-associated outbreaks included information on year of outbreak, median age of patients, agent, serovar, food incriminated, food category, main reason, number of cases, number of cases that were laboratory-confirmed, number of hospitalizations, deaths, and location and cases with HUS for the *E. coli* related outbreaks. The variables that had enough data to be compared were statistically descriptive using mainly tables and graphs statistics in Excel[®] or SPSS (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.)

126 **Results**

The two organisms causing most reported meat-related outbreaks were verotoxin-producing Escherichia coli (VTEC) and Salmonella. 127 The details of the *E. coli* outbreaks (n=33) is shown in Table 1. The details of the Salmonella outbreaks (n=21) is shown in Tables 2. 128 In the E. coli outbreaks, the total number of reported cases was 1966, of which 1543 (78.4%) were laboratory confirmed. The number 129 of cases requiring hospitalization was 476 (24.2 %), of whom 233 (48.9 %) cases had a hemolytic-uraemic syndrome (HUS), and the 130 reported deaths were 32 (1.6 %). While in the Salmonella outbreaks the total number of all reported cases were 2279, of whom 1891 131 (83 %) were laboratory confirmed. The number of reported cases requiring hospitalization was 94 (4.1 %), and seven (0.3 %) were 132 reported dead. Other organisms linked to meat-associated outbreaks, but less frequently reported, were Staphylococcus aureus, 133 Bacillus cereus, Clostridium perfringens, Clostridium botulinum, and Listeria monocytogenes. 134

135 Outbreaks due to *E. coli*

In our survey, 16/33 (48.5 %) of the VTEC outbreaks were reported from the USA. Most (n=29) of the outbreaks, were caused by 136 serovar O157:H7 (87.8%), while the other four outbreaks were caused by the O111:H8, O26:H11, O111, and O103:H25. As shown 137 in Figure 1, fresh processed meat products was the category most frequently implicated, in 17/33 (51.5%) of the outbreaks. The 138 second meat category most frequently implicated was raw cured fermented sausages, linked to 11/33 (33.3 %) of the outbreaks. As 139 shown in Figure 2, the most extensive outbreak, caused by *E. coli* O157:H7, with more than 600 cases was in 1992/93, in the USA, 140 and hamburgers were incriminated as the source of infection. The highest number of outbreaks (5) was seen in 2009 as shown in 141 Figure 3. Four of the outbreaks had more than 100 cases. Three had 51 – 100 cases, 20 had 10 – 50 cases, while six had less than 142 10 cases. 143

Table 3 shows the distribution of HUS cases by the total cases within a meat product category and out of the total cases. HUS cases were reported in raw cured fermented sausages (16.4%), cooked meat products (13.4%), fresh processed meat (10.3%), and unknown meat products (3.6%). The corresponding percentage of HUS cases out of all cases was 5.9% in fresh processed meat, 3.2
in cooked meat products, 2.6 in raw cured fermented sausages, and 0.1 in unknown meat products. In our survey, HUS was
diagnosed in at least one patient in 79.4 % of the outbreaks. In six of the outbreaks with *E. coli*, there were more than 10 cases of
HUS in each outbreak. In three of those outbreaks, all the cases developed HUS. Of those, two outbreaks were caused by Raw Cured
Fermented Sausages, while fresh processed meats were incriminated in the third outbreak.

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152 Outbreaks caused by Salmonella species

As shown in Figure 4, in total, there were 8 serovars that caused those outbreaks. The most common serovar causing Salmonella-153 related outbreaks was S. Typhimurium, involved in 61.9 % (13/21) of the total number of outbreaks. Figure 3 shows the time trends 154 which is the number of reported outbreaks per year. There were four outbreaks in 2005, of which the largest outbreak, with 525 cases 155 of infection, occurred in Germany in the same year, where raw minced pork and fermented sausages were implicated, and it was 156 caused by S. Bovimorbificans. The meat category most frequently implicated in the outbreaks (10/21) was raw cured fermented 157 sausages (47.6 %). The spectrum of serovars isolated from raw cured fermented sausages was broad, as 5 out of the 8 different 158 reported serovars were involved. Fresh processed meats and cooked meat products were implicated in 23,8 % of the outbreaks. We 159 did not record any Salmonella outbreak in peer-reviewed journals from 2010 – 2015. 160

161 Outbreaks caused by other bacterial pathogens

There were very few reported red meat related outbreaks caused by other pathogens, other than VTEC and *Salmonella*. For some pathogens, there are simply too few outbreaks with identified food vehicles to estimate attribution. Regarding outbreaks caused by toxins of *C. botulinum*, an outbreak in Taiwan was attributed to fermented goat meat (Tseng, Tsai et al. 2009) and a special outbreak in Alaska was attributed to fermented beaver tail and paw (CDC 2001). 166 Clinical listeriosis mainly occurs in particular at-risk groups: pregnant women, elderly people, immunocompromised people, unborn 167 babies, and neonates (Maertens de Noordhout, Devleesschauwer et al. 2014). Human listeriosis is a relatively rare, but serious 168 zoonotic disease associated with high hospitalization and high lethality rates in these vulnerable populations. Of all the zoonotic 169 diseases under EU surveillance, listeriosis causes one of the most severe human diseases, but few outbreaks are reported each year 170 and very few of them are associated with meat and meat products. Except for one outbreak reported in 2013, related to meat and 171 meat products with 34 cases, listeriosis outbreaks involved two to four cases each, resulting in 51 cases, 11 hospitalizations and 2 172 deaths (EFSA 2015).

A multistate outbreak of listeriosis was reported in the United States in 1998 that caused illness in 108 persons residing in 24 states and caused 14 deaths and four miscarriages or stillbirths (Graves, Hunter et al. 2005). The outbreak was associated with contaminated hot dogs. In a study in the USA on foods implicated in outbreaks, (1998 – 2008) it was reported that out of the confirmed outbreaks related to meat, 4/208 (1,9 %) were caused by *Bacillus cereus*, 71/208 (34,1 %) were due to *Clostridium perfringens*, and 45/208 (21,6 %) were due to *Staphylococcus aureus* (Bennett, Walsh et al. 2013).

Food handling by a food worker after food preparation was mainly involved in *Staphylococcus* outbreaks, as the organism but not the toxins are usually eliminated by cooking and pasteurization. In contrast to *C. perfringens* and *S. aureus*, *B. cereus* outbreaks were most commonly associated with rice or fried rice dishes (Stewart 2005, Stenfors Arnesen, Fagerlund et al. 2008).

182 Discussion

Out of 9,6 million estimated annual domestically acquired foodborne illnesses in the United States, 1998 – 2008, with known etiology, caused by bacterial, viral, parasitic and chemical agents, 1,174,257 (12.2 %) were attributed to meat. Out of all foodborne illnesses (3,645,773) due to bacterial agents, in the study, 844,006 (23.2 %) were attributed to meat (Painter, Hoekstra et al. 2013). In the same study, an estimated 130/862 (15.1 %) deaths each year due to bacterial agents were attributed to meat, and an estimated 5,238/35,979 (14.6 %) of annual hospitalizations due to bacterial agents were attributed to meat. Among the 839 strong evidence outbreaks of salmonellosis reported by 24 European Union member states in 2013, pig meat and products thereof accounted for 7.7 %, while bovine meat and products thereof were identified as a source vehicle in 3.6 % (EFSA 2015).

In the EU, where the most commonly reported VTEC serovar in 2013 was, as in previous years, O157 (48.9 %) of cases with known serovar and serovar O26 was the second most common in meat (EFSA 2015). This was in agreement with our study as the most commonly isolated serovar was also O157. Between 1983 and 2002, in a study in the USA, of human non-O157 Shiga toxin-producing *E. coli* (STEC) isolates from persons with sporadic illnesses, the most common serovars were O26 (22%), O111 (16%), O103 (12%), O121 (8%), O45 (7%), and O145 (5%) (Brooks, Sowers et al. 2005). The more frequent isolation of non-O157 STECs has been shown to correlate nicely with the gradual introduction of culture-independent enzyme immunoassay tests in laboratories (Gould, Walsh et al. 2013).

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In 2014, 13 of the member states in the EU reported 39 outbreaks where VTEC was reported as the causative agent (excluding waterborne outbreaks). These outbreaks involved 270 cases and 34 hospitalizations, and eight of these outbreaks were caused by VTEC O157. Meat and meat products were not incriminated in the strong evidence supported outbreaks, but four outbreaks were categorized originating from "bovine meat and products thereof" in the weak-evidence outbreaks (EFSA 2015). In the same publication, 23 Member states in the EU reported a total of 1,048 food-borne outbreaks (225 strong-evidence, 823 weak-evidence) caused by *Salmonella* (excluding one strong-evidence water-borne outbreak) (EFSA 2015). These outbreaks involved 9,226 cases, 1,944 hospitalizations, and 14 deaths. Distribution of food vehicles in strong-evidence outbreaks caused by *Salmonella* in the EU, 2014, was 225 outbreaks (9.3 % of the outbreaks) were attributed to pig meat and products thereof, 3.1 % to meat and meat products, 2.7 % to buffet meats, and 2.2% to bovine meat and products thereof.

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208 S. Typhimurium was the serovar most frequently (40 %) implicated in pigs and pig meat as well as bovine meat in strong-evidence 209 outbreaks reported in the European Union (EFSA 2015). In a study in the United States, thirty serovars caused beef related outbreaks 210 during 1973-2011, with the most common being Typhimurium (16 outbreaks), Newport (15), and Enteritidis (8). This is in agreement 211 with our findings as the most common serovar causing *Salmonella*-related outbreaks was *S*. Typhimurium. Outbreaks caused by 212 serovars Newport and Typhimurium also accounted for more illnesses and hospitalizations than any other single serovar (Laufer, 213 Grass et al. 2015).

The *Listeria* outbreak from Canada (Currie, Farber et al. 2015) demonstrated the need for improved listeriosis surveillance, strict control of *L. monocytogenes* in establishments producing ready-to-eat foods, and advice to vulnerable populations and institutions. However, even though being ready-to-eat products, no reported outbreak has been connected to raw cured fermented sausages through all these years. This strongly indicates that bacteriological surveillance for *Listeria* and corrective actions like retractions or recalls, from these products are not risk-based, e.g. Food safety criteria (EU Commission 2005).

We had to confine the analysis to those variables reported in most outbreaks in our study. This highlights an important gap in the literature. The medical community tends to report on outbreak and case entities but focus very little on characterizing the incriminated

products. The food science community tends to study the potential growth, survival, or decimation of pathogens under conditions 221 relevant for production and distribution of foods. Similarly, National public health institutes have a long tradition of reporting outbreaks 222 in scientific journals like Eurosurveillance or Morbidity and Mortality Weekly Report (MMWR). National Food Authorities do not have 223 the same tradition, and management of outbreaks and crises tend to stop after governmental actions, like a retraction, recalls, and 224 closure of production premises, take place. The rationale for corrective actions undertaken is seldom peer reviewed. Authorities have 225 paid less attention to quality aspects of foods, and laboratory services are in many countries outsourced. Multidisciplinary 226 competences are needed to draw sound conclusions from outbreak data, and it is our opinion that a deeper and applied understanding 227 of microbiology, processing steps and technological aspects of industrial production is needed, as well as peer-reviewed publishing 228 of risk and event management. 229

Surveillance systems vary between countries and thereby the likelihood that an outbreak is reported also depends on the country and its reporting systems (Callejon, Rodriguez-Naranjo et al. 2015). Outbreaks were mainly reported from industrialized countries, and apparently represent a bias from available resources or priorities.

It has been reported that the more extensive an outbreak, the more likely it is to represent a major and unusual failure in food safety
systems, the more likely it is to have been noticed and thoroughly investigated, and the more likely it is that the vehicle will be identified
(Batz, Hoffmann et al. 2012, Callejon, Rodriguez-Naranjo et al. 2015).

Outbreaks from a non-conformant batch or resulting from systematic errors in large food producers are more easily detected in public surveillance systems (Callejon, Rodriguez-Naranjo et al. 2015). From England and Wales only 3 % of outbreaks reported to national surveillance systems were published in peer-reviewed literature (O'Brien, Gillespie et al. 2006). It is also reported that, when the outbreak size varies by food category, attribution percentages based on a number of cases become skewed towards those foods more likely to cause extensive outbreaks (Batz, Hoffmann et al. 2012). An effect of increased awareness and intensified laboratory testing increases the likelihood of detection. Increased notification rates were observed in the EU in the two consecutive years (EFSA 242 2015) also for other serovars than O157 following the large outbreak caused by VTEC O104:H4 in Europe in 2011 (EFSA 2011).
243 Since the large outbreak in 1993, minced meat products have been put at the front of investigators' minds when STEC outbreaks
244 occur, while a lot of other food items have emerged as essential sources or vehicles (Lynch, Tauxe et al. 2009, Heiman, Mody et al.
245 2015).

Based on calculation of Publication Bias Index (PBI) in the UK, it has been reported that peer-reviewed publications underestimate those outbreaks that are due to red meat and meat products, poultry, fish, egg and egg products while overestimating the impacts of milk and milk products (O'Brien, Gillespie et al. 2006). Hence, the freshly processed meat category, containing big volume products, might be relatively overrepresented among the reported outbreaks.

250 Methods for source attribution

There are several methods for attribution of foodborne illnesses to their source. Five basic approaches to source attribution have been reported (Batz, Hoffmann et al. 2012).

We categorized the meats according to the definitions given in the European Union Legislation and found them comprehensive and relevant.

Attribution approaches also differ in their points of attribution, where "point of production" approaches focus on primary food production activities, whereas "point of consumption" approaches, focus on food vehicles that directly lead to exposure (e.g., *E. coli* O157 in hamburgers) (Batz, Doyle et al. 2005, Batz, Hoffmann et al. 2012). Primarily, the outbreak papers tended to focus on the point of consumption (case-controls, bacteriological analyses of products), and secondarily the investigation turns at the point of production. Both governmental and industrial risk managers need insight in these investigations beyond the determination of the source of infection.

262 Food matrices and pathogen

The food matrix may affect virulence. In addition, more likely, serious illnesses where patients are hospitalized, are probably more 263 frequently detected and reported. Our results show that the majority of STEC outbreaks were rather small outbreaks compared to 264 Salmonella outbreaks. The median number of cases was 21 for outbreaks caused by E. coli and 58 for Salmonella, respectively. 265 Generally, outbreaks from small food producers are not easily detected as they cannot be easily distinguished from sporadic cases. 266 Geographical or organizational collaboration and exchange of information are crucial for identification of outbreaks and sources of 267 infection when the distribution of patients gets complicated in time or space. Our results indicate that likelihood for detection and 268 notification depends on the severity of disease and not at least the presence of pathognomonic symptoms (HUS) or deviating 269 bacteriological properties (sorbitol fermenting E. coli O157). Another example illustrating the impact of unusual appearance in the 270 laboratory, was an outbreak caused by a rare Salmonella phagevar (14b) easily distinguished in the laboratory from other S. Enteritidis 271 isolates (Guerin, Nygard et al. 2006). 272

A shift has been observed in the type of beef implicated, from roast to ground beef (Laufer, Grass et al. 2015). While delicatessenstyle roast beef cooked in commercial processing establishments was the predominant type during the 1970s and early 1980s, regulations on cooking and processing virtually eliminated this problem by 1987 and ground beef emerged as an important vehicle in the 2000s (Laufer, Grass et al. 2015). In our survey, *S.* Typhimurium related outbreaks were mainly caused by fresh processed sausages and the main reason for food implication was undercooking or inappropriate hygienic practices during preparation. Interestingly, no reported *Salmonella* outbreak has occurred after 2010, where meat and meat products have been incriminated as a source of infection. Possibly this reflects improved meat hygiene, and not a publication bias.

280 Food production systems

In our survey, about 50 % of the *E. coli* outbreaks, worldwide, were reported from the USA. It is reported, that regarding O157, including sporadic cases, 88 % were traced to ground beef and 89 % occurred in the US. High level of ground beef consumption at fast food restaurants and the availability of *E. coli* O157 diagnostic methods were hypotheses explaining the large number of US outbreaks and cases (Hussein 2006). However, this trend was not seen from the *Salmonella* data, where only 2 out of 21 outbreaks caused by meats were reported from the USA. This is probably partly due to a significantly different prevalence in value chains, maybe consumption patterns, while medical, including diagnostic tools, and reporting systems are unlikely explanatory factors. However, different production systems that may relatively favour STEC but not *Salmonella* could also be of interest.

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289 Risk management

Categorization schemes used for broad evaluation of risks across the entire food supply chain are likely to be quite different from 290 those useful for targeted risk management (Batz, Hoffmann et al. 2012). Risk managers need to combine information both on 291 outbreaks, incidence rates and pathogens' abilities to survive and grow to perform appropriate HACCP-analyses and make risk-based 292 priorities. It is important that outbreak reports consider the relevant products' characterizations for pathogen growth and survival. A 293 zero-risk level does not exist. An important question is therefore whether an outbreak occurred as a consequence of human errors 294 like sublethal heat treatment or evitable cross-contamination, or if the outbreak is a result of an unlikely event. The Food Business 295 Operators (FBO) are responsible for producing safe food. The trade-off between having food to eat and trust in safe consumption 296 cannot be omitted. It is therefore our opinion that the reactions towards the FBOs should be conditional depending on the likely 297 causation of outbreaks; it is a significantly different case when an outbreak may result from blameworthy errors or neglecting hygienic 298 rules or principles, or if the outbreak is due to a systematic but accepted weakness of the regulations, product or the process. 299

300

301 Potential biases

We searched for the terms, "meat, fermented, outbreaks" as we were interested in particular, to illustrate different risks posed from 302 raw cured fermented meats and other main product categories. The inclusion of the term 'fermented' may have generated a bias 303 towards identifying more outbreaks generated by fermented meats. But we used different search resources to capture as many 304 outbreaks as possible. We carried out a thorough search for published outbreaks in the literature. Outbreaks that occurred in the 305 less developed countries and those that were reported in other languages than English, as well as many of those reported to 306 national surveillance programs may have been missed. Outbreaks that may cause many severe clinical outcomes or cause many 307 deaths, or where incentives are given to produce publications, may result in publication bias. As such, the representativeness of our 308 data remains uncertain. 309

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311 Conclusions

The recognition of dry fermented sausages as a potential threat to food safety has been recognized by several countries and measures has been taken to reduce the risks. Thus, the aims of the study were to review global outbreaks where red meat and meat products were incriminated as a source for outbreaks, with a focus on fermented meats. Our review seems to indicate that the number of reported outbreaks linked to meats may have declined over the last decades. Meat-related outbreaks are still dominated by *Salmonella* and VTEC. It is difficult to be certain on whether this trend is real, as there are many reporting potential biases in this area. We were not able to find enough reports to conclude on the potential risk for the public linked to cured, fermented sausages.

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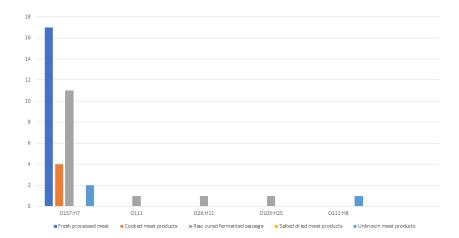
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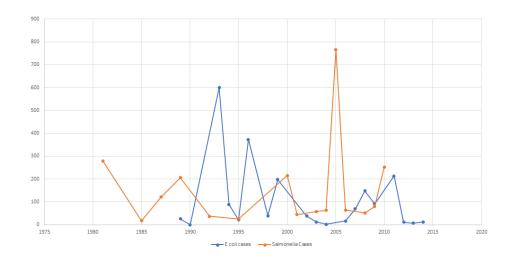
541 Figure 1. The distribution of *E. coli* serovars identified in the reported outbreaks as related to the meat categories implicated

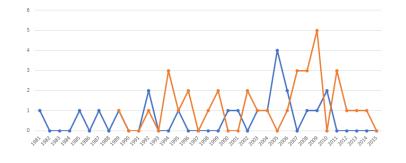
542 Figure 2. The size of the reported *E. coli* and *Salmonella* outbreaks as related to the total reported number of cases per outbreak-543 year

544 Figure 3. Time-line trend graph for the reported E. coli and Salmonella outbreaks that shows number of outbreaks per year

545 Figure 4. The distribution of *Salmonella* serovars identified in the reported outbreaks as related to the meat categories implicated







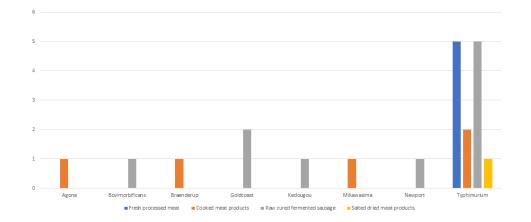


Table 1. Outbreaks caused by Shiga toxin-producing *E. coli*

Outbreak Year	Biovar	Food incriminated	Food category	Main reason	No. of cases	Age median	Laboratory- confirmed	Cases with HUS	Hospital- ization	Death	Location	Reference
1989	O157H7	Turkey roll/ tinned frankfurter sausages/ pork pie	Cooked meat products	cross- contamination	26	25	13	1	6	0	England	(Salmon, Farrell et al. 1989)

1992/ 1993	O157H7	Hamburgers	Fresh processed meat	undercooked	600	6	501	39	39	3	USA	(Obrien, Melton et al. 1993, Brandt, Fouser et al. 1994, Bell, Griffin et al. 1997)
1994	O157H7	Hamburgers	Fresh processed meat	undercooked	8	NA	7	NA	NA		UK	(Willshaw, Thirlwell et al. 1994)
1994	O157H7	Roast beef/waldrof salat	Cooked meat products	undercooked	61	28	35	0	0	0	USA	(Rodrigue, Mast et al. 1995)
1994	O157H7	Dry-Cured Salami	Raw cured fermented sausage	No errors in food handling observed	20	6	20	1	3		USA	(Alexander, Boase et al. 1995, CDC 1995, Tilden, Young et al. 1996)
1995	O111	Semi-Dry Fermented Sausage (mettwûrst)	Raw cured fermented sausage	short maturation?	21	NA	20	21	20	1	Australia	(Paton, Ratcliff et al. 1996, Jureidini, Henning et al. 1997, Henning, Tham et al. 1998)
1996	O157H7	(Mortadella) Teewürst	Cooked meat products, Raw cured fermented sausage	Raw meat?	28	NA	12	28	12	3	Germany	(Ammon, Petersen et al. 1999)
1996	O157H7	contaminated cooked meats	Cooked meat products	cross- contamination	345	63	279	34	120	16	Scotland	(Cowden, Ahmed et al. 2001, Dundas, Todd et al. 2001)
1998	O157H7	Genoa salami	Raw cured fermented sausage	short maturation?	39	16	36	2	14		Canada	(Williams, Isaacs et al. 2000)
1999	O111H8	Various	NA	NA	55	16	2	2	2		USA	(Brooks, Bergmire-Sweat et al. 2004)

1999	O157H7	Salami	Raw cured fermented sausage	NA	143	12	143	6	42	0	Canada	(MacDonald, Fyfe et al. 2004)
2002	O157H7	Fermented sausage	Raw cured fermented sausage	NA	30	19	29	9	13	0	Sweden	(Sartz, De Jong et al. 2008)
2002	O157H7	Minced meat	Fresh processed meat	Undercooked	8	14	7	3	3	0	USA	(Vogt and Dippold 2005)
2003	O157H7	Tenderized marinated steak	Fresh processed meat	undercooked	12	NA	10	1	0	0	USA	(Laine, Scheftel et al. 2005)
2004	O157H7	Dry-fermented pork salami	Raw cured fermented sausage	NA	2	60	2	0	2	0	Italy	(Conedera, Mattiazzi et al. 2007)
2006	O103H25	Dry cured sausage	Raw cured fermented sausage	NA	16	NA	15	10	14	1	Norway	(Schimmer, Nygard et al. 2008)
2007	O157H7	Beef cooked	Cooked meat product	cross- contamination	9	70	9	NA	NA	1	Scotland	(Stirling, McCartney et al. 2007, McCartney, Cowden et al. 2010)
2007	O157H7	Frozen ground patties	Fresh processed meat	undercooked	40	NA	40	2	25	0	USA	(CDC 2007)
2007	O26H11	Organic fermented beef sausage	Raw cured fermented sausage	NA	20	2	20	0	0	0	Denmark	(Ethelberg, Smith et al. 2009)
2008	O157H7	Ground beef	Fresh processed meat	NA	64	21	64	2	38	0	USA	(CDC 2010)
2008	O157H7	Ground beef	Fresh processed meat	NA	35	18,5	35	1	22	0	USA	(CDC 2010)
2008	O157H7	Ground beef	Fresh processed meat	undercooked	49	NA	49	NA	27		USA	(CDC 2008)
2009	O157H7	Fermented deer sausage	Raw cured fermented sausage	non-compliant small scale production	5	6	5	2	5	0	USA	(Ahn, Russo et al. 2009)

2009	O157H7	Steak tartare	Fresh processed meat	undercooked	17	41	17	0	7	0	Holland	(Greenland, de Jager et al. 2009)
2009	O157H7	Beef primals, ground beef	Fresh processed meat	undercooked	23	NA	17	2	16	0	USA	(CDC 2009)
2009	O157H7	Ground beef	Fresh processed meat	NA	26	NA	24	5	19	2	USA	(CDC 2009)
2009	O157H7	Beef tenderized	Fresh processed meat	NA	21	34	21	1	9	0	USA	(CDC 2010)
2011	O157H7	Lebanon bologna beef semi-dry fermented	Raw cured fermented sausage	NA	14	13,5	14	0	3	0	USA	(CDC 2011)
2011	O157H7	Beef raw	Fresh processed meat	undercooked	181	NA	55	34	NA	5	Japan	(Watahiki, Isobe et al. 2014)
2011	O157H7	frozen ground beef	Fresh processed meat	NA	18	NA	12	18	6	0	France	(King, Loukiadis et al. 2014)
2012	O157H7	Ground beef	Fresh processed meat	undercooked	11	14	11	8	NA	NA	Denmark	(Soborg, Lassen et al. 2013)
2013	O157H7	Beef tartare	Fresh processed meat	undercooked	7	NA	7	1	2	0	Canada	(Gaulin, Ramsay et al. 2015)
2014	O157H7	Ground beef	Fresh processed meat	undercooked	12	25	12	0	7	0	USA	(CDC 2014)

554

555 *Not available

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Table 2: Reported outbreaks caused by Salmonella spp.

Outbrea k Year	Biovar	Food incriminated	Food Categor y	Main reason	No. of case s	Age media n	Laborator y- confirmed	Hospitalizatio n	Deat h	Location	Reference
1981	Newport	Salami	Raw cured fermente d sausage	NA*	279	NA	279	2	NA	Australia	(Taplin 1982)
1985	Typhimurium	Bologna fermented sausage	Raw cured fermente d sausage	NA	17	NA	17	0	0	Holland	(van Netten, Leenaerts et al. 1986)
1987	Typhimurium	Salami sticks Germany	Raw cured fermente d sausage	short maturation?	121	6	101	19	NA	England	(Cowden, O'Mahony et al. 1989)
1989	Typhimurium	cold roasted pork	Cooked meat products	Inadequate heating	206	NA	31	19	0	England	(Maguire, Codd et al. 1993)
1992	Mikawasima	Döner kebab	Cooked meat products	Cooking & handling faults/contaminati on	9	25	9	0	0	England	(Synnott, Morse et al. 1993)
1992	Typhimurium	Cooked ham re- contaminated	Cooked meat products	Faulty cooking	28	NA	28	2	1	Wales, UK	(Llewellyn, Evans et al. 1998)
1995	Typhimurium	Lebanon bologna Semidry fermented sausage	Raw cured fermente d sausage	bad procedures	26	NA	26	NA	NA	USA	(Sauer, Majkowski et al. 1997)
2000	Braenderup	Meat pies	Cooked meat products	bad procedures	215	NA	215	NA	NA	Switzerland	(Rossier, Urfer et al. 2000)
2001	Goldcoast	Fermented sausage	Raw cured fermente d sausage	NA	44	54	44	NA	NA	Germany	(Bremer, Leitmeyer et al. 2004)

2003- 2004	Typhimurium	Ground beef	Fresh processe d meat	NA	58	49	30	11	0	USA	(Dechet, Scallan et al. 2006)
2004	Typhimurium	Salami corallina Fermented pork salami	Raw cured fermente d sausage	undercooked	63	7,5	63	NA	NA	Italy	(Luzzi, Galetta et al. 2007)
2005	Bovimorbifica ns	Pork raw minced/ fermented sausage (Zwiebelmettwur st)	Raw cured fermente d sausage	NA	525	NA	525	NA	1	Germany	(Gilsdorf, Jansen et al. 2005)
2005	Typhimurium	Salami Italian	Raw cured fermente d sausage	undercooked	32	NA	15	NA	NA	Sweden	(Hjertqvist, Luzzi et al. 2006)
2005	Typhimurium	Capaccio Italian	Fresh processe d meat	NA	40	NA	32	NA	0	Denmark	(Ethelberg, Sorensen et al. 2007)
2005	Typhimurium	Beef Italian steak tartare	Fresh processe d meat	raw meat consumption	169	NA	32	NA	NA	Holland	(Kivi, Hofhuis et al. 2007)
2006	Kedougou	Salami danish style	Raw cured fermente d sausage	NA	54	NA	54	NA	1	Norway	Emberlan d KE et al. 2006
2006	Typhimurium	Spanish chorizo	Salted dried meat products	undercooked	10	NA	10	NA	NA	Norway/Denmar k/	(Nygard, Lindstedt et al. 2007)
2008	Typhimurium	Fresh pork	Fresh processe d meat	NA	51	54	51	NA	4	Norway, Denmark Sweden	(Bruun, Sorensen et al. 2009)
2009	Goldcoast	Salami Mantovano	Raw cured fermente d sausage	raw meat consuption	79	50	79	NA	NA	Italy	Scavia et al. 2013

2010	Agona	Precooked meat	Cooked meat products	undercooked	163		163	NA	NA	Ireland	(Nicolay, Thornton et al.
2010	Typhimurium	Ground beef/ossenworst	Fresh processe d meat	undercooked	90	22	97 %	46 %	NA	Holland	2011) (Friesema, Schimmer et al. 2012)

559 NA* Not available

Table 3: Meat product categories related to reported cases with Hemolytic Uremic Syndrome (HUS)

Meat category	Cases With HUS	Total cases within category	HUS within category	HUS of all cases (N=1966)
Fresh processed meat	117	1132	10.3%	5.9%
Raw cured fermented sausage	51	310	16.4	2.6
Cooked meat products	63	469	13.4	3.2
Unknown meat products	2	55	3.6	0.1
Salted dried meat products	NA*	NA		
Sum ALL	233	1966	11.8	11.8

563 NA* No outbreak was reported due to this category