Application de l'attribution dans divers pays européens

Troisième article
Attribution de source appliquée à *Salmonella* dans différents pays européens

Article en préparation pour soumission à Foodborne Pathogens and Disease

Dans le cadre du projet « Human illness source attribution » du réseau d'excellence Med-Vet-Net, la méthode d'attribution par typage microbiologique, préalablement développée par le Danemark (Hald, Vose et al. 2004), a été adaptée dans 6 pays européens, dont la France. L'article qui suit présente ces démarches au travers des données de surveillance utilisées par chacun des pays, leurs caractéristiques (nombre de sources considérées, nombre de sérotypes inclus, mode de typage des souches…), les hypothèses posées et les résultats d'attribution obtenus. Il discute ensuite l'hétérogénéité des résultats d'attribution par source entre les différents pays, l'importance constante des cas exogènes (résultant d'un voyage) et l'absence de convergence pour certains pays.

Cet article est en préparation pour soumission à Foodborne Pathogens and Disease.

Salmonella source attribution in different European countries

S.M. Pires[1*], G. Nichols[2], H. Whalstrom[3], A. Kaesbohrer[4], H. Spitznagel[4], W. Van Pelt[5], E. Snary[6], P. Nally[6], C. Frank[7], J. David[8], A. Baumann[9], T. Hald[1]

[1] National Food Institute, Technical University of Denmark, Lyngby, Denmark.

2 Health Protection Agency Centre for Infections, 61 Colindale Avenue, London NW9 5EQ, United Kingdom

[3] National Veterinary Institute, SE-75189 Uppsala, Sweden

[4]

[5] Epidemiology and Surveillance Unit, National Institute for Public Health and the Environment, Bilthoven, The Netherlands.

[6] Veterinary Laboratories Agency, Surrey, KT12 5JN, England.
[7]

[8] French Food Safety Agency, BP 90203, 35302 Fougères, France

[9] Department of Epidemiology, National Institute of Public Health, National Institute of Hygiene, Poland

* Corresponding author: Sara Monteiro Pires, National Food Institute, Technical University of Denmark. Mørkhøj Bygade 19, DK-2860 Søborg, Denmark. Tel: 45 5115 7464; Fax: + 4572347028. Email: smpi@food.dtu.dk.

Abstract

Salmonella spp. is a major cause of human gastroenteritis in Europe. Several countries have implemented interventions to control *Salmonella* in food-producing animals and foods. However, knowledge on the impact of such interventions in the incidence of salmonellosis in humans is sparse. Under the scope of the "Human Illness Source Attribution" working group supported by Med Vet Net (WP 28), we adapted a previously developed microbial subtyping approach for the attribution of human salmonellosis to specific sources in six European countries. The model estimates the number of domestic and sporadic cases caused by different *Salmonella* subtypes as a function of the distribution of these subtypes in the animal-food sources, the amount of food source consumed, and the differences between subtypes and sources in their ability to cause disease. The approach was adapted to surveillance data from Germany, the United Kingdom, the Netherlands, Sweden, Poland, and France. Adaptations were made according to data features and availability, and the results were interpreted in light of the differences in public health, animal and food surveillance, and food consumption figures. National source attribution models were successfully developed for the UK, Sweden, the Netherlands and France; the attempted models for Germany and Poland did not provide appropriate convergence. Results suggest that the most important sources of human salmonellosis vary between countries, and that international travel is the single most important cause of disease in the majority of the investigated countries. A comparison of both methods and results shows that the successful adaptation of this approach is dependent on the quality and representativeness of the available data. The model is a useful tool to estimate the most important sources of salmonellosis in the countries, and we encourage other countries to apply source attribution approaches to assist risk management and public health decisions.

1 Introduction

Human salmonellosis is a major cause of disease in Europe. In 2006, the incidence of human salmonellosis in European Union Member States (MS) was 34.6 per 100,000 inhabitants (EFSA, 2007). A wide variability is observed amongst the countries, and incidence estimates ranged from 3.0 to 321.5 per 100,000 population in the different countries (EFSA, 2007). This variability also reflects differences in surveillance and reporting systems in European countries.

During the last decades, several countries have implemented intervention programmes to prevent and control foodborne diseases, particularly foodborne zoonoses (Wegener et al., 2003; EFSA, 2006). However, precise measure of the public health impact of such interventions has been difficult, in part because the contribution of specific sources to the burden of foodborne diseases is often unknown. To prioritize appropriate food safety interventions, it is crucial to attribute the human disease burden of each foodborne infection to specific sources (Pires et al., 2009)..

In order to get a better understanding of the mechanism behind the dynamics in the occurrence of *Salmonella* infections in humans, Hald *et al* (2004) developed a *microbial subtyping approach* for source attribution. The method estimates the number of human cases attributable to each of the major animal-food sources. The method is routinely applied by the Danish Zoonosis Centre, National Food Institute, and its results are published in the Annual Report on Zoonoses in Denmark (e.g. Anon., 2006). Microbial subtyping has proved to be a valuable tool in focusing food safety interventions to the appropriate animal reservoir in Denmark, and provides an example of potential synergy between quantitative risk assessment and public health surveillance (Wegener et al., 2003;Hald et al., 2004).

An attempt to adapt the model to other European countries' data was made under the scope of the "Human Illness Source Attribution" working group supported by Med Vet Net (WP 28). National source attribution models for *Salmonella* were developed for Germany, United Kingdom, the Netherlands, Sweden, Poland, and France. The method was adapted according to the availability and features of the data, and the interpretation of results took into account differences in public health processes, animal and food production, and food consumption figures. We present a comparison of the methods and results from these models and the model applied to Danish surveillance data.

2 Material and Methods

2.1 Model overview

The model is built on the basis of the method described by Hald *et al.* (2004), where *Salmonella* subtypes isolated from animals and foods in a given year are compared with subtypes isolated from humans. The objective is to estimate the number of human cases that can be attributed to each source. The method is developed under a Bayesian framework and allows for the estimation of the contribution of additional factors, other than the prevalence of each type on the food/ source and the amount of food consumed, to the number of people infected with a particular type. These factors account for the differences in the ability of different *Salmonella* subtypes to cause disease and of different sources to act as a vehicle for infection.

The basic model attribution equation is

$$\lambda_{ji} = P_{ij} * m_j * a_j * q_i \qquad \text{(Equation 1)},$$

where λ_{ji} is the expected number of cases per type *i* and source *j*, P_{ij} is the prevalence of type *i* in source *j*, m_j is the amount of source available for consumption in the country, a_j is the source-dependent factor for source *j*, and q_i is the bacteria dependent factor for type *i*. The source and subtype related factors a_j and q_i were defined as uniform prior distributions. q_i for phage types within *S.* Enteritidis were fixed to 1, and all remaining q_i estimates are relative to this one.

2.2 Data used in the model

The original model attributes human sporadic and domestic *Salmonella* infections to specific sources based on the number of laboratory-confirmed infections caused by each *Salmonella* subtype, travel information for each case, prevalence of each subtype in the different sources, and amount of source available for consumption in the country. The number of outbreak cases per type (except 1 case) is subtracted from the total number of cases

reported per type to estimate the number of sporadic cases. The remaining outbreak-related cases are in the end added to the output of the model. Travel information and amount of food source available for consumption are not an absolute data requirement, and the model can be adapted without these parameters.

The variables and data differed between countries (Tables 1 and 2). This reflects differences in data availability with regards to typing of *Salmonella* isolates, travel information, number of sources tested, and testing of imported foods.

The sources included in the models also differed between the countries. These differences reflect not only availability of data, and thus coverage of national surveillance programmes, but also differences in consumption habits and in the importance of the sources. Cases were attributed to an "unknown" source if they were caused by subtypes not found in the sources considered in the model, or caused by subtypes grouped into "other serotypes", which the model could not attribute to any of the sources.

All models were run in the WinBUGS 1.4 software with five independent Markov chains of 40,000 iterations, each starting with a different set of initial values for the prior distributions. Convergence was monitored using the methods described by Gelman and Rubin (Gelman and Rubin, 1992) and was considered to have occurred when the variance between the different chains was not larger than the variance within each individual chain, and when the chains had reached a stable level.

The Swedish model

In the period between the 1st of July 2004 and the 31st of June 2006, 1,296 laboratory-confirmed sporadic cases, 227 outbreak-related cases and 5,859 travel-related cases were reported in Sweden. All *Salmonella* isolates were serotyped, and isolates of the serotypes Enteritidis and Typhimurium were phage typed. Salmonellosis sporadic cases were attributed to 10 sources: *imported food (including human foreign cases), pigs, cattle, layers, broilers, geese, passerine birds, seagulls, hedgehogs* and *unknown*. Data from travel related cases were included in the model as an addition to the available data on food. "Food" was considered as a single source, and grouped isolates from samples from different imported foods sampled at the retail level. The final model included 81 *Salmonella* subtypes, including "*Salmonella* others", which grouped subtypes that only caused few cases of disease and subtypes not found in any of the considered sources.

The UK model

In the United Kingdom, a total of 41,264 lab-confirmed cases were reported to the Health Protection Agency between 2003 and 2005. All *Salmonella* isolates were serotyped, and isolates of the serotypes Enteritidis and Typhimurium were phage typed. Human reported cases included information on travelling abroad, although there is evidence that this was not completed for all travel related cases. Human salmonellosis domestic sporadic cases were attributed to 6 domestic animals-food sources, *game bird* and *unknown*. The final model included 55 types (including "others").

The Dutch model

A total of 1,232 sporadic cases, reported in 2006, were included in the Dutch model and attributed to 4 sources: pigs, cattle, boilers and layers. All *Salmonella* isolates were serotyped, and isolates of the serotypes Enteritidis and Typhimurium were phage typed. The travel-related cases were extracted before modelling, and the proportion of the total salmonellosis cases attributed to *travelling* was added again to the output of the model. The dataset did not include human cases caused by subtypes not found in the animal sources. The final set included 48 types (including "others", which grouped the subtypes causing only few human cases).

The German model

44,294 human salmonellosis cases were reported in Germany. These were attributed to 6 sources: pork, beef, chicken, eggs, turkey and reptiles. All *Salmonella* isolates were serotyped, and isolates of the serotypes Enteritidis and Typhimurium were phage typed. Travel information was available for cases caused for all *Salmonella* serotypes, but not for phage types within *S*. Enteritidis and *S*. Typhimurium. Data on the amount of source available for consumption (m_j) of each source was included in the model; m_j for the source *reptiles* was assumed to be not available. The model included 67 types (including "others", which grouped isolates not found in the considered sources and infrequent subtypes).

The Polish model

The Polish dataset included 32,187 laboratory-confirmed cases, reported in 2005 and 2006. All isolates were serotyped, but no phage typing information was available. The data did not

include travel information. Nine sources, including domestic animal foods, aquatic products and wild animals, were considered in the model: pork, beef, poultry, eggs, shellfish, other animals, guinea fowl, buffalos and wild game.

The French model

The adaptation of the model to French data involved more substantial changes. The adaptation of the source account model to *Salmonella* French data was made at the French Food Safety Agency (AFSSA). The French dataset for 2005,.includes 9076 domestic sporadic lab-confirmed human cases as well as active surveillance data on layers, broilers, turkeys, pigs and cattle and passive surveillance data on those 5 channels plus sheep, ducks, other poultry and sea products. Data features include the serotyping of all *Salmonella* isolates and further subtyping of *S*. Enteritidis and *S*. Typhimurium by clusters of antimicrobial resistance profiles. The model included travel information and consumption data for the included sources. Sporadic *Salmonella* infections are being attributed to pigs, cattle, broilers, layers, turkeys, ducks, sheep, other poultry and sea products. The human data are provided by the National Reference Center for Salmonella and the National Public Health Institute (Institut de Veille Sanitaire). Regarding the agro-food sector, the active data are provided by the Food Directorate (Agriculture Ministry) and the passive data, by the Salmonella Network (French Food Safety Agency).

The Danish model

For the purpose of comparison of methods and results, we present the output of the Danish model (as described above and by Hald et al. (2004)) applied to Danish *Salmonella* surveillance data from 2007. In this model, cases caused by 54 *Salmonella* subtypes (including "others", which grouped isolates not found in the considered sources and infrequent subtypes) were attributed to eight sources: pork, beef, table-eggs, chicken, imported pork, imported beef, imported chicken and imported turkey.

3 Results

Adaptations of the *Salmonella* source attribution model were successful for data from the United Kingdom, Sweden, the Netherlands, and France. The models from Germany and Poland did not provide appropriate convergence, and thus results were not analyzed and are not presented. *Salmonella* source attribution estimates for France are in progress (David et al., in preparation).

The proportion of cases attributed to the main sources varied considerably between the three countries (table 3). In the UK, the food-source causing a higher proportion of cases was chicken, followed by table eggs and pork. In contrast, the majority of the salmonellosis cases in the Netherlands were estimated to be attributed to table eggs, followed by beef and pork. In Sweden, the most important source was *food*, which comprises cases caused by imported foods; wildlife sources, and the animal sources layers, cattle and chicken, all causing a very low proportion of cases (<1%), followed in order of importance.

Results suggest that international travel was the single most important cause of salmonellosis in the UK and Sweden. Likewise, the majority of salmonellosis in Denmark was attributed to travel. The proportion of cases attributed to travel in Sweden and in the Netherlands correspond to reported travel-related cases, and were not estimated. The proportion of cases attributed to an unknow source varied between 20 and 37% in the UK, Sweden and Denmark.In the Netherlands, only around 4% of the cases were attributed to *unknown,* but these cases correspond only to infections caused by infrequent types and do not include cases caused by subtypes not isolated from the sources considered in the model*.* As a consequence, this estimate is not comparable with the previous ones. The proportion of outbreak-related cases was higher in Netherlands, representing around 11% of the total cases of reported salmonellosis.

The UK and the Swedish models attributed human salmonellosis to sources not included in the other models. In the UK, around 2% of the cases were attributed to lamb, and 1.4% to the consumption of turkey. The Swedish model attributed around 6.8% of human disease to imported foods, and cases were also attributed to wildlife sources; around 0.2% could be attributed to geese, 0.2% to pass birds, 0.09% to seagulls, and 0.3% to hedgehogs.

The relative importance of the source (a_j) and the subtype (q_i) related factors differed between the countries (table 4). Results are not directly comparable and should not be contrasted in absolute numbers. Chicken and eggs were on the top three of the most importance countries for two countries. Regarding the ability of *Salmonella* subtypes to

cause disease, the order of importance varied in all countries, and only *S.* Newport was common to the top subtypes with highest ability to cause disease in two of the countries (UK and the Netherlands).

4 Discussion

The Danish source attribution model was adapted to attribute human salmonellosis in the UK, Sweden and The Netherlands. The three models differed in the number of *Salmonella* subtypes, number of sources, and type of sources included. A comparison of results was only possible for the sources included in the three models. These estimates were further compared with the results of the original model, applied to attribute human salmonellosis in Denmark.

A comparison of the relative proportion of the cases attributed to the common sources included in the three models and in the Danish source attribution model revealed that the contribution of the main animal-food sources varied between countries. *Table-eggs* was estimated to be the most important source of *Salmonella* infections in the Netherlands and Denmark, and a major contributer for human salmonellosis in the UK; in Sweden, this source was estimated to be of minor importance. Chicken was estimated as the major source of salmonellosis in the UK, and results of the Dutch model suggest cattle is a very important source of disease in the country. Travel was estimated to be the single most important cause of disease in the UK, Sweden and Denmark; in the Netherlands, travel-related cases were not modelled, and cases reported with a history of travelling were added to the output of the model. The presented proportion could therefore be an underepresentation of the true importance of international travel to human salmonellosis in the Netherlands.

In Sweden, the majority of the cases was acquired abroad or derived from the consumption of imported foods. A very low proportion of the cases was attributed to any of the food-animal sources. The low estimated proportion of cases attributed to domestic food-animals is explained by the very low prevalence of *Salmonella* in all food producing animals in the country. Sweden's *Salmonella* control program covering the entire food chain, from feed to fork, was implemented over 50 years ago, and interventions have proven successful in

reducing both the levels of *Salmonella* in the whole production chain and the burden of human salmonellosis attributed to domestic sources.

Even though the model provided appropriate convergence, the results of the Dutch model were not coherent with results from a previously developed source attribution approach that utilized the same data (Van Pelt et al., 1999;Valkenburgh et al., 2007). The principle of this method is very similar to the model developed by Hald et al. (2004), but the statistical methods differ. Despite these differences, we would expect results to be similar. However, the order of importance of the four sources included in the estimates differ, and the original Dutch approach attributes 29% of cases to table eggs, 21% to pigs, 11.6% to chicken and 11% to cattle compared to 41% for table eggs, 11% for pigs, 16% for cattle and 0.6% for chickens in this model.

The relative importance of the estimated source-dependent factors (a_j) was substantially variable in the three developed models and Denmark. In all models, these factors account for relative differences in food consumption, sensitivity of the surveillance programmes, variability of the sampling schemes and specific characteristics of the foods that may influence their ability to act as a vehicle for infection, e.g. fat content, preparation and processing, etc. It is also noteworthy that these estimates should not be compared in absolute numbers, especially between countries that do not include food consumption data in the models (e.g. UK, Sweden, the Netherlands) and countries that do (Denmark).

The *Salmonella* subtypes with highest ability to cause disease varied significantly in the three countries. These estimates account for differences in the survivability of the various *Salmonella* subtypes along the food chain, and potentially differences in their pathogenicity to humans. However, the method is a sort of "black box" model and the q_i values do not translate into virulence of the specific subtypes. In addition, it is expected the most important subtypes in different countries are a reflection of the occurrence of subtypes in those countries, as well of the different types of sources the population is exposed to.

The model developed for Poland did not converge. The available data had little discriminatory power (only serotype information), and merged information for multiple years. Despite the discriminatory power of the German data, which included serotyping and phage typing of the isolates, the model developed for Germany also did not provide appropriate convergence.

An adaptation of the source account model to *Salmonella* French data is in progress at the French Food Safety Agency.

Conclusion

The successful adaptation of the model is totally dependent on the quality and representativeness of the available data. Still, the approach has proved useful for the attribution of human salmonellosis, and therefore for the identification of the most important sources of *Salmonella* in different countries. We conclude that the presented source attribution approach is a valuable tool for the implementation of public health intervention strategies in different countries, and to point out areas for future research and data collection.

References

Gelman, A., Rubin, D., 1992. Inference from iterative simulations using multiple sequences (with discussion). Statistical Sciences 7, 457-511.

Hald, T., Vose, D., Wegener, H.C., Koupeev, T., 2004. A Bayesian approach to quantify the contribution of animal-food sources to human salmonellosis. Risk Anal. 24, 255-269.

Pires, S.M., Evers, E.G., van, P.W., Ayers, T., Scallan, E., Angulo, F.J., Havelaar, A., Hald, T., 2009. Attributing the human disease burden of foodborne infections to specific sources. Foodborne Pathog. Dis. 6, 417-424.

Valkenburgh, S., Oosterom, R., Van Stenvers, O., Aalten, M., Braks, M., Schimmer, B., Giessen, A., Van Pelt, W., Langelaar, M. Zoonoses and zoonotic agents in humans, food, animals and feed in the Netherlands 2003-2006. RIVM rapportnummer:330152001 ISBN-13, 978-90-6960-184-7. 2007.
Ref Type: Report

Van Pelt, W., Van De Giessen, A.W., Leeuwen, W.J., Wannet, W., Henken, A.M., Evers, E.G. Oorsprong, omvang en kosten van humane salmonellose. Deel 1. Oorsprong van humane salmonellose met betrekking tot varken, rund, kip, ei en overige bronnen. Infectieziekten Bulletin , 240-243. 1999.
Ref Type: Report

Wegener, H.C., Hald, T., Lo Fo, W.D., Madsen, M., Korsgaard, H., Bager, F., Gerner-Smidt, P., Molbak, K., 2003. Salmonella control programs in Denmark. Emerg. Infect. Dis. 9, 774-780.

Country	Typing		Travel	Food consumption data
	Serotyping	Phage typing		
UK	+	+	+	-
Sweden	+	+	NM*	-
Netherlands	+	+	NM*	-
France	+	+**	+	+
Germany	+	+	+	+
Poland	+	-	-	-
Denmark	+	+	+	+

*NM: not modelled
** : other subtyping method
+: Data included in the model
-: Data not included in the model

<u>Table 1</u>: Variables used in the different European models

Country	Sources				
	Food/ Dom. Animals	Food/ Game	Food/ Seafood	Food/ Imported	Wildlife
UK	+	+	-	-	-
Sweden	+	+	-	+*	+
Netherlands	+	+	-	-	-
France	+	-	+	-	-
Germany	+	-	-	-	Reptiles
Poland	+	+	+	-	+
Denmark	+	-	-	+	-

*Imported food and "foreign cases" as a proxy for imported food
+: Data included in the model
-: Data not included in the model

<u>Table 2</u>: Sources included in the different European models

Source	UK	Sweden	Netherlands	Denmark
Pigs/pork	3.4 - 3.7	0.002 - 0.3	7.6 - 15.2	3.6 – 9.7
Cattle/Beef	0.1 - 0.25	0.003 - 0.3	12.3 - 20.1	0.2 – 1.6
Broilers/Chicken	15.2 - 15.8	0.008 - 0.2	0.2 - 1.8	0.1 – 1.8
Layers/Eggs	8.8 - 9.3	0.08 - 0.3	37.5 - 44.5	8.9 – 13.2
Turkey	1.1 - 1.7	NE	NE	NE
Lamb	2.0 - 2.3	NE	NE	NE
Game birds	0.6 - 0.7	NE	NE	NE
Food	NE	6.2 - 7.5	NE	NE
Wildlife†	NE	0.3-0.9	NE	NE
Travel	37.8	81.9	16.40	46.3
Outbreaks	5.8	2.9	10.80	4.4
Unknown	25.1 - 25.8	7.3 – 6.6	1.0 - 7.8	20.0 – 26.8

NE: not estimated
* "Unknown" in The Netherlands does not represent cases caused by types that were not identified in the described sources
** Travel related cases in the Netherlands were not modelled, but added to the final output of the model
†Includes geese, passerine birds, seagull and hedgehog

Table 3: Estimated proportion of cases of human salmonellosis attributed to specific sources in the UK, Sweden, the Netherlands and Denmark (95% CI)
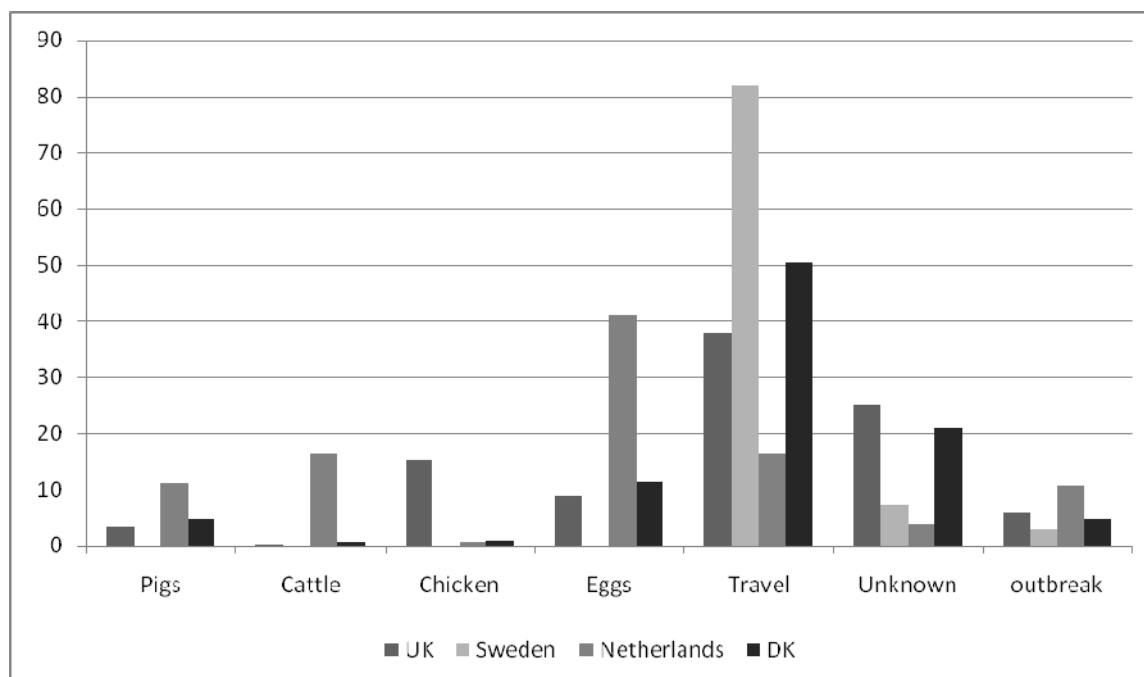

Fig. 1: Estimated proportion of cases attributed to specific sources in the UK, Sweden, The Netherlands and Denmark
* "Unknown" in The Netherlands does not represent cases caused by types that were not identified in the described sources
** Travel related cases in the Netherlands were not modelled, but added to the final output of the model
***Percentages do not add to 100%; some sources excluded

		a_j				q_i	
UK							
Chicken	15250	[14610,	15900]	S. Newport	2215	[1700,	2855]
Eggs	10030	[9469,	10590]	S. Hadar	57.4	[34.1,	89.4]
Lamb	3507	[2648,	4407]	S. Arizonae	44.7	[30.4,	63.3]
Sweden				**Sweden**			
Chicken	26	[91.6,	0.3]	S. Napoli	214.9	[127,	332.2]
Hedgehog	19.2	[88.0,	0.1]	S. Typhimurium NST	130.2	[59.6,	231.5]
Seagull	12.1	[80.9,	0.0]	S. Typhimurium DT12	117.2	[57.7,	200.6]
Netherlands				**Netherlands**			
Eggs	3.5	[3.2,	3.8]	S. Corvallis	162.2	[9.0,	468]
Cattle	2.1	[1.4,	3.0]	S. Muenchen	38.4	[16.4,	75.3]
Pig	0.3	[0.2,	0.4]	S. Newport	30.2	[12.0,	61.3]
Denmark				**Denmark**			
Beef	$4.21*10^{-6}$	$[7.41*10^{-9}$,	$1.75*10^{-5}]$	S. Typhimurium DT104 Q	243.3	[6.4,	852.5]
Imported beef	$4.21*10^{-6}$	$[7.41*10^{-9}$,	$1.75*10^{-5}]$	S. Thompson	74.8	[22.1,	99.2]
Eggs	$8.06*10^{-7}$	$[6.47*10^{-7}$,	$9.73*10^{-5}]$	S. Senftenberg	66.6	[22.0,	98.4]

Table 4: Estimated source- (a_j) and food-dependent factors (q_i) for the UK, Sweden, the Netherlands and Denmark, mean and 95% CI