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Attributing foodborne salmonellosis in humans to animal reservoirs in the European Union using a multi-country stochastic model

L. V. DE KNEGT*, S. M. PIRES AND T. HALD

National Food Institute, Division of Epidemiology and Microbial Genomics, Technical University of Denmark, Denmark

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SUMMARY

A Bayesian modelling approach comparing the occurrence of *Salmonella* serovars in animals and humans was used to attribute salmonellosis cases to broilers, turkeys, pigs, laying hens, travel and outbreaks in 24 European Union countries. *Salmonella* data for animals and humans, covering the period from 2007 to 2009, were mainly obtained from studies and reports published by the European Food Safety Authority. Availability of food sources for consumption was derived from trade and production data from the European Statistical Office. Results showed layers as the most important reservoir of human salmonellosis in Europe, with 42·4% (7 903 000 cases, 95% credibility interval 4 181 000–14 510 000) of cases, 95·9% of which was caused by *S.* Enteritidis. In Finland and Sweden, most cases were travel-related, while in most other countries the main sources were related to the laying hen or pig reservoir, highlighting differences in the epidemiology of *Salmonella*, surveillance focus and eating habits across the European Union.

Key words: Foodborne zoonoses, risk assessment, *Salmonella*, source attribution, surveillance.

INTRODUCTION

Unsafe food is related to several kinds of diseases, ranging from diarrhoeal syndromes to various forms of cancer. It has been estimated that foodborne or waterborne diarrhoeal diseases were responsible for 2·2 million deaths per year worldwide, 1·8 million of which were children [1]. *Salmonella enterica* is considered one of the leading causes of gastroenteritis and bacteraemia in the world [2, 3], being estimated to cause 93·8 million human cases and 155 000 deaths every year [4]. In the European Union (EU), *S.* Enteritidis and *S.* Typhimurium are the most frequently reported serovars, but a wide range of other serovars frequently cause disease in humans and thus are of public health significance [3, 5]. Human infection is most often foodborne, but other routes of infection, namely contact with animals and environmental transmission, have been identified [6, 7].

To design and prioritize effective food safety interventions, it is important to identify which foods are vehicles for specific illnesses [8]. This process is called *source attribution*, and it can be based on different approaches, such as analysis of outbreak data, analysis of sporadic cases, microbial subtyping, comparative exposure assessment, intervention studies and expert elicitations [8]. Methods for source attribution are intended to provide countries with tools for priority setting in relation to human foodborne and

* Author for correspondence: Dr L. V. De Knegt, Technical University of Denmark, National Food Institute, Division of Epidemiology and Microbial Genomics, Mørkhøj Bygade 19, Building H, 2860 Søborg, Denmark.
(Email: ledkn@food.dtu.dk)

zoonotic diseases both at the national and regional level, being a critical tool for decision-making aimed at reducing human zoonotic infections faster and more effectively [9].

Hald *et al*. [10] developed a Bayesian approach based on microbial subtyping for attribution of human cases of salmonellosis to animal reservoirs in Denmark. It made use of Denmark's extensive surveillance and data collection system to identify the main *Salmonella* subtypes responsible for human cases and compare them with those found in six animal-food sources. The model was further developed by Pires & Hald [11] to accommodate information from different time periods, and adapted by Mullner *et al*. [12] to apply it to *Campylobacter*.

Other EU Member States (MS) have performed *Salmonella* source-attribution studies based on the cited methods, e.g. Sweden [13] and The Netherlands [14]. A EU-wide source-attribution approach based on outbreak data was also developed [15]; this model attributed disease at the EU region level and did not provide estimates at country level. So, the relative contribution of different food sources for human salmonellosis in the remaining individual countries within Europe had still not been assessed.

This paper presents a study in which the Hald model was adapted to use EU-harmonized data reported by 24 MS to attribute human cases of salmonellosis to their respective animal reservoirs at both country and EU level.

METHODS

Data availability

All utilized data covered the period between 2007 and 2009. EU animal-food production and trade data were available as published by the Statistical Office of the European Union (EUROSTAT) [16]. Data on the prevalence of *Salmonella* serovars in animals and food were available from the EU-wide Baseline Studies (BS) conducted in different animal species [17–20] and from the European Union Summary Reports (EUSR) as published by the European Food Safety Authority (EFSA) from 2006 to 2009 [21–24]. Data on the number and serovar distribution of human cases reported to the European Surveillance System (TESSy) from 2007 to 2009 were extracted on 6 July 2010 and provided by the European Centre for Disease Prevention and Control (ECDC) through EFSA, except for Poland and Portugal, which directly provided additional datasets with more detailed serovar information. Human data included both case-based and aggregated data and were complemented with other data sources (e.g. national monitoring or laboratory surveillance data not published in the EUSRs) when necessary and possible. One of the main obstacles for the use of these data is the underreporting of cases. It is generally understood that the real (and generally unknown) number of illnesses in the population is considerably larger than the number of cases reported in the surveillance system. Moreover, the level of underreporting varies strongly between countries, depending on differences in organization and effectiveness of local surveillance systems [25, 26]. This was taken into consideration by multiplying the country-specific underreporting factors (UFs) estimated by Havelaar *et al*. [27] to the reported sporadic cases. The UFs were fitted as lognormal distributions, following the methodology described in Hald *et al*. [28]. The number of cases originally reported in the datasets obtained, the UFs and the resulting adjusted totals can be seen in Table 1.

Data management

Isolates not classified up to the serovar level or reported in aggregated form were reassigned to specific serovars according to proportions observed in previous studies, in the same dataset or in other references, depending on the availability of data in each case. Isolates classified as serogroups were distributed among serovars pertaining to them, in accordance with the Kauffman–White–Le Minor scheme [29]. For sporadic human cases, the main reference dataset used to obtain the proportions for the reassignment was the WHO Global Foodborne Infections Network (GFN) Country Databank (CDB) [30], which contains the 15 most commonly identified *Salmonella* serovars among human and non-human sources in 84 countries. Animal isolates were reassigned based on proportions found in the BS datasets. Isolates identified as monophasic variants of *S*. Typhimurium (e.g. *S*.1,4,[5],12:i:- or *S*.4,[5],12:i:-) were reassigned to *S*. Typhimurium [31]. Outbreak-related cases were reassigned using the proportions observed in the outbreak dataset, because some serovars may be more prone to generate outbreaks than others, and thus the proportions observed in reported sporadic cases may not apply. At the EU level, a total of 9·1% of sporadic cases had to be reassigned to specific serovars, varying from zero in Portugal to 73·5% in

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Table 1. *Human cases of salmonellosis reported in the modelling dataset before and after adjusting for underreporting (UFs with 95% credibility intervals)*

Country	Reported	UF (95% CrI)	Adjusted (95% CrI)
Austria	8487	11 (1·6–33·6)	93 357 (13 579–285 163)
Belgium	11 066	3·5 (0·3–12·5)	38 731 (3320–138 325)
Bulgaria	3899	718·5 (112–2141)	2 801 432 (435 518– 8 345 810)
Cyprus	471	173·2 (26·8–523·8)	81 577 (12 623–246 710)
Czech Republic	38 842	28·9 (4·3–86)	1 122 534 (167 021–3 340 412)
Denmark	7497	4·4 (0·7–13·1)	32 987 (5248–98 211)
Estonia	1341	16·9 (2·4–51·8)	22 663 (3218–69 464)
Finland	8228	0·4 (0–1·2)	3291 (0–9874)
France	20 319	26·9 (4–82)	546 581 (81 276–1 666 158)
Germany	127 330	9·8 (1·5–29·3)	1 247 834 (190 995–3 730 769)
Greece	1927	1228·5 (189–3668)	2 367 320 (363 240–7 068 621)
Hungary	19 091	66·8 (10·2–199·1)	1 275 279 (194 728–3 801 018)
Ireland	1264	5·4 (0–27·2)	6826 (0–34 381)
Italy	10 205	71·7 (10·7–214)	731 699 (109 194–2 183 870)
Latvia	2665	43·3 (6·6–134·9)	115 395 (17 589–359 509)
Lithuania	7643	59·1 (8·7–182·1)	451 701 (66 494–1 391 790)
Luxembourg	479	4·5 (0–21·4)	2156 (0–10 251)
Malta	371	222·7 (33·7–663)	82 622 (12 503–245 973)
The Netherlands	4168	26·3 (3·6–84·8)	109 618 (15 005–353 446)
Poland	30 963	114·1 (17·2–338·2)	3 532 878 (532 564–10 471 687)
Portugal	1513	2082·9 (318–6267)	3 151 428 (481 588–9 481 820)
Romania	2351	349·9 (48–1128)	822 615 (112 848–2 651 458)
Slovakia	19 399	53·2 (7·6–165·4)	1 032 027 (147 432–3 208 595)
Slovenia	11 265	40·3 (4·9–133·2)	453 980 (55 199–1 500 498)
Spain	12 033	214·2 (32·7–638·9)	2 577 469 (393 479–7 687 884)
Sweden	3002	0·5 (0·1–1·6)	1501 (300–4803)
UK	36 666	7·3 (1·1–22·6)	267 662 (40 333–828 652)
EU-27	392 485	57·5 (8·8–171·4)	22 567 888 (3 453 868–67 271 929)

UF, Underreporting factor; CrI, Credibility interval.

Greece. Records with travel information referred as 'unknown' and considered as domestic cases corresponded to 27% of all cases reported, varying from zero in Austria, Belgium, Czech Republic, Estonia, Hungary, The Netherlands, Slovakia and Spain, to 100% in France. No outbreak cases were reported by Cyprus, Greece, Italy, Luxembourg, Malta or the UK. Among countries which reported outbreaks, the total percentage of reassigned cases was 8·2%, ranging from zero in 13 countries to 46·7% in France. Concerning the animal data, reassigned records corresponded to 4·4% of the total for broilers, 8·6% for pigs, 0·8% for turkeys, 27·8% for layers and 51·3% for cattle. The number of countries in which reassignments were necessary varied from five in broilers to 11 in pigs, and the largest reassigned percentage was observed for cattle in the UK (92·1%).

Concerning the consumption data, the domestic amount of a product available in a country was estimated as domestic production minus export, whereas the amount of imported food available for consumption in MS A originating from MS B was estimated as import minus re-export (when re-export was relevant). That was done in order to consider the intra-community food trade and its impact on the incidence of human salmonellosis in importing countries. Trade between EU countries and third-party countries was not considered. To assess the assumption that the EUROSTAT trade could be used as an approximation for consumption data, the final trade dataset was compared with consumption data from the Food and Agriculture Organization (FAO) [32]. A proportional similarity index between the two datasets was calculated, obtaining 91% similarity. Thus, the data was considered appropriate for inclusion in the model.

Based on data quality, food-animal sources included in the final model were broilers, pigs, turkeys and laying hens (as the animal reservoir for eggs). Since neither harmonized EU monitoring data nor

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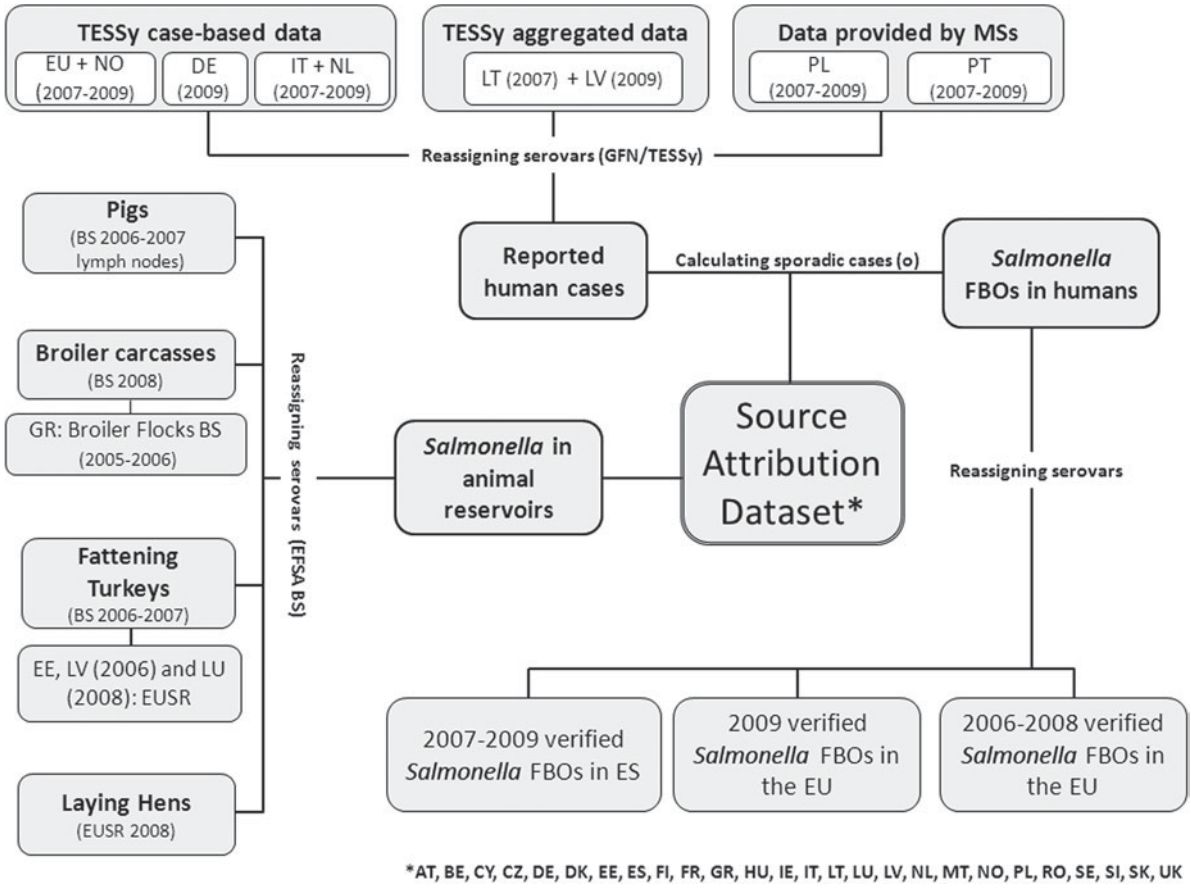

Fig. 1. The final *Salmonella* dataset (not including trade data). (*Source-attribution dataset: AT, Austria, BE, Belgium, CY, Cyprus, CZ, Czech Republic, DK, Denmark, EE, Estonia, FI, Finland, FR, France, DE, Germany, GR, Greece, HU, Hungary, IE, Ireland, IT, Italy, LV, Latvia, LT, Lithuania, LU, Luxembourg, MT, Malta, NO, Norway, NL, The Netherlands, PL, Poland, RO, Romania, SK, Slovakia, SI, Slovenia, ES, Spain, SE, Sweden, UK.) FBO, Foodborne outbreaks.

BS data were available for the cattle reservoir, this source was excluded from the final model due to poor data quality, which would significantly compromise the validity of the model results. As for MS, 24 were included in the model: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, The Netherlands and the UK. Bulgaria and Romania, which were part of the initial list, were excluded for lack of appropriate human or animal data, respectively. Twenty-two serovars were selected to be specifically addressed, based on their presence and importance in humans and in the main animal reservoirs in a 5-year period: *S.* Agona, *S.* Anatum, *S.* Bovismorbificans, *S.* Braenderup, *S.* Brandenburg, *S.* Bredeney, *S.* Derby, *S.* Enteritidis, *S.* Hadar, *S.* Heidelberg, *S.* Infantis, *S.* Kentucky, *S.* Kottbus, *S.* Livingstone, *S.* London, *S.* Mbandaka, *S.* Montevideo, *S.* Newport, *S.* Rissen, *S.* Saintpaul, *S.* Typhimurium and *S.* Virchow. Albeit important in humans in most of the 24 countries, *S.* Dublin, *S.* Ohio and *S.* Stanley were not included in the list because *S.* Stanley was not isolated from the animal sources considered for the source-attribution model, and *S.* Dublin and *S.* Ohio became irrelevant after the cattle reservoir was removed. Serovars not included in the above list were aggregated as 'Others'.

Data management was performed using SAS Enterprise Guide, SAS/STAT® User's Guide, v. 8 (SAS Institute Inc., USA). Data origin and countries providing information for each food-animal reservoir, reported human cases and cases related to foodborne *Salmonella* outbreaks are summarized in Figure 1. A detailed description and discussion of the data management steps, challenges and appraisal of the final quality appear in de Knegt *et al.* [33].

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Model overview

The presented approach for source attribution by microbial subtyping works by comparing the number of human cases caused by different subtypes of a pathogen with the distribution of the same subtypes in different food-animal sources, utilizing a collection of temporally and spatially related isolates from multiple sources and humans.

The model attributes sporadic domestic cases to food-animal sources. A sporadic case is defined as a subject that could not be associated with a recognized foodborne disease outbreak. Outbreak-related cases are added to the final results of the model, being attributed to the source implicated in the outbreak, if that is known. If not, they are considered outbreaks with unknown source. As *Salmonella* subtypes are clonally distributed among animal hosts [10], the model attribute cases at the animal reservoir level. This means that in general, cases caused by pork are attributed to pigs, eggs to layers, chicken meat to broilers and so on, but if a pork food preparation is contaminated during processing with a subtype originally found in broilers, the resulting cases are attributed to broilers, not pigs.

The model was built in a Bayesian framework based on the method described by Hald *et al.* [10]. In that model, *Salmonella* subtype distributions in animals in a given country in a certain time period are compared with the subtype distribution in humans in the same country in the same period.

The objective was to estimate the number of reported human cases that can be attributed to each source in each country, based on (1) the number of laboratory-confirmed infections caused by each *Salmonella* serovar in each country, including possible outbreak or travel information for each case, (2) prevalence of each serovar in the different sources in each country, and (3) amount of food source available for consumption in each country broken down by the country of origin. Due to the non-availability of animal data for the same years as the human data, it was decided to use a cross-sectional approach, using data from the EFSA BS and assuming that the serovar profiles presented in them would be representative of the 3-year period the human data referred to. The model was adapted to accommodate data from multiple countries, thereby adding a third dimension to the original model (in addition to subtype and food-animal source-related factors), and was based on the distribution of serovars in humans and food-animal sources. Another addition to the original model was the use of trade data as a surrogate for consumption. This creates a scenario in which it is possible to differentiate the country of origin of the food from the country where the human cases were reported, and apply the corresponding country-specific *Salmonella* prevalences to the sources. As a consequence, it is also possible to estimate the number of cases reported in a country which are attributable to a source from other country(ies).

Model parameters and specifications

The model takes into account the number of cases caused by a serovar, the prevalence of each serovar in each source in each country, the underreporting multipliers in each country, and relative impact of a set of unknown factors, as described in Hald *et al.* [10]. The unknown factors were included as multi-parameter priors, and account for the differences in the ability of different subtypes to cause disease and of different sources to act as vehicles for infection. Multiple loops were included to accommodate data from the 24 countries. An overview of the model parameterization can be drawn as:

$$a_{cj} \sim \text{Uniform}\,(0, 100),$$
$$q_i \sim \text{Uniform}\,(0, 100),$$
$$\lambda_{ci} \sim \text{Poisson}\,(o_{ci}),$$
$$\lambda_{ci} = \sum_{j=1\,k=1}^{n} \lambda_{ckji},$$
$$\lambda_{ckji} = p_{kij} * m_{ckj} * a_{cj} * q_i,$$

where: (1) λ_{ckji} is the expected number of cases per serovar i and source j reported in country c and caused by food produced in country k; (2) p_{kij} is the prevalence of serovar i in source j in country k; (3) m_{ckj} is the amount of source j available for consumption in country c produced in country k; when a source is domestically produced in the country of attribution, $c{=}k$; (4) a_{cj} is the source-dependent factor for source j in country c; (5) q_i is the subtype-dependent factor for serovar i. The source-dependent factor a_{cj} was assumed to vary between countries, accounting for variability in consumption patterns and preferences not captured by m_{ckj}, also including general variations between sources, e.g. bacterial load/concentration in the food and processing, handling or preparation practices. The subtype-dependent factor q_i is a one-dimensional parameter, meaning that it is a property of the *Salmonella* serovar and assumed independent

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Table 2. *Parameters used to estimate the number of sporadic cases of salmonellosis attributable to the animal sources*

Notation	Description	Estimation
i (1–22)	*Salmonella* serovar	—
j (1–4)	Food-animal source	
c (1–24)	Country where the human case was reported	
k (1–24)	Country of origin of the food product*	
o_{ci}	Observed cases caused by serovar i in country c	Data
ob_{ci}	Observed cases caused by serovar i known to be outbreak related in country c. For each outbreak, one case was subtracted so that one outbreak contributed with one sporadic case.	Data
yt_{ci}	Observed cases caused by serovar i in country c that was reported as travel-related	Data
p_{kji}	Prevalence of serovar i in source j in country k	Data
m_{ckj}	Amount of source j available for consumption in country c produced in country k*	Data
a_{cj}	Source-dependent factor for source j and country c	dunif(0,max a_{cj})
q_i	Subtype-dependent factor for serovar i	dunif(0,max q_i)
uf_c	Underreporting factor for country c	dllnorm(μ,σ)
$spdo_{ci}$	Total number of sporadic cases caused by serovar i in country c	$o_{ci}-yt_{ci}-ob_{ci}+1$

* If the food is produced and consumed in the same country, $c=k$.

of the country of infection. The q_i prior for *S.* Enteritidis is defined as 1, and all other q_i values are estimated relatively to this one. The amount of food source available for consumption in the country where a *Salmonella* case was reported considers both domestically produced and imported foods (m_{ckj}). The number of human sporadic and domestic cases attributed to each source per country (λc_{ji}) is estimated assuming a Poisson distribution of the observed number of sporadic cases per subtype per country (o_{ci}). After attribution, sporadic reported cases were multiplied by the correspondent UF in each MS. Model parameters are presented in Table 2.

The model was built in WinBUGS 1.4 (http://www.mrc-bsu.cam.ac.uk/bugs/), which uses Markov Chain Monte Carlo (MCMC) with Gibbs sampling as a default to obtain summary values for posterior distributions. Five independent chains ran for 40 000 iterations each to obtain the values for a_{cj} and q_i. Each chain had a different set of starting values for the priors, widely dispersed in the target distribution. Chain convergence was monitored using the methods described by Gelman & Rubin [34] and was considered to have occurred when the variance between the different chains was no larger than the variance within each individual chain, and when the chains had reached a stable level.

RESULTS

The most important source of human salmonellosis at the EU level was estimated to be the laying hen reservoir (i.e. eggs), with 42·4% [7 903 000 cases, 95% credibility interval (CrI) 4 181 000–14 510 000] of cases, followed by 31·1% attributed to pigs (5 800 000 cases, 95% CrI 2 973 000–11 100 000). Broilers and turkeys were estimated to be less important sources of *Salmonella*, contributing with 12·6% (2 350 000 cases, 95% CrI 736 300–6 194 000) and 3·8% (702 400 cases, 95% CrI 325 500–1 590 000), respectively. A total of 1·6% (292 400 cases, 95% CrI 150 700–562 700) of all salmonellosis cases were reported as being travel-related, and 0·1% (13 848) of cases were reported as being part of outbreaks with unknown source. Cases which could not be attributed to any of the sources included in the model corresponded to 8·5% of the total (1 578 000 cases, 95% CrI 828 400–2 951 000).

The most important serovars contributing to human salmonellosis originating from the animal reservoirs are presented in Table 3. Of all *S.* Enteritidis infections, 63% (7 504 000 cases, 95% CrI 3 964 000–13 770 000) were attributed to laying hens, whereas 90·8% of *S.* Typhimurium originated from pigs (2 950 000 cases, 95% CrI 1 510 000–5 663 000). Compared to infections attributed to layers and pigs, a large proportion of cases were caused by other serovars in other sources, such as 4·5% *S.* Infantis in broilers (106 600 cases, 95% CI 32 560–284 500) and 9·2% *S.* Newport (226 296 cases, 95% CrI 84 379–567 930) or 4·5% *S.* Saintpaul (33 580 cases, 95% CrI 18 052–62 443) in turkeys. In those sources, these serovars were not the most frequently associated with cases, but still constituted a significant burden.

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Table 3. *Estimated proportion of human reported cases by food-animal source and the top-5 serovars within each source*

Animal source associated with cases							
Broilers		Layers		Pigs		Turkeys	
Serovar	%	Serovar	%	Serovar	%	Serovar	%
Enteritidis	85·0	Enteritidis	95·0	Typhimurium	50·9	Enteritidis	27·9
Infantis	4·5	Typhimurium	1·4	Enteritidis	38·2	Typhimurium	18·6
Typhimurium	2·5	Infantis	1·3	Derby	1·8	Newport	9·2
Virchow	2·9	Virchow	1·0	Infantis	1·1	Saintpaul	4·5
Kentucky	0·6	Kentucky	0·2	Newport	2·3	Hadar	19·0
Others	4·5	Others	1·0	Others	5·7	Others	21·0
Total cases	2 348 384	Total cases	7 899 435	Total cases	5 789 456	Total cases	702 335

When looking at attribution within specific countries, 13 MS (Austria, Czech Republic, Estonia, Germany, Greece, Hungary, Latvia, Lithuania, Luxembourg, Slovenia, Slovakia, Spain, UK) had the laying hen reservoir estimated as the most important source of salmonellosis. Pigs were the larger contributor for salmonellosis in eight (Belgium, Cyprus, Finland, France, Ireland, Italy, Poland, Sweden) MS, and the proportion of disease attributed to layers and pigs were similar in The Netherlands. Imported turkey meat and domestic broilers had a localized importance in Denmark and Portugal, respectively. The majority of *Salmonella* infections in Finland, Sweden and, to a lesser extent, Denmark, Ireland and the UK were reported as travel-related (Fig. 2). Online Appendix A contains the country-specific attribution tables.

As mentioned earlier, a feature of this model is its ability to estimate the country of origin of cases attributed in other countries, as country-specific prevalences and amounts are used. When considering all sources together, Poland was estimated to be the most important source country for human salmonellosis in the EU, contributing 21·3% of cases (3 563 710 cases, 95% CrI 911 750–10 818 900), followed by 18·4% from Spain (3 081 090 cases, 95% CrI 898 170–9 056 800) and 14·5% from Portugal (2 422 142 cases, 95% CrI 361 368–8 508 397). Country-specific estimates with 95% CrIs are shown in online Appendix B. Cases reported in the country of origin are also included in the total, which means that the 3 563 710 cases 'originating' from Poland included cases reported in Poland, not only in other countries. Looking at the numbers in Appendix B it can be seen that the impact of the country of origin varied with the source. As an example, 55·6% of cases (1 305 000 cases, 95% CrI 198 500–4 535 000) attributed to broilers were estimated to 'originate' from Portugal, while cases attributed to turkeys were mostly related to Spain (43·1% or 302 600 cases, 95% CrI 55 350–1 029 000) and pigs to Poland (24·2% or 1 402 000 cases, 95% CrI 257 000–4 721 000) and Spain (22·5% or 1 306 000 cases, 95% CrI 423 700–3 556 000). The majority of cases attributed to layers originated from Greece (21·5% or 1 701 000 cases, 95% CrI 256 400–5 944 000), Spain (17·9% or 1 414 000 cases, 95% CrI 406 000–4 286 000) and Poland (16·3% or 1 287 000 cases, 95% CrI 492 000–316 000).

Concerning the factors simulated to estimate the ability of food sources to act as a vehicle for disease (a_{cj}) or of different serovars to cause disease (q_i), layers had the highest value of a_{cj} in 11 countries (Austria, Czech Republic, Estonia, Germany, Greece, Hungary, Lithuania, Luxembourg, Latvia, Slovenia, Slovakia) and turkeys in 10 (Belgium, Cyprus, Denmark, Finland, France, Ireland, The Netherlands, Spain, Sweden, UK). In Italy and Poland, the highest a_{cj} was estimated for pigs, whereas in Portugal this occurred for broilers. The highest values of q_i were estimated for *S.* Kentucky, *S.* Newport, *S.* Virchow and *S.* Typhimurium. Values estimated for a_{cj} and q_i are shown in online Appendices C and D.

DISCUSSION

This study represents the first attempt to conduct source attribution of human salmonellosis in most European countries. Results suggest that layers were the most important source of salmonellosis in the EU in the study period, being responsible for over

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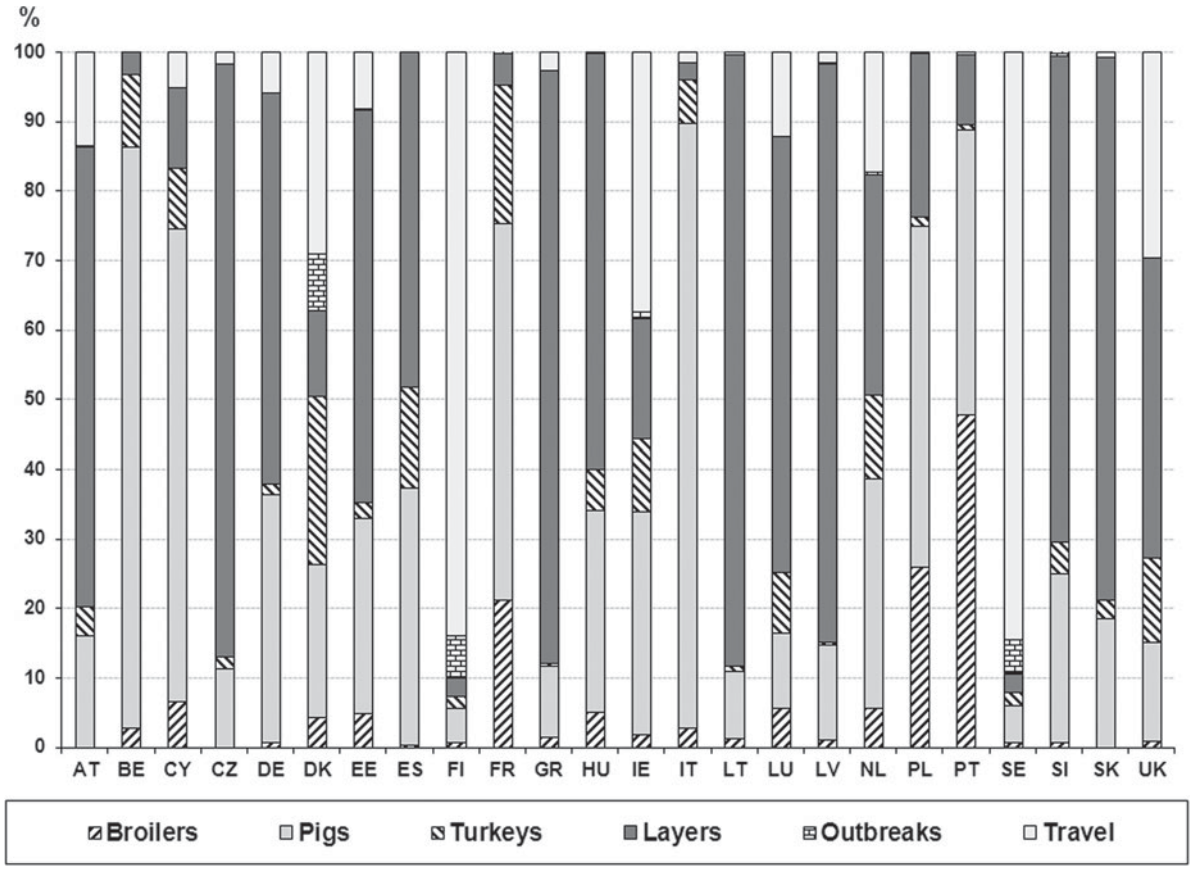

Fig. 2. Proportion of *Salmonella* human cases attributed to food animal reservoirs, travel and outbreaks in 24 EU Member States, 2007-2009 (median %). For explanation of abbreviations see Figure 1 legend.

40% of all *Salmonella* infections. At the country level, layers were estimated as the most important source in 13/24 countries, followed by pigs, which were the most important source in eight countries. Turkeys were revealed as particularly important only in Denmark and broilers in Portugal. The identification of the most important sources of salmonellosis is a step for prioritization of actions and interventions aimed at reducing the public health burden of disease.

These attribution estimates took into account the amount of food produced and traded between countries as reported to the EUROSTAT database. The underlying assumption was that these data reflected the real flow of foodstuffs and consequent exposure in the countries. However, the dataset used was built based on production, imports, exports and poultry trade datasets, and their quality and consistency depend on factors such as the recording and reporting of information by the countries. It is an important feature in this model that the relative contribution of food-animals produced in different countries is dependent not only on the *Salmonella* prevalence in a source in an exporting country, but also on the amount imported from that country. This is a point in which the EU model differs from the way single-country models work: in a single-country model, m_j works as a subset of a_j, as they have the same dimensions [10, 11, 13]; for each source, there is only one value of m and one value for the prevalence of a subtype in that source. The m_j, therefore, has the role of weighting the contribution of the different sources, which is, up to a point, already reflected in a_j, In the multi-country model, m in a reporting country is composed by subsets of m from different countries or origin of the food sources, each one with its own prevalence. For that reason, even if an exporting country has a very high prevalence in a source, this prevalence will have little impact in an importing country if the amount imported is very small, particularly if another country with a low prevalence exports very large amounts which can, ultimately, 'dilute' the high prevalence found in the first country. In short, the amount imported ultimately drives the $m*p$ in the model formula, particularly when large differences

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in trade volume are observed, and so the quality of the trade data has a large impact on the observed results.

Trade data may also not necessarily reflect the primary origin of the food. It is not uncommon to import food products into one country in which the foods are then repacked and relabelled and exported to other countries. This may also happen for food products imported from third-party countries. A consequence of this will be that cases are attributed to EU countries, which may not be the primary producers of the food in question. Unfortunately, it is not possible to quantify the impact of this since the information necessary to assess this is not available at the EU level.

Travel-related cases had a localized importance in Northern Europe, notably in Scandinavian countries. Although data quality issues underline any interpretations of the travel data, these results are corroborated by other studies for at least two countries. A previous source attribution study in Sweden allocated 82% of *Salmonella* infections as travel-related [13], and results of the Danish source account for the same period [35] found a proportion of travel-related *Salmonella* cases varying between 22 and 46%, which, although higher than estimated by the EU model, accounted for the probability of a case with unknown travel information having been travelling abroad before onset of symptoms, and so add more 'possible' travelers. Other countries, such as Spain, had zero cases attributed to international travel, as no travel information was reported. For this model, cases that were reported as acquired outside the country were considered as travel-related cases, and all cases without specific information otherwise were assumed to be domestically acquired. That resulted in the data available being dependent on the patients being asked whether they had been travelling abroad before onset of symptoms, and the information being registered centrally. For that reason, travel-related disease is expected to be underestimated. Differences between patients travelling within or outside Europe were not assessed, as this information was only available for a few MS.

The use of UFs has proved important when considering the effect of source and country contributions at the EU level. This is particularly clear for broilers: this reservoir was the most important only in Portugal, but the use of an UF multiplied its impact within the EU by 2082·9 (mean value), increasing both the relative contribution of broilers and of Portugal to the total cases of salmonellosis, when compared to the original numbers. A similar effect can be observed for the contribution of Greece to the total cases attributed to layers. It should therefore be noted that most of the cases 'originated' by countries with large UFs were reported in those same countries, so one should be careful when interpreting these results as countries 'exporting' cases to the rest of the EU. Limitations of the use of the UFs include the fact that they have been calculated based on incidence data from returning Swedish travellers [25] and on a burden of illness study from The Netherlands [27]. Therefore, they bring along a set of assumptions related to the eating habits and exposures of Swedish travellers and to the current *Salmonella* incidence in The Netherlands. Some of the values seem extreme, like for Portugal (2082·9) and Sweden (0·5), and may require a more careful interpretation when used for countries standing alone. However, as a measure of relative contribution among countries within the EU, the UF-adjusted numbers were considered a better reflection of reality than the raw reported data. Further considerations about the limitations of UFs are described in the original paper [27], as well as de Knegt *et al.* [33].

As there was a large variation in the availability of data from the EFSA BS or EU- harmonized monitoring and surveillance of food sources between MS, only broilers, laying hens, pigs and turkeys could be included in the model. This can result in the misplacing of some cases when their 'correct' source is not included. As an example, it is expected that some cases that should be attributed to beef could be attributed to pigs instead, as *S.* Typhimurium is a common serovar in both sources. However, it should be noted that when the Danish model started being applied, it only included five sources, and it was still a powerful tool in guiding the decisions for the targeted actions regarding broilers, pigs and table eggs that markedly decreased the prevalence of *Salmonella* in these sources in the last decade [36, 37]. Fruits and vegetables, which are also recognized as sources of salmonellosis, were not included. This happened because the approach employed attributes cases to the original animal reservoirs, meaning that infections caused by fruits and vegetables contaminated with faeces from production animals would be traced to the animal reservoir.

The use of serovar as subtyping level, which resulted from the scarcity or absence of data on further subtyping levels (phage typing, antimicrobial resistance profiles), can also result in misattribution of cases. A good example is *S.* Enteritidis, which is present in all sources [17–20]. Without more specific

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differentiation between subtypes found in each reservoir, cases are likely to be 'cross-attributed' among sources. In countries where travel information was not provided, the misattribution of *S.* Enteritidis cases may include the attribution of cases which are actually travel-related to the animal reservoirs. In MS with reasonably good travel data it can be seen that a large proportion of the *S.* Enteritidis infections are linked to travel, indicating that the same situation could be found in MS with poor or no travel data. In that scenario, travel-related cases would be wrongly attributed to one of the sources included in the model, as also observed by Hald *et al.* [28]. A large proportion of cases was attributed to 'unknown sources' in some countries. This category receives cases caused by serovars not found in any of the animal reservoirs in the country, and where there was no positive information on travel. Large differences between countries are therefore explained by the assumption that cases with no travel information were domestic and by the lack of outbreak data in some countries. Finally, the limited number of sources included in the model undoubtedly also explains a proportion of the cases in the unknown category, since cases infected with serovars from reservoirs not included in the model will go to this category as well.

The values of q and a can be regarded as multiplication factors that indicate the impact a specific subtype and food source has on the number of human cases. For q, this may be interpreted as a way of accounting for 'theoretical' differences in the subtypes' virulence and/or their ability to survive in the food chain. As for a, it may account for general differences in bacterial load in the product and preparation habits before consumption [8, 11]. Based on the data available, the posterior values are estimated as

$$a_{cj} * q_i = (\lambda_{ckji}/(p_{kij} * m_{ckj})),$$

Because q and a are estimated considering each food/subtype combination (i.e. a multi-parameter prior), the ranking of results for each parameter alone may not correspond to findings of studies which focused specifically on virulence factors or survival of *Salmonella* in food sources [3, 38].

Despite data limitations and the consequent uncertainty in the results, the source-attribution estimates are considered valid as a first indication of which sources are most important for human salmonellosis in several countries. Limitations include the variability in the human surveillance systems in place in the countries, as well as the different details with which serovar information is reported for both human and animal-food sources. Such uncertainties cannot be statistically quantified, but should be borne in mind when interpreting the results. The relative importance of different food-animal sources was found to vary between countries according to differences in prevalences, trade and consumption patterns and preferences, as well as animal and food production systems, also highlighting regional differences in the focus of surveillance systems in place in EU MS. The results are expected to be useful for the delineation of risk management strategies in the EU. An application of the methods presented here was recently published in an EFSA report [39], where the EU model was used with data collected after the implementation of the EU-harmonized reporting of *Salmonella* in breeding and layer hens. The obtained estimates clearly show the impact of such programmes, when compared to our results [39]. Therefore, the application of the model on a regular basis and the analysis of its results over the years allows, for example, for the evaluation of the impact of implemented control activities, which would also be a way of validating the results.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268814001903.

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DECLARATION OF INTEREST

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