
SYSTEMATIC REVIEW

Source attribution of human salmonellosis using a meta-analysis of case-control studies of sporadic infections

A. R. DOMINGUES^{1*}, S. M. PIRES¹, T. HALASA² AND T. HALD¹

¹ National Food Institute, Technical University of Denmark, Søborg, Denmark

² National Veterinary Institute, Technical University of Denmark, Copenhagen, Denmark

(Accepted 18 October 2011; first published online 8 December 2011)

SUMMARY

Salmonella is an important cause of human illness. Disease is frequently associated with foodborne transmission, but other routes of exposure are recognized. Identifying sources of disease is essential for prioritizing public health interventions. Numerous case-control studies of sporadic salmonellosis have been published, often using different methodologies and settings. Systematic reviews consist of a formal process for literature review focused on a research question. With the objective of identifying the most important risk factors for salmonellosis, we performed a systematic review of case-control studies and a meta-analysis of obtained results. Thirty-five *Salmonella* case-control studies were identified. In the meta-analysis, heterogeneity between studies and possible sources of bias were investigated, and pooled odds ratios estimated. Results suggested that travel, predisposing factors, eating raw eggs, and eating in restaurants were the most important risk factors for salmonellosis. Sub-analyses by serotype were performed when enough studies were available.

Key words: Epidemiology, food safety, public health, *Salmonella*.

INTRODUCTION

Salmonella is a major cause of foodborne disease in both the industrialized and the developing world [1–3]. Although *Salmonella* is a frequent cause of foodborne outbreaks, the majority of the reported cases are sporadic. Infections are frequently associated with foodborne transmission, but other routes of exposure, such as direct contact with live animals and person-to-person transmission, have also been identified [4–7]. Identifying the most important sources of human foodborne disease is essential for prioritizing food-safety interventions and setting public health goals [8].

Several types of studies have been performed to identify possible sources of apparently sporadic human infections. Case-control studies are the most commonly used analytical epidemiological approach. Typically, selected patients (cases) and a corresponding group of asymptomatic and therefore assumed uninfected individuals (controls) are interviewed, and the relative role of exposures is estimated by comparing the frequency of exposures among cases and controls. When infections are associated with an exposure, the proportion of cases attributed to the exposure can be calculated and this measure is defined epidemiologically as the ‘population attributable fraction’ (PAF) [9]. PAFs can be used to partition the human disease burden to specific sources [10]. Alternatively, the relative importance of risk factors can provide an indication of which sources or routes of exposure are responsible for a higher burden of

* Author for correspondence: Miss A. R. Domingues, National Food Institute, Technical University of Denmark, Mørkhøj Bygade 19, DK-2860 Søborg, Denmark.
(Email: arco@food.dtu.dk)

disease. Case-control studies are a valuable tool to identify potential risk factors for human infections, including sources and predisposing, behavioural or seasonal factors [11]. In addition to individual case-control studies, a systematic review (SR) of published case-control studies of sporadic infections of a given foodborne disease can provide a comprehensive summary of the estimated measures of association and PAFs for each exposure, and this can be combined to estimate the overall burden of illness attributed to each exposure.

SRs consist of a formal process for literature review focused on a specific research question, and include the identification of relevant literature, quality assessment of relevant studies, summarization or statistical analysis of data, and conclusions [12, 13]. The intent of SRs is to apply review methods that minimize systematic and random errors, and thus minimize the introduction of bias and provide reliable basis for the decision-making process. Meta-analysis consists of an analysis of the summarized statistics of the studies provided by the SR.

This SR and meta-analysis aimed at comparing the relative importance of risk factors for cases of *Salmonella*, thus providing information for source attribution of human salmonellosis and delineation of interventions to reduce the burden of disease.

MATERIALS AND METHODS

Literature search

A literature search was conducted in February 2008, and was limited to the languages English, German, Portuguese, Spanish, and Danish. Relevant studies were identified using a combination of key words in the databases Medline, Science Direct, Agricola, CAB International, Biosis, FSTA, ISI Web of Science, and Web of Knowledge. In addition to published peer-reviewed studies, relevant studies published as conference proceedings and in scientific reports were also searched. A combined search was performed, looking for case-control studies of *Salmonella* spp. and *Campylobacter* spp. sporadic infections.

The search was conducted using a combination of (1) general terms, related to case-control studies and risk factors, and (2) *Campylobacter* and *Salmonella* terms. Citations were collected, de-duplicated and managed in web-based software (SRS 4.0, TrialStat! Corporation, Canada).

An additional traditional literature search, using the same search terms but without assistance of SR software, was performed in February 2010, and new references were added to the previously retrieved studies.

Relevance screening

All references were independently reviewed by two reviewers, and it was sufficient that one reviewer considered it relevant for the reference to pass to the quality assessment step of the SR. Relevance of studies was assessed on the basis of specific inclusion criteria: (1) focus on human disease; (2) focus on *Campylobacter* or *Salmonella*; (3) focus on sporadic disease; (4) reference describing a case-control study.

Quality assessment

Methodological soundness was assessed by two reviewers on the basis of the following study quality criteria: (1) statistical power above 80%, if information was available (if the power of the study was not mentioned, the reviewers were asked to evaluate the reference based on the other criteria); (2) case definition implying laboratory confirmation of the diagnosis; (3) random selection of controls; (4) comparability of cases and controls; (5) control for potential confounding factors (matching); (6) acceptable matching criteria for matched study designs (e.g. age and gender); (7) exposure window for cases and controls acceptable (maximum 10 days) and comparable; (8) response rates for cases and controls acceptable; (9) appropriate statistics; (10) the studies provided the odds ratio (OR) with the 95% confidence interval (CI) of the effect of each exposure based on conditional logistic regression; (11) acceptable study design (the reviewers assessed the overall quality assessment criteria and decided on the inclusion or exclusion of the reference).

The non-compliance with a single criterion was not sufficient to reject a study. Instead the reviewer was asked to do an overall assessment based on all criteria, and studies not fulfilling two or more criteria were excluded. If the two reviewers disagreed on the acceptance of a study, a third reviewer was consulted.

Data extraction

Data from studies that passed the previous steps were manually extracted by one of two reviewers using a

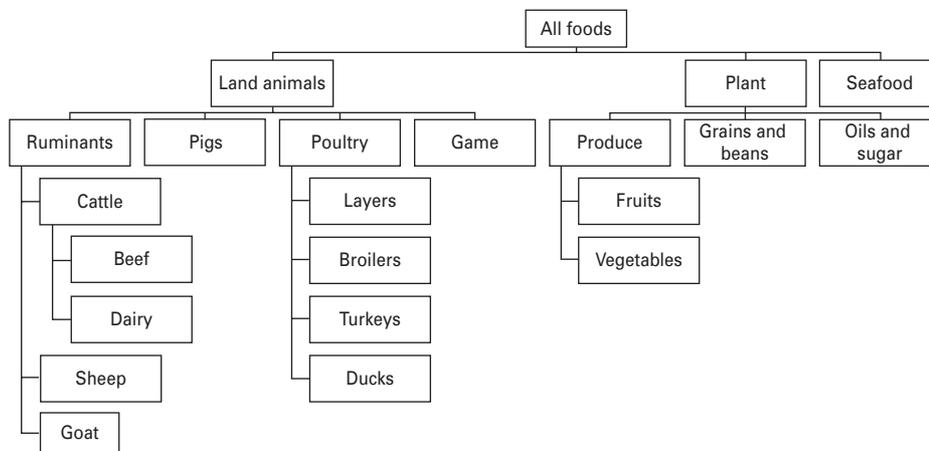


Fig. 1. Categorization of foods (based on [33]).

standardized form. The data extracted included country and time period of the study, age stratification of the population, study design parameters (e.g. matched or unmatched study), and outcome of the study (ORs for specific risk factors together with the 95% CIs).

Data analysis

Two separate meta-analyses were performed to compare and combine information from different studies. The meta-analysis presented here focuses on sporadic salmonellosis. The *Campylobacter* study will be described in a forthcoming paper [14]. All risk factors were stratified according to source-categorization schemes and location of exposures.

Source categorization

Exposures were categorized in six main groups: *food*, *direct contact with live animals*, *environment*, *person-to-person*, *predisposition* and *travel*. Additionally, *food preparation* risk factors were included for specific food routes with the purpose of distinguishing between the impact of exposure through consumption of foods and through handling of food items.

Risk factors from the main groups *food* (Fig. 1) and *direct contact with live animals* were sub-categorized in a hierarchical scheme of mutually exclusive categories. Environmental transmission routes included drinking water, exposure to recreational waters, and exposure to contaminated environments (e.g. playgrounds) or objects (e.g. bottles). In general, categorizations were based on (1) main reservoirs of the pathogen, (2) main routes of transmission from the reservoir to the susceptible population, and

(3) important predisposing and behavioural factors for human exposure (e.g. occupational exposure to farm animals or daily contact to pets). The main groups *person-to-person*, *predisposition* and *travel* were not sub-categorized. Predisposing factors included previous intake of drugs (e.g. antimicrobials and anti-acids), or pre-existing chronic disease, and were analysed individually.

Location of exposures

Risk factors from the main group *food* were further classified as *household* or *outside the household*, according to the setting of the exposure. The location of exposure corresponds to where the food was consumed or exposure occurred (e.g. cafe/restaurant, institution, home).

Meta-analysis procedure

Outcome parameters. The ORs and 95% CIs per risk factor from each study were pooled in a meta-analysis using commercial software [15]. Some studies presented more than one risk factor that could be integrated in the same categorization stratum (e.g. 'eating beef' and 'eating ground beef'). For these cases, a combined effect was calculated per study [15], so that a study with several risk factors in the same stratum did not have more influence on the total effect. When a study had more than one risk factor in the same main category (e.g. the food category *chicken*) but classified in a different location category (e.g. 'eating chicken at home' and 'eating chicken outside home'), each factor was treated individually. Similarly, risk factors belonging to the same category but describing consumption of raw or undercooked foods were treated separately.

Table 1. *Systematic review statistics*

Level	Reviewers/ reference	Total references	References passed	References excluded	References not analysed
Relevance screening	2	1295	131	1164	—
Quality assessment	2	131	72	46	13*
Added references	1	1	1	—	—
Data extraction	1	73	72	0	—
<i>Salmonella</i> references	—	34	—	—	—

* Full text references could not be found, and a proper quality assessment was not possible.

Studies are designed differently, conducted in different time periods and on different populations, which can create heterogeneous study populations [16]. Moreover, if only a small number of studies for a risk factor is available, homogeneity between groups could be apparent, but this would be a consequence of low statistical power and not due to actual lack of differences. Therefore, a random-effects model was used to calculate the pooled ORs [17].

The meta-analysis was designed to assess the influence of the factors age of the study population, geographical region, and study period in the final outcome. Regional analyses were performed according to the United Nations regions (see <http://www.un.org/depts/dhl/maplib/worldregions.htm>). For each stratum, we calculated (1) a pooled OR and 95% CI per group (age, region, time period, serotype), and (2) a total pooled OR and 95% CI based on all groups [15]. The meta-analysis was performed only when at least four studies were available [16, 18] for each stratum.

Publication bias. The publication bias was assessed using Duval & Tweedie's trim-and-fill method [19], Begg & Mazumdar's rank correlation test [20], and Egger's regression test [21]. When significant publication bias and change in the estimated pooled ORs were detected, the number of studies necessary to reverse the overall pooled effect was calculated using Orwin's fail-safe N method [22]. The influence of a single study was also examined using the one-study-removed method [23]. If significant publication bias existed, the pooled ORs were estimated after correcting for the bias, based on Duval & Tweedie's trim-and-fill method.

A significant publication bias was considered to exist when adjustment for the bias altered a previous conclusion or when the confidence limits of the unadjusted and the adjusted ORs did not overlap.

RESULTS

Systematic review

From 1295 identified references, 131 passed the relevance screening, 72 passed the quality assessment stage, and data was extracted from 71. Full text references could not be found for 13 references, which therefore did not pass to the data extraction phase. One reference was added after a posterior non-SR. Results of the SR process are summarized in Table 1.

From the 72 references, 34 investigated risk factors of sporadic salmonellosis and 38 focused on sporadic campylobacteriosis [14]. *Salmonella* case-control studies were conducted between 1989 and 2003 in 11 different countries. Two studies analysed exposures in children and five studies interviewed only individuals above 10 or 15 years of age. Some studies investigated risk factors for specific serotypes: 10 studies focused on *S. Enteritidis*, and few studies limited analyses to other serotypes. Overall, the number of cases and controls interviewed varied between 22 (small scale studies) and 7618 (community studies). All studies were published in English. The Appendix presents the complete list of *Salmonella* studies collected in the SR.

Meta-analysis of risk factors of human sporadic salmonellosis

Results show that international travel (OR 6.5, 95% CI 3.81–11), the previous intake of anti-acids (OR 2.9, 95% CI 1.5–5.7), pre-existing medical condition (OR 2.8, 95% CI 1.98–4), previous intake of antimicrobials (OR 2.23, 95% CI 1.65–3.00), eating raw eggs (OR 2.78, 95% CI 1.87–4.10), and eating in a restaurant (OR 2.74, 95% CI 1.74–4.32) were the most important risk factors for human salmonellosis in the overall study population (Table 2).

Table 2. The odds ratio (OR) together with the 95% confidence interval (CI) for the risk factors for sporadic salmonellosis

Risk factor	OR (95% CI)	Publication bias outcome
Direct contact with animals		
Pets	1.82 (1.30–2.50)	No significant bias
Farm animals	2.46 (1.73–3.48)	No significant bias
Environmental transmission		
Recreational waters	2.25 (0.75–6.81)	No significant bias
Drinking untreated water	2.30 (1.05–5.01)	No significant bias
Food		
Restaurant	2.74 (1.74–4.32)	No significant bias
Beef	0.68 (0.52–0.89)	No significant bias
Beef, <i>S. Enteritidis</i>	0.54 (0.37–0.79)	No significant bias
Beef at home	0.59 (0.45–0.78)	No significant bias
Chicken	0.95 (0.64–1.40)	No significant bias
Chicken, <i>S. Enteritidis</i>	0.75 (0.46–1.23)	No significant bias
Chicken in restaurant	2.02 (1.17–3.50)	No significant bias
Undercooked chicken	3.15 (0.67–14.8)	Bias was rejected
Dairy	0.57 (0.40–0.81)	No significant bias
Eggs	1.26 (0.90–1.80)	No significant bias
Eggs, <i>S. Enteritidis</i>	1.45 (0.79–2.66)	No significant bias
Undercooked eggs	2.78 (1.87–4.10)	Bias was rejected
Undercooked eggs, <i>S. Enteritidis</i>	2.12 (1.41–3.17)	No significant bias
Fish	0.77 (0.35–1.70)	No significant bias
Vegetables	0.60 (0.39–0.92)	No significant bias
Fruits	0.47 (0.19–1.15)	No significant bias
Meat	0.74 (0.55–0.99)	No significant bias
Pork	0.64 (0.47–0.88)	No significant bias
Sausages	1.07 (0.53–2.16)	No significant bias
Turkey	0.55 (0.33–0.91)	No significant bias
Food preparation		
Handling eggs	0.87 (0.50–1.51)	No significant bias
Travel	6.48 (3.81–11.0)	No significant bias
Travel, <i>S. Enteritidis</i>	8.83 (2.04–38.3)	No significant bias
Predisposing factors		
Antimicrobials	2.23 (1.65–3.00)	No significant bias
Antimicrobials, <i>S. Typhimurium</i>	2.78 (1.88–4.10)	No significant bias
Medication (H2Inib)	2.94 (1.53–5.66)	No significant bias
Chronic disease	2.81 (1.98–4.00)	No significant bias

H2Inib, Proton inhibitors medication.

Consumption of undercooked or raw eggs and chicken in a restaurant were the only food items identified as relevant for human disease in the analysis, and environmental routes (both drinking and recreational waters), direct contact with pets and farm animals, and various predisposing factors proved to play a role in human salmonellosis. The results of the analyses focusing on serotypes suggested that travelling abroad and consumption of eggs are particularly important risk factors for *S. Enteritidis* infection,

while previous intake of antimicrobials was the only risk factor identified for *S. Typhimurium*. Available studies did not allow for an analysis by region or age group. Figure 2 shows the relative importance of risk factors and routes of exposure to *Salmonella*, including *Salmonella* serotypes.

Significant publication bias was not identified in any of the analyses. When the number of studies in the analyses was small, the one-study-removed method frequently indicated the existence of influential

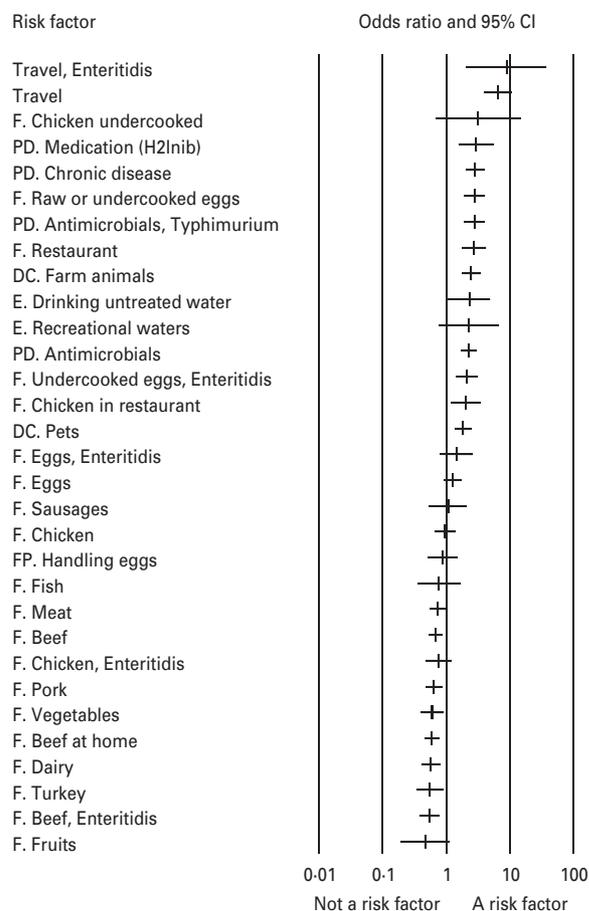


Fig. 2. Relative importance of risk factors for sporadic salmonellosis (odds ratio and 95% CI). F, Food; DC, direct contact with animals; E, environmental transmission; PD, predisposing factors; FP, food Preparation; H2Inib, proton inhibitors medication.

studies. For instance, Figure 3 shows the change in the pooled OR for the risk factor *eating undercooked chicken* when the corresponding study was removed. It shows that removing the study [24] suggests that eating undercooked chicken in a restaurant is a strong risk factor for sporadic salmonellosis (OR 7.09, 95% CI 1.14–43.98). In the analysis of the risk factor *eating raw or undercooked eggs*, the funnel plot showed a lack of symmetry around the pooled OR (Fig. 4). Duval & Tweedie's trim-and-fill method suggested adding six studies (solid symbols, ●) to the left side of the plot to reach complete symmetry, which would result in a shift of the OR with the 95% CI towards the null effect (the black diamond below the x-axis) reducing the effect of eating raw or undercooked eggs as a risk factor for salmonellosis. This was supported by Egger's regression test that indicated a strong association between study size and study effect

(intercept = 2.82, s.e. = 0.55, $P < 0.01$). However, Begg & Mazumdar's correlation test suggested an absence of correlation between study size and study effect ($\tau = 0.3$, $P = 0.1$), and the one-study-removed method did not indicate the existence of influential studies. In the analysis of *eating undercooked chicken*, Duval & Tweedie's trim-and-fill method suggested adding two studies to the right side of the plot to reach complete symmetry (results not shown). This would lead to a shift in the OR from 3.15 (95% CI 0.67–14.8) to 8.4 (95% CI 1.04–67), suggesting that eating undercooked chicken is a risk factor for sporadic salmonellosis. Using the one-study-removed method, an influential study was identified (Fig. 3). In both cases, the existence of publication bias was rejected.

DISCUSSION

This SR followed a rigorous search strategy to identify all potentially relevant peer-reviewed case-control studies of sporadic salmonellosis. Collected studies were conducted in different countries and time periods (see Appendix), designed with different settings, and sometimes focused on specific age groups within the population. The quality of the studies also varied, and was evaluated on the basis of defined methodological criteria during the formal process of the SR, and not judged on an individual basis by the reviewers.

The risk factors extracted from individual studies were categorized according to main source-classification schemes, and the meta-analyses of collected data were carried out per risk factor stratum, analysing information from all references that assessed the impact of that specific factor on the risk of disease. This categorization implied the harmonization of risk-factor labelling, which may have resulted in loss of information from individual studies. Nonetheless, it allowed for the integration and meta-analysis of results from all collected studies. Additionally, risk factors were included in the analysis only if they were investigated in four or more case-control studies. This criterion resulted in the exclusion of risk factors from the meta-analysis, which may also have resulted in the loss of evidence and potentially biased estimates.

The meta-analysis of sporadic salmonellosis studies highlighted international travel as the most important risk factor for human *Salmonella* infections. Other source attribution studies published in several

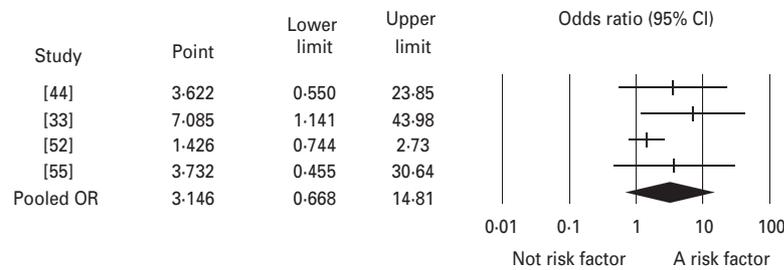


Fig. 3. Forest plot of the change in the pooled odds ratio (OR) of the risk of sporadic salmonellosis following eating undercooked chicken together with the 95 % confidence interval (CI), when the corresponding study was removed. The pooled OR represents the effect including the four studies. Study [24] is identified as influential, and when it is removed from the analysis, the pooled OR changes from 3.15 (95 % CI 0.67–14.81) to 7.09 (95 % CI 1.14–43.98).

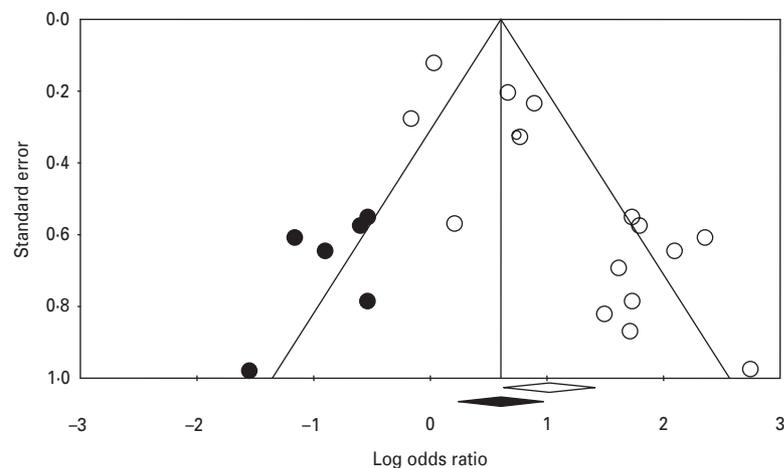


Fig. 4. Funnel plot of the logarithm odds ratio of 16 studies (○) quantifying the effect of eating undercooked or raw eggs on the risk of sporadic salmonellosis. The solid symbols (●) are the potential missing studies according to Duval & Tweedie’s trim-and-fill method (if they had existed, the pooled effect would have shifted slightly towards the null effect; the black diamond below the x-axis). The white diamond represents the pooled odds ratio with the 95 % confidence interval unadjusted for publication bias.

countries have identified travel as an important contributor to human salmonellosis, namely in Denmark [25, 26], Sweden [27], and several other European Member States [28]. Travel is expected to be important for the burden of human salmonellosis in countries with relatively low levels of *Salmonella* in domestic animals and foods and where the population travels frequently, particularly developed countries. Most of the collected studies were conducted in industrialized countries (see Appendix), and all studies included in the meta-analysis for the risk factor travel came from the developed world.

Regarding food products, our analysis only identified eggs eaten undercooked or raw, and chicken consumed in a restaurant as risk factors for salmonellosis. These findings are supported by all *Salmonella* source attribution studies available in the literature

(see e.g. [26, 29, 30]). The fact that our results did not identify other foods as relevant for salmonellosis may be explained by the inclusion of evidence from several studies conducted in a variety of countries throughout the world. On the one hand, studies frequently pose questions to interviewed cases and controls differently, for example asking about the degree of cooking of foods or not, and this may result in different signals in the importance of specific foods for disease. On the other, the contribution of each food to *Salmonella* infections varies between countries as shown by [24], but the studies included in this meta-analysis did not allow for regional analyses, and thus geographical differences could not be investigated.

Our results suggest that direct contact with live animals (pets and farm animals) and environmental

routes, namely drinking and swimming in recreational waters, are important contributors for human salmonellosis. Non-foodborne routes have been previously identified as important routes of transmission of *Salmonella* (see e.g. [4]), but most source attribution methods applied so far focus solely on foods. Additionally, intervention measures aimed at controlling salmonellosis have traditionally focused on the food chain. Thus, these results provide valuable information for the attribution of human salmonellosis cases and can be used to direct interventions or raise awareness in the population for risk factors of infection.

The meta-analysis included studies investigating risk factors for infections *Salmonella* spp. and studies focusing on specific serotypes. Some serotypes have more frequently been associated with specific animal sources and foods (e.g. *S. Enteritidis* with eggs, *S. Dublin* with cattle and beef), while others may have a broader range of sources (e.g. *S. Typhimurium* with several animal species and meats), and the weight of each serotype on the overall number of studies could influence the final general results of a meta-analysis. Nonetheless, because the distribution of studies focusing on the most important serotypes and on *Salmonella* spp. was balanced (see Appendix), we found the potential bias irrelevant.

The analyses by serotype could be conducted only for the most frequent *Salmonella* serotypes in the human population, *S. Enteritidis* and *S. Typhimurium*. The analysis identified travel and eggs as important risk factors for infection with *S. Enteritidis*, and this is in line with other epidemiological evidence provided by studies focusing on this serotype [26]. Only predisposing factors were identified as relevant for *S. Typhimurium*, which is thought to be a reflection of the low number of studies conducted for this serotype alone.

In the context of source attribution, we did not draw conclusions on factors associated with a statistically significant reduced risk of disease (odds ratio <1). This is justifiable in the light of the potential impact of bias inherent to individual case-control studies (e.g. due to misclassification of exposures due to lack of accuracy of recall), and thus to the final meta-analysis. While this is true for all exposures and all data that originate from patients' and controls' interviews, it is particularly important when making inferences on the protective effect of specific exposures, which may eventually also be routes for infection.

The statistical analysis took into account the potential innate heterogeneity of studies by using the random-effects model [17]. Potential factors that could explain the heterogeneity were further investigated using classification. Publication bias results have shown the absence of significant bias. In the analysis of eating raw or undercooked eggs, Duval & Tweedie's trim-and-fill method suggested adding six studies (Fig. 4, solid symbols, ●) to the left side of the plot to reach complete symmetry. Adding these missing studies would reduce the effect of eating undercooked or raw eggs as a risk factor for sporadic salmonellosis. The apparently missing studies are small- or medium-sized studies, which increases our suspicions that those studies could have been conducted, but not published, because they do not show interesting results [18, 31]. Eating raw or undercooked eggs has been recognized as a source of *Salmonella* and the confidence limits of the OR before and after correction for publication bias overlap; therefore, the publication bias was rejected. In the analysis of eating undercooked chicken, Duval & Tweedie's trim-and-fill method suggested adding two studies to the right side of the plot to reach complete symmetry (results not shown). Adding these studies would suggest that eating undercooked chicken is a risk factor for salmonellosis. Chicken meat is a known source of *Salmonella*, as we also show in our current study. Nonetheless, the two missing studies show quite interesting results, and one of them is a large study, which suggests the study would have been published if it had been conducted. The one-study-removed method identified an influential study [32], which is expected when there are only few studies available for the analysis [18]. In this analysis, only four studies were available in which bias could have been observed due to the small sample size. It is recommended that accepting or rejecting a bias should be solely based on rational and biological reasons, and not only based on statistical tests [18]. Because we could not rationally explain the omission of these two studies given our rigorous search criteria, we rejected the publication bias and deemed it a correct meta-analysis.

We conclude that a SR and meta-analysis of case-control studies are valuable tools to collect and analyse available information on risk factors of sporadic cases of pathogens commonly transmitted through foods. The approach can be applied to a variety of pathogens, and results can be used to assist risk management decisions and identify and prioritize areas for interventions.

APPENDIX. Reference, country, subtype, time period, and number of cases and controls interviewed of case-control studies of sporadic salmonellosis collected in the systematic review

Reference	Country	Subtype	Time period	No. of cases	No. of controls
[32]	France	<i>S. Typhimurium</i>	1995	108	105
[34]	Netherlands	<i>S. Enteritidis</i>	2002–2003	167	3119
[35]	USA	<i>S. Newport</i>	2002–2003	214	1154
[36]	Canada	<i>S. Heidelberg</i>	2003 (Jan.–May)	95	95
[37]	Canada	<i>S. Typhimurium</i>	1999–2000	258	258
[38]	USA	<i>Salmonella</i> spp.	1996	22	39
[39]	USA	<i>S. Typhimurium</i>	1996–1997	166	317
[40]	USA	<i>S. Javiana</i>	2001	55	109
[41]	USA	<i>S. Newport</i>	1999–2002	32	94
[42]	UK	<i>Salmonella</i> spp.	1997–1998	99	99
[43]	Trinidad & Tobago	<i>S. Enteritidis</i>	1998–1999	46	92
[44]	USA	<i>S. Enteritidis</i>	1996	43	86
[45]	France	<i>S. Typhimurium</i>	1996	108	105
[46]	UK	<i>Salmonella</i> spp.	1993	143	854
[47]	Switzerland	<i>Salmonella</i> spp.	1993	223	223
[48]	UK	<i>S. Virchow</i>	1994	88	182
[49]	USA	<i>S. Enteritidis</i>	1989–1990	106	212
		<i>S. Typhimurium</i>			
[50]	USA	<i>S. Enteritidis</i>	2002–2003	218	742
[51]	Australia	<i>S. Mississippi</i>	2001–2002	59	219
[52]	USA	<i>Salmonella</i> spp.	1989	120	265
[53]	Australia	<i>S. Birkenhead</i>	2001–2002	111	234
[54]	Spain	<i>Salmonella</i> spp.	1989–1990	117	84
[55]	UK	<i>S. Enteritidis</i>	1997	64	64
[56]	USA	<i>Salmonella</i> spp.	2002–2004	442	928
[57]	USA	<i>Salmonella</i> spp.	1998–1999	115	115
[58]	USA	<i>S. Enteritidis</i>	1994 (summer)	58	98
[59]	USA	<i>Salmonella</i> spp.	1993–1995	90	264
[60]	USA	<i>S. Dublin</i>	1979–1980	32	62
[61]	UKA	<i>S. Typhimurium</i>	1993	83	235
[62]	Denmark	<i>S. Enteritidis</i>	1997–1999	455	507
[63]	USA	<i>S. Enteritidis</i>	1997	35	59
[64]	USA	<i>S. Enteritidis</i>	1996–1997	182	345
[65]	USA	<i>S. Heidelberg</i>	1996–1997	44	83
[66]	USA	<i>Salmonella</i> spp.	1996–1997	463	7618
[67]	Norway	<i>S. Typhimurium</i>	1990–1002	41	82

ACKNOWLEDGEMENTS

Financial support was provided by the EU Network of Excellence MedVetNet.

DECLARATION OF INTEREST

None.

REFERENCES

1. **EFSA.** The community summary report on trends and sources of zoonoses, zoonotic agents, antimicrobial resistance and foodborne outbreaks in the European Union in 2006. EFSA, 2007.
2. **Mead PS, et al.** Food-related illness and death in the United States. *Emerging Infectious Diseases* 1999; **5**: 607–625.
3. **Mølbak K, Olsen JE, Wegener H.** Salmonella infections. In: Riemann HP, Cliver DO, eds. *Foodborne Infections and Intoxications*, 3rd edn. London: Elsevier, 2006, pp. 57–136.
4. **Baker MG.** A recurring salmonellosis epidemic in New Zealand linked to contact with sheep. *Epidemiology and Infection* 2007; **135**: 76–83.
5. **Neimann J, et al.** A case-control study of risk factors for sporadic campylobacter infections in

- Denmark. *Epidemiology and Infection* 2003; **130**: 353–366.
6. Wallace MA, Thompson G. Salmonellosis in a nursing home patient on enteral feeding. *American Journal of Infection Control* 2006; **34**: 97.
 7. Engberg J. Contributions to the epidemiology of Campylobacter infections. A review of clinical and microbiological studies. *Danish Medical Bulletin* 2006; **53**: 361–389.
 8. Pires SM, *et al.* Attributing the human disease burden of foodborne infections to specific sources. *Foodborne Pathogens and Disease* 2009; **6**: 417–424.
 9. Clayton D, Hills M. *Statistical Models in Epidemiology*. Oxford, New York, Tokyo: Oxford University Press, 1993.
 10. Stafford RJ, *et al.* Population-attributable risk estimates for risk factors associated with Campylobacter infection, Australia. *Emerging Infectious Diseases* 2008; **14**: 895–901.
 11. Engberg J. Contributions to the epidemiology of Campylobacter infections. A review of clinical and microbiological studies. *Danish Medical Bulletin* 2006; **53**: 361–389.
 12. Khan K, *et al.* Systematic reviews to support evidence-based medicine. *Preventive Veterinary Medicine* 2009; **87**: 213–228.
 13. Sargeant JM, *et al.* The process of systematic review and its application in agri-food public-health. *Preventive Veterinary Medicine* 2006; **75**: 141–151.
 14. Domingues A, *et al.* Source attribution of human campylobacteriosis using a meta-analysis of case-control studies of sporadic infections. *Epidemiology and Infection* (in press).
 15. Biostat Institute Inc. *Comprehensive meta-analysis. Meta-Analysis Manual*. Englewood, New Jersey, USA, 2008.
 16. Halasa T, *et al.* Meta-analysis of dry cow management for dairy cattle. Part 2. Cure of existing intramammary infections. *Journal of Dairy Science* 2009; **92**: 3150–3157.
 17. Borenstein M. *Introduction to Meta-Analysis*. Chichester, UK: John Wiley & Sons Ltd, 2009.
 18. Halasa T, *et al.* Meta-analysis of dry cow management for dairy cattle. Part 1. Protection against new intramammary infections. *Journal of Dairy Science* 2009; **92**: 3134–3149.
 19. Duval S, Tweedie R. A nonparametric ‘trim and fill’ method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association* 2000; **95**: 89–98.
 20. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50**: 1088–1101.
 21. Egger M, *et al.* Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* 1997; **315**: 629–634.
 22. Orwin R. A fail-safe N for effect size in meta-analysis. *Journal of Educational Statistics* 1983; **8**: 157–159.
 23. Dohoo I, Martin S, Stryhn H. *Veterinary Epidemiological Research*. Charlottetown, Prince Edward Island, Canada: AVC, 2003.
 24. Pires SM, *et al.* Salmonella source attribution in different European countries. *Proceedings of the Food Micro Conference, Aberdeen, Scotland*, 2008.
 25. Hald T, *et al.* A Bayesian approach to quantify the contribution of animal-food sources to human salmonellosis. *Risk Analysis* 2004; **24**: 255–269.
 26. Pires SM, Hald T. Assessing the differences in public health impact of salmonella subtypes using a bayesian microbial subtyping approach for source attribution. *Foodborne Pathogens and Disease* 2010; **7**: 143–151.
 27. Ekdahl K, *et al.* Travel-associated non-typhoidal salmonellosis: geographical and seasonal differences and serotype distribution. *Clinical Microbiology and Infection* 2005; **11**: 138–144.
 28. Pires SM, *et al.* Using outbreak data for source attribution of human salmonellosis and campylobacteriosis in Europe. *Foodborne Pathogens and Disease* 2010; **7**: 1351–1361.
 29. Havelaar AH, *et al.* Attribution of foodborne pathogens using structured expert elicitation. *Foodborne Pathogens and Diseases* 2008; **5**: 649–659.
 30. Greig JD, Ravel A. Analysis of foodborne outbreak data reported internationally for source attribution. *International Journal of Food Microbiology* 2009; **130**: 77–87.
 31. Ferguson CJ. Evidence for publication bias in video game violence effects literature: a meta-analytic review. *Aggression and Violent behavior* **12**: 470–482.
 32. Delarocque-Astagneau E, *et al.* Risk factors for the occurrence of sporadic Salmonella enterica serotype typhimurium infections in children in France: a national case-control study. *Clinical Infectious Diseases* 2000; **31**: 488–492.
 33. Painter JA, *et al.* Recipes for foodborne outbreaks: a scheme for categorizing and grouping implicated foods. *Foodborne Pathogens and Disease* 2009; **6**: 1259–1264.
 34. Doorduyn Y, *et al.* Risk factors for Salmonella Enteritidis and Typhimurium (DT104 and non-DT104) infections in The Netherlands: predominant roles for raw eggs in Enteritidis and sandboxes in Typhimurium infections. *Epidemiology and Infection* 2006; **134**: 617–626.
 35. Varma JK, *et al.* Highly resistant Salmonella Newport-MDRampC transmitted through the domestic US food supply: a FoodNet case-control study of sporadic Salmonella Newport infections, 2002–2003. *Journal of Infectious Diseases* 2006; **194**: 222–230.
 36. Currie A, *et al.* Frozen chicken nuggets and strips and eggs are leading risk factors for Salmonella Heidelberg infections in Canada. *Epidemiology and Infection* 2005; **133**: 809–816.
 37. Dore K, *et al.* Risk factors for Salmonella Typhimurium DT104 and non-DT104 infection: a Canadian multi-provincial case-control study. *Epidemiology and Infection* 2004; **132**: 485–493.
 38. Rowe SY, *et al.* Breast-feeding decreases the risk of sporadic salmonellosis among infants in FoodNet sites. *Clinical Infectious Diseases* 2004; **38** (Suppl. 3): S262–S270.

39. Glynn MK, *et al.* Prior antimicrobial agent use increases the risk of sporadic infections with multidrug-resistant *Salmonella enterica* serotype Typhimurium: a FoodNet case-control study, 1996–1997. *Clinical Infectious Diseases* 2004; **38** (Suppl. 3): S227–S236.
40. Srikantiah P, *et al.* *Salmonella enterica* serotype Javiana infections associated with amphibian contact, Mississippi, 2001. *Epidemiology and Infection* 2004; **132**: 273–281.
41. Gupta A, *et al.* Emergence of multidrug-resistant *Salmonella enterica* serotype Newport infections resistant to expanded-spectrum cephalosporins in the United States. *Journal of Infectious Diseases* 2003; **188**: 1707–1716.
42. Parry SM, *et al.* Risk factors for salmonella food poisoning in the domestic kitchen – a case control study. *Epidemiology and Infection* 2002; **129**: 277–285.
43. Indar-Harrinauth L, *et al.* Emergence of *Salmonella enteritidis* phage type 4 in the Caribbean: case-control study in Trinidad and Tobago, West Indies. *Clinical Infectious Diseases* 2001; **32**: 890–896.
44. Sobel J, *et al.* The pandemic of *Salmonella enteritidis* phage type 4 reaches Utah: a complex investigation confirms the need for continuing rigorous control measures. *Epidemiology and Infection* 2000; **125**: 1–8.
45. Delarocque-Astagneau E, *et al.* Risk factors for the occurrence of sporadic *Salmonella enterica* serotype typhimurium infections in children in France: a national case-control study. *Clinical Infectious Diseases* 2000; **31**: 488–492.
46. Banatvala N, *et al.* Salmonellosis in North Thames (East), UK: associated risk factors. *Epidemiology and Infection* 1999; **122**: 201–207.
47. Schmid H, *et al.* Risk factors for sporadic salmonellosis in Switzerland. *European Journal of Clinical Microbiology and Infectious Disease* 1996; **15**: 725–732.
48. Willocks LJ, *et al.* *Salmonella virchow* PT 26 infection in England and Wales: a case control study investigating an increase in cases during 1994. *Epidemiology and Infection* 1996; **117**: 35–41.
49. Hedberg CW, *et al.* Role of egg consumption in sporadic *Salmonella enteritidis* and *Salmonella typhimurium* infections in Minnesota. *Journal of Infectious Diseases* 1993; **167**: 107–111.
50. Marcus R, *et al.* Re-assessment of risk factors for sporadic *Salmonella* serotype Enteritidis infections: a case-control study in five FoodNet Sites, 2002–2003. *Epidemiology and Infection* 2007; **135**: 84–92.
51. Ashbolt R, Kirk MD. *Salmonella* Mississippi infections in Tasmania: the role of native Australian animals and untreated drinking water. *Epidemiology and Infection* 2006; **134**: 1257–1265.
52. Kass PH, *et al.* Disease determinants of sporadic salmonellosis in four northern California counties. A case-control study of older children and adults. *Annals of Epidemiology* 1992; **2**: 683–696.
53. Beard F, *et al.* Risk factors for sporadic *Salmonella* Birkenhead infection in Queensland and northern New South Wales: a case control study. *NSW Public Health Bulletin* 2004; **15**: 172–177.
54. Bellido-Blasco JB, *et al.* Risk factors for the occurrence of sporadic *Campylobacter*, *Salmonella* and rotavirus diarrhea in preschool children. *Anales de pediatria (Barcelona)* 2007; **66**: 367–374.
55. Hayes S, *et al.* Undercooked hens eggs remain a risk factor for sporadic *Salmonella enteritidis* infection. *Communicable Disease and Public Health* 1999; **2**: 66–67.
56. Jones TF, *et al.* A case-control study of the epidemiology of sporadic *Salmonella* infection in infants. *Pediatrics* 2006; **118**: 2380–2387.
57. Kohl KS, *et al.* Relationship between home food-handling practices and sporadic salmonellosis in adults in Louisiana, United States. *Epidemiology and Infection* 2002; **129**: 267–276.
58. Passaro DJ, *et al.* Epidemic *Salmonella enteritidis* infection in Los Angeles County, California. The predominance of phage type 4. *Western Journal of Medicine* 1996; **165**: 126–130.
59. Schutze GE, *et al.* Epidemiology and molecular identification of *Salmonella* infections in children. *Archives of Pediatrics & Adolescent Medicine* 1998; **152**: 659–664.
60. Taylor DN, *et al.* *Salmonella dublin* infections in the United States, 1979–1980. *Journal of Infectious Diseases* 1982; **146**: 322–327.
61. Wall PG, *et al.* A case control study of infection with an epidemic strain of multiresistant *Salmonella typhimurium* DT104 in England and Wales. *Communicable Disease Reports. CDR Reviews* 1994; **4**: R130–R135.
62. Mølbak K, Neimann J. Risk factors for sporadic infection with *Salmonella enteritidis*, Denmark, 1997–1999. *American Journal of Epidemiology* 2002; **156**: 654–661.
63. Trepkova MJ, *et al.* An increase in sporadic and outbreak-associated *Salmonella enteritidis* infections in Wisconsin: the role of eggs. *Journal of Infectious Diseases* 1999; **180**: 1214–1219.
64. Kimura AC, *et al.* Chicken consumption is a newly identified risk factor for sporadic *Salmonella enterica* serotype Enteritidis infections in the United States: a case-control study in FoodNet sites. *Clinical Infectious Diseases* 2004; **38** (Suppl. 3): S244–S252.
65. Hennessy TW, *et al.* Egg consumption is the principal risk factor for sporadic *Salmonella* serotype Heidelberg infections: a case-control study in FoodNet sites. *Clinical Infectious Diseases* 2004; **38** (Suppl. 3): S237–S243.
66. Mermin J, *et al.* Reptiles, amphibians, and human *Salmonella* infection: a population-based, case-control study. *Clinical Infectious Diseases* 2004; **38** (Suppl. 3): S253–S261.
67. Kapperud G, Stenwig H, Lassen J. Epidemiology of *Salmonella typhimurium* O: 4–12 infection in Norway: evidence of transmission from an avian wildlife reservoir. *American Journal of Epidemiology* 1998; **147**: 774–782.