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Source Attribution of Human Salmonellosis: An Overview of Methods and Estimates

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Abstract

Reducing the burden of foodborne salmonellosis is challenging. It requires identification of the most important food sources causing disease and prioritization of effective intervention strategies. For this purpose, a variety of methods to estimate the relative contribution of different sources of *Salmonella* infections have been applied worldwide. Each has strengths and limitations, and the usefulness of each depends on the public health questions being addressed. In this study, we reviewed the source attribution methods and outcomes of several studies developed in different countries and settings, comparing approaches and regional differences in attribution estimates. Reviewed results suggest that illnesses and outbreaks are most commonly attributed to exposure to contaminated food, and that eggs, broiler chickens, and pigs are among the top sources. Although most source attribution studies do not attribute salmonellosis to produce, outbreak data in several countries suggest that exposure to raw vegetables is also an important source. International travel was also a consistently important exposure in several studies. Still, the relative contribution of specific sources to human salmonellosis varied substantially between studies. Although differences in data inputs, methods, and the point in the food system where attribution was estimated contribute to variability between studies, observed differences also suggest regional differences in the epidemiology of salmonellosis.

Introduction

Salmonellosis is a growing public health concern in both the developed and developing worlds. *Salmonella* spp. have a variety of animal reservoirs and routes of transmission that can result in human infection. However, the majority of infections in developed countries are thought to be caused by foodborne exposures (Scallan *et al.*, 2011). Reducing the burden of foodborne salmonellosis is challenging; it requires identification of the most important food sources causing disease and prioritization of effective intervention strategies. A variety of methods to estimate the relative contribution of different food sources to human foodborne disease have been developed, including the microbial subtyping approach,

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comparative exposure assessment, epidemiological analysis of sporadic cases, analysis of data from outbreak investigations, and expert elicitation (Pires *et al.*, 2009). Each of these approaches has strengths and limitations, and the usefulness of each depends on the public health questions being addressed. In this study, we reviewed methods and results of several source attribution studies of *Salmonella* spp. developed in different countries, and compared the approaches and regional differences in the results.

Overview of Source Attribution Methods

Approaches to source attribution can be grouped broadly into four categories: microbiological, epidemiological, expert elicitation, and intervention studies (Pires *et al.*, 2009). Methods in all categories have been used to estimate the sources of salmonellosis in different subpopulations, and some have applied attribution results beyond the original study population.

One of the most frequently used methods for source attribution of salmonellosis is the microbial subtyping approach. The principle is to compare the subtypes of isolates obtained from different sources (e.g., animals, food) with those isolated from humans. This approach requires characterization of the etiologic agent by subtyping methods (e.g., phenotypic or genotypic subtyping), and depends on strong associations between dominant subtypes and a specific reservoir or source. Using a collection of temporally and spatially related isolates from various sources, this approach estimates the number of laboratory-confirmed, sporadic (i.e., illnesses not associated with outbreaks) human cases attributable to each source; thus, it is facilitated by an integrated foodborne disease surveillance program that collects isolates from the major food sources, as well as from human cases of infection.

Another microbiological approach to source attribution is the comparative exposure assessment. The principle is to determine the relative importance of the known transmission routes by estimating the human exposure to the hazard via each route. For each known route, this approach requires information on the prevalence and quantity of the hazard in the source, the changes in these throughout the transmission chain, and the frequency of human exposure by each route (e.g., consumption data). With this information, the total exposure in the population associated with each transmission route is estimated. These estimates are used to partition the total number of illnesses caused by the specific hazard to each transmission route, proportionally to the total exposure from all routes. The estimates of exposure for each route can be subsequently combined with a dose–response model to predict the number of infections in the population from each route.

Epidemiological approaches to source attribution include analyses of data from sporadic case–control studies and analyses of information collected during outbreak investigations. Case–control studies of sporadic, laboratory-confirmed infections are the most commonly used approach to determining the importance of possible risk factors for illness, including sources and predisposing, behavioral, or seasonal factors. Population-attributable fractions (PAFs) from case–control studies are used to estimate the proportion of laboratory-confirmed illnesses in the target population attributable to each source (Greenland and Robins, 1998). A systematic review of published case–control studies of a given hazard

can provide an overview of the relevant exposures and risk factors for disease, as well as a summary of estimated PAFs generalized to a broader population. A PAF derived from a meta-analysis of several case–control studies can be combined with an estimate of the total number of illnesses in a population caused by that hazard to estimate the number of illnesses attributable to each exposure.

Many foodborne outbreak investigations are successful in identifying the specific contaminated source or ingredient that transmitted the causative agent. By conducting an analysis of data collected during outbreak investigations, the most common foods involved in outbreaks can be identified. A simple descriptive analysis or summary of outbreak investigations is useful for quantifying the relative contribution of different foods to outbreak illnesses. However, outbreak data have also been used to estimate the total number of illnesses in the population attributable to different foods. The approaches used to extrapolate the results of outbreak investigations to estimate the sources of illness in the population also include methods to estimate the contaminated ingredients in “complex” foods (i.e., foods containing ingredients from different food categories). By assigning a probability to each ingredient corresponding to the likelihood that it was the source of the outbreak, data from both simple (i.e., a single contaminated ingredient or a food containing multiple ingredients belonging to a single food category) and complex foods implicated in outbreaks can be used to attribute foodborne illnesses to sources. A source attribution method using data from both simple and complex foods was developed by Painter *et al.* (2006, 2013) and adapted by Pires *et al.* (2010, 2011a, 2012).

Expert opinions may be used to fill data gaps, to combine data from different studies and scientific approaches into a single estimate, or as an alternative source-attribution method when other methods are not feasible or useful to address a public health question (EFSA, 2008). Expert judgments are subjective and may be biased by many factors, including the background and scientific expertise of the respondents. Expert elicitations have also been used to partition the estimated number of foodborne illnesses in the population to foodborne, environmental, contact with animals and their environments, and human-to-human transmission pathways.

The implementation of *Salmonella* control programs focused on particular foods and the subsequent evaluation of their public health impact on a population constitute large-scale intervention studies that can be used to estimate the proportion of illnesses in the population due to those foods. Examples include intervention programs established in Denmark during the 1990s (Wegener *et al.*, 2003) followed by studies that measured reduction of human salmonellosis (Wegener, 2010), and the measures to control the epidemic of *Salmonella* enterica serotype Enteritidis introduced in the United Kingdom (O’Brien, 2013) followed by an analysis of the decline in human cases.

Each of these methods has different data requirements and may estimate sources for different subpopulations of human illness (i.e., laboratory-confirmed sporadic illnesses, outbreak-associated illnesses, and illnesses in the general population) at different points of the farm-to-consumption chain (production or exposure), and therefore their utility will vary depending on both the hazard and surveillance data available. The variety of methods

available for source attribution of foodborne illness has been described in detail by Pires *et al*. (2009), as well as description of the data requirements of each approach (Pires, 2013).

Overview of Published Studies

Many source attribution studies for *Salmonella spp*. using national or regional foodborne disease data have been published in recent years. Several research groups work in this area, including research teams in Denmark, United States, New Zealand, and The Netherlands. We conducted a comprehensive literature review to collect all published studies attributing human salmonellosis to the responsible sources. In addition to a web-based literature search, we have identified published studies referenced in other publications and through personal contacts in the scientific community.

The strengths and weaknesses of each method influence their utility to a specific attribution question, and results should be interpreted in light of these method characteristics (Table 1). Data availability often drives the selection of the source attribution approach used. The microbial subtyping approach has been used in several countries, and it was recently adapted to two sets of data in France to study the impact of data quality on the attribution results (David *et al*., 2013). In contrast, the comparative exposure assessment approach has only been applied using data from Denmark (Pires, 2009). Table 2 provides an overview of the country or region of origin and methods used in recently published studies. We present, compare, and discuss the main findings of these studies.

Microbial subtyping

The microbial subtyping approach originally described by Hald *et al*. (2004) is routinely applied in Denmark to estimate the relative contribution of domestic and imported food-animal sources to sporadic salmonellosis. The proportion of cases acquired abroad is also estimated, as is the proportion of disease that cannot be attributed to any of the known sources (Anon., 2011). Results from 2010 estimated that domestically produced pork was the food most likely to cause illness in the country (15%), followed by imported pork (5%), imported beef (2%), and table eggs (2%) (Table 3). Nearly half of the reported *Salmonella* infections (47%) were estimated to be acquired during international travel. When the same model was applied to data from Sweden (Whalström *et al*., 2011), results indicated that over 80% of the *Salmonella* cases were acquired abroad and that domestic food-producing animals were responsible for less than 1% (Table 3).

The Hald approach was also applied to data from several European Union (EU) countries in a model that used data from the European Center for Disease Control and the European Food Safety Authority (EFSA) (Pires *et al*., 2011a). The model was applied to data from 24 Member States and attributed human sporadic salmonellosis to four animal reservoirs: pigs, broiler chickens, laying hens, and turkeys. Results showed that the relative contribution of sources varied between regions and countries (Table 3). In contrast to independent results from Denmark, this model estimated that in the EU the laying hen reservoir (eggs) was the most important source (44% of cases), followed by pigs (27%). This was driven by results of analyses for Eastern, Northern, and Southern Europe, where layers contributed between 30% and 59% of salmonellosis. Results for food sources of disease among Western

EU states were more similar to those from Denmark, with pork being the leading food source (44%), and turkeys (4%) and broilers (3%) less important. The estimated contribution of broilers was low, representing less than 1% of the total reported *Salmonella* cases in Denmark and Sweden, and around 3% in EU countries overall (Table 3). International travel was a less important source of salmonellosis in the EU overall (9%) than in Northern EU (which includes Denmark and Sweden), where it was responsible for an estimated 33% of infections. Overall, 4% of reported illnesses were related to outbreaks with unknown source, and 9% of the cases could not be attributed to any source included in the model (Table 3).

The Hald microbial subtyping model (Hald *et al.*, 2004) was also adapted to national surveillance data from Japan, the United States, and New Zealand. In Japan, data collected between 1998 and 2007 was used to estimate the number of human *Salmonella* illnesses attributable to each of the major food animal reservoirs (Toyofuku *et al.*, 2011). Eggs were estimated to be the most important source, responsible for over 50% of cases in most years. Broilers and pigs were the second most important sources, depending on the year, while cattle were seldom associated. The U.S. model adaptation (Guo *et al.*, 2011) estimated the relative proportions of domestically acquired sporadic *Salmonella* infections resulting from contamination in six food sources sampled at processing sites in the United States from 1998 through 2003. Unlike results from the EU analysis, broilers were estimated to be the most important food source of domestic sporadic cases of salmonellosis (48%) for all study years. Additional sources were ground beef (28%), turkey (17%), egg products other than intact shell eggs (6%), intact beef (1%), and pork (< 1%).However, lacking data from other sources, the U.S. model estimated that all *Salmonella* illnesses were associated with the six modeled food sources, and did not attribute any illnesses to travel, shell eggs, produce, or other sources. The New Zealand model included several modifications that allow it to be more easily adapted to countries without intensive surveillance systems (Mullner *et al.*, 2009). The model attributed the majority of the *Salmonella* illnesses to pork (60%), followed by poultry (21%) and beef and veal (12%); eggs (3%) and lamb (1%) were estimated to be minor sources.

Analysis of data from outbreak investigations

Statistical analyses of outbreak data have been used in several countries to attribute illnesses to sources and examine changes in the foods causing outbreaks over time. A statistical analysis of data from *Salmonella* outbreaks in Canada from 1996 to 2005 (Ravel *et al.*, 2009) showed that produce was the most frequent cause of outbreaks (29%), followed by poultry (15%), other meats (15%), dairy products (9%), and seafood (6.6%). In contrast to findings in other regions, attribution to eggs was low, causing only 5% of outbreaks. In 13% of outbreaks, the implicated food was “complex,” and the contaminated ingredient was not identified or estimated through modeling.

In another study, outbreaks of salmonellosis reported in New Zealand from 2000 to 2009 were analyzed (King *et al.*, 2011). The study included an analysis of outbreak settings, main transmission pathway, and food sources. Foodborne transmission was reported for 63% of the 123 outbreaks for which only 1 mode of transmission was reported, followed by person-to-person (32%), waterborne (3%), and zoonotic (2%). The results of this analysis

support the hypothesis that salmonellosis is primarily a foodborne disease in New Zealand, but the study did not identify important food vehicles.

A similar analysis of *Salmonella* outbreaks was conducted in Latin America and the Caribbean (Pires *et al.*, 2012). Data from 20 countries for the period 1993 through 2010 were collected. Overall, eggs, meat products, vegetables, chicken, grains and beans, and pork were the most important sources of salmonellosis. When outbreaks with an unknown source were excluded, results showed a substantial increase from the 1990s to the 2000s in the proportion of illnesses attributed to eggs (from 17% to 43%) and pork (4%–9%), and minor increases in the relative contribution of vegetables (10%–12%). In contrast, the proportion of illnesses attributed to meat products (29%–9%) and chicken (12%–6%) decreased in the same period. The method was also applied to obtain source attribution estimates for Japan (Pires *et al.*, 2011b). Data included the study period 2000–2009 and also attributed disease to both food sources and water. Estimates suggested that eggs were the most important food source, and that the proportion of illnesses attributed to this source increased in the second half of the decade. Among illnesses attributed to a known source, vegetables followed eggs in importance, contributing 13% of illnesses from 2000 to 2004 and 17% from 2005 to 2009, followed by grains and beans (12% from 2000 to 2004 and 12.4 from 2005 to 2009). All remaining food sources were of minor importance. However, over 80% of reported outbreaks did not implicate a contaminated source, and therefore could not be used in the model.

A statistical analysis of outbreak data collected in the United States was conducted to determine significant changes over time in the proportion of outbreaks and outbreak illnesses attributable to each food category using information from outbreaks implicating simple foods (Gould *et al.*, 2013). In this analysis, *Salmonella* outbreaks were most commonly associated with poultry (includes both chicken and turkey; 30%) and eggs (24%). Other food categories showed much lower attribution proportions: pork at 9% and beef at 8%. Although changes in the proportions of outbreaks associated with eggs, poultry, beef, pork, and vine-stalk vegetables were observed, only the change associated with the proportion attributed to eggs was statistically significant, decreasing from 33% in 1998–1999 to 15% in 2006–2008.

Probabilistic models using information from both simple and complex foods implicated in outbreaks have been applied in several countries and regions to attribute the estimated number of *Salmonella* infections in the population to food sources (Table 4). Such a model was applied to data from 27 EU Member States, Norway, and Switzerland. It attributed all *Salmonella* illnesses, both sporadic and outbreak-associated, occurring between 2007 and 2009 to water and 19 food sources based on the attribution proportions estimated from outbreaks with known sources (Table 4) (Pires *et al.*, 2011a). Eggs were estimated to be the most important source, followed by pork, chicken, the general category “meat and poultry,” and dairy products. The proportion of *Salmonella* outbreaks attributed to an unknown source and to various food sources varied substantially among EU regions (Table 4). A higher proportion of illnesses were attributed to eggs in Eastern Europe (84%) and Southern Europe (74%) than in other regions. Pork followed eggs in importance in Western Europe (17%), whereas vegetables were estimated to be a major contributor in Northern Europe (19%).

Chicken (ranking second to fourth, depending on region) and dairy products (ranking third to fifth, depending on region) were important in all regions.

Using a similar approach, outbreak data collected by the U.S. Centers for Disease Control and Prevention (CDC) Foodborne Disease Outbreak Surveillance System from 1998 through 2008 was used in a recently published source attribution study (Painter *et al.*, 2013). The model used data on the number of illnesses associated with outbreaks implicating either a simple or complex food in a probabilistic model attributing the estimated number of domestically acquired foodborne *Salmonella* illnesses (Scallan *et al.*, 2011) to food categories. In this analysis, vine-stalk vegetables and poultry (includes both chicken and turkey) were estimated to be the most common sources, responsible for 21% and 19% of illnesses, respectively (Table 4). These were followed by eggs (15%) and the fruits and nuts category (13%).

Systematic review of case–control studies

To identify the most important risk factors for sporadic cases of salmonellosis, a systematic review of case–control studies and a meta-analysis of study results was performed (Domingues *et al.*, 2012). Thirty-five *Salmonella* case–control studies published in 11 countries were identified (Australia, Canada, Denmark, France, the Netherlands, Norway, Spain, Switzerland, Trinidad and Tobago, United States, and United Kingdom). Results showed that international travel, medical predispositions (i.e., intake of antiacids, pre-existing medical condition, and previous intake of antimicrobials), eating raw eggs, and eating in a restaurant were the most important risk factors for sporadic human salmonellosis. Consumption of undercooked or raw eggs and chicken in a restaurant were the only food items identified as exposure risks for human disease in the analysis; environmental routes (both drinking and recreational waters), direct contact with pets and farm animals, and various predisposition factors proved to play major roles in human salmonellosis. The results of the analyses focusing on serotypes suggested that traveling abroad and consumption of eggs are particularly important risk factors for *Salmonella* enterica serotype Enteritidis infection, while previous intake of antimicrobials was the only risk factor identified for Typhimurium. The studies did not allow for an analysis by region or age group.

Expert elicitation

Expert elicitations have estimated the proportion of all *Salmonella* illnesses in the population that can be attributed to foodborne transmission. In 1999, Mead *et al.* partially relied on expert opinions to estimate that 95% of U.S. salmonellosis was foodborne (Mead *et al.*, 1999). Later estimates of the total number of foodborne illness in the United States published by Scallan *et al.* (2011) were similar, with 94% of domestically acquired salmonellosis estimated to be foodborne. Hall and Kirk performed an expert elicitation with experts from public health and food safety fields in Australia, where 87% of the *Salmonella* illnesses cases were attributed to foodborne sources (Hall and Kirk, 2005). Estimates of foodborne transmission of *Salmonella* in New Zealand based on expert elicitation were much lower, with a most likely value of 61% (Cressey and Lake, 2005).

An expert elicitation study was conducted to estimate the fractions of several causes of enteric illness transmitted by five major pathways globally (food, environment, direct contact, human-to-human transmission, and travel) and by 11 foods (Havelaar *et al.*, 2008). The study estimated that, for *Salmonella*, 55% of cases are foodborne and that eggs are the most important food source (22%), followed by poultry (15%), pork (14%) and beef and lamb (13%). Another expert elicitation study performed by Hoffmann *et al.* (2007) in the United States used 45 experts, including leading food safety scientists, public health officials, and policy experts. Results suggested that 35% of U.S. foodborne *Salmonella* illnesses can be attributed to poultry, 22% to eggs, 12% to produce and 11% to beef. An expert elicitation conducted in Canada showed that, among *Salmonella* illnesses transmitted through food, poultry (34%–42%), eggs (19%–21%), produce (8%–18%), and pork (7%–8%) were the main sources (Davidson *et al.*, 2011). The initial results of the Canadian expert elicitation were widely diverse. Because disagreements between experts clustered in two distinct subgroups for certain pathogens, the authors used external information to choose the estimates derived from one subgroup of experts. Because of differences in the selection of experts, the elicitation tool, and the analysis of results, comparison of results from different expert elicitations should be made with care.

Discussion

Salmonellosis is a leading bacterial cause of foodborne illness in many developed countries. To inform prevention strategies, several approaches to source attribution have been applied to data collected in several countries. The results of these studies suggest that illnesses and outbreaks are most commonly attributed to food exposures, and eggs and broiler chickens are among the top food sources. Although most types of source attribution studies do not attribute *Salmonella* infections to produce commodities, studies using outbreak data in several countries suggest that produce is also a significant source. Attribution to international travel is also consistent among studies, but none provided specific information regarding countries associated with higher infection risks. Other studies have analyzed available data on human salmonellosis acquired during international travel (Ekdahl *et al.*, 2005; Havelaar *et al.*, 2012; Kendall *et al.*, 2012), but these data have not been used to attribute salmonellosis to different countries or regions.

Each approach to source attribution has different data requirements and method uncertainties, and attributes illness from different subpopulations to various points of the farm-to-consumption chain. These differences in data and methods contribute to the observed variability in estimates across the studies. Nonetheless, comparisons of the relative contribution of different foods and transmission pathways among different countries highlight regional differences in the epidemiology of salmonellosis.

Estimates of source attribution will vary depending upon the approach used. Case–control studies of sporadic illnesses and analyses of outbreak data both attribute illnesses to contamination at the point of consumption or the point of direct contact. However, case–control studies estimate attributable fractions by comparing the exposure distributions among sporadic cases and population-based controls after controlling for potentially confounding variables and estimating the excess risk associated with specific exposures.

While attribution estimates for a range of food and nonfood exposures in the population can be obtained using case–control studies, the population-attributable fractions from these studies reflect the results of statistical models and are prone to limitations such as recall bias and reliance on several assumptions (Levine, 2007). In contrast, outbreak investigations directly determine the causal transmission route of illnesses, but these data can only attribute to exposures causing multiple illnesses clustered in time, in a single exposure location, or linked by the same etiologic agent subtype. As a result, attributable fractions obtained from case–control studies represent very different measures from those determined by outbreak analyses, and assumptions are required to generalize estimates from outbreak data to non-outbreak-related illnesses in the population. Microbial subtyping methods have also been used to attribute both sporadic and outbreak illnesses to sources. Attributable fractions determined by microbial subtyping analyses are based on variations in food contamination, and so represent very different measures from those determined by analyses of outbreaks or case–control studies. Assessing the degree to which estimates using these three data sources (outbreaks, case–control studies, and microbial subtypes of isolates from sources and ill persons) vary can help investigators determine data gaps and methods to improve estimates. However, analyses using data obtained from differing points in the farm-to-table continuum would be expected to produce different estimates.

The microbial subtyping approach requires estimates of *Salmonella* prevalence in all possible sources of human infection at the point of attribution for assumptions associated with this approach to be valid. All but the U.S. and New Zealand microbial subtyping models included a category “unknown” to account for sources of salmonellosis not specified in the model; in these two countries, all domestically acquired infections were assumed to be foodborne. Likewise, variation in the food regulatory and surveillance systems between countries also contributes to differences in the inherent model assumptions associated with the point in the food chain where source attribution estimates are derived. For example, in Sweden *Salmonella* surveillance in food animals includes regular sampling of production animals. Consequently, use of these subtyping models includes the assumption that all human infections are attributable to these farm sources, either directly through contact with farm animals or their food products, or indirectly via contamination of the environment or cross-contamination of other foods. In contrast, in the United States, regulation and collection of surveillance data on meat products is primarily at the point of slaughter and processing, so attribution to only this point in the food production chain includes the assumption that all infections result from exposure to animal food products or foods cross-contaminated by animal food products. Sampling strategies also vary among surveillance systems, depending upon the goals of the program. Thus, variation in food surveillance programs contributes to differences between countries to reliably estimate contamination prevalence among different sources. Baseline surveys of food animal sources conducted in the EU and the United States contributed prevalence data to subtyping models. Likewise, routine surveillance of production animals conducted in Sweden and other countries also provide good prevalence estimates. However, many countries conduct risk-based sampling, targeting surveillance to farms and facilities where contamination is most likely, and in these countries adaptations to the model are needed as was done in the United States, Japan, and New Zealand. These differences in data sources and modeling methods also limit direct

comparisons of attribution estimates across studies using similar approaches but data from different sources.

Country-specific differences in human surveillance systems also contribute to data-dependent variability in attribution estimates. Detection and reporting of human *Salmonella* infection is dependent upon healthcare and public health infrastructures, health-seeking behavior in the populations under surveillance, and diagnostic laboratory systems. These differences can bias human data available for attribution. For example, health-seeking behavior and laboratory testing practices may cause surveillance data to be over-representative of more susceptible populations such as the young, elderly, and those with chronic conditions (Scallan *et al.*, 2006). The degree to which these populations are over-represented may vary globally across cultures and levels of access to healthcare. In addition, differences in outbreak surveillance and reporting practices can also contribute to variability in the results of attribution analyses. Not all countries routinely collect data for nonfoodborne outbreaks. In 2009, the United States expanded national surveillance capacity to collect data on nonfoodborne outbreaks, resulting in a lower proportion of *Salmonella* outbreaks being attributed to food sources than previously estimated (Hall *et al.*, 2013). Likewise, criteria for outbreak reporting can vary between reporting jurisdictions. In some regions, outbreaks are more likely to be reported when a specific contaminated source is confirmed by isolation of the pathogen or agent in the food, while other public health agencies may report all outbreaks investigated, regardless of the level of certainty associated with the transmission pathway or implicated source. In regions or countries where these types of surveillance bias are prevalent, attribution studies may overestimate the importance of sources associated with susceptible subpopulations or transmission pathways more likely to lead to identification of a contaminated source.

In addition to method- and data-dependent sources of variability, attribution estimates reflect underlying differences in the epidemiology of salmonellosis in different countries and regions. For example, there were several differences in the observed distributions of *Salmonella* subtypes in food sources among EU countries (EFSA, 2008); and serotype Heidelberg was among the top four subtypes causing U.S. illnesses, but was not among the top 10 in the EU study (EFSA, 2008; Guo *et al.*, 2011). Likewise, differences in human consumption, international travel, and contact with water and animals play a role in the importance of specific sources of salmonellosis among different countries or regions. In the microbial subtyping model of Denmark, pork was the most commonly consumed food, whereas chicken was most commonly consumed in the U.S. model (Hald *et al.*, 2004; Guo *et al.*, 2011). Several studies found international travel to be a significant source of *Salmonella* infection. Collection of data on the country or region visited by ill persons can provide information on relative risks of travel to those regions (Kendall *et al.*, 2012; Ekdahl *et al.*, 2005).

In spite of the limitations in comparing source attribution estimates derived from different studies and countries, there are relevant observations regarding common sources of salmonellosis globally. Better understanding of the global burden and source attribution of salmonellosis will contribute to improved prevention strategies. This overview provides several insights and highlights opportunities for future studies. First, several approaches

to attribution of salmonellosis to specific sources are available, and should be applied in more countries, according to the data sources available, to improve our knowledge of the epidemiology of this pathogen globally. The results of this overview suggest that all approaches can provide important information regarding the sources of pathogens that contribute the greatest burden of illness. Secondly, future studies of salmonellosis should attempt to identify countries or regions of the world where travel may be most associated with risk of *Salmonella* infection. This knowledge, coupled with the results of microbial subtyping studies or outbreak investigations exploring imported food sources of *Salmonella*, may be useful to prevention efforts targeting imported foods. Finally, food product surveillance systems may increase sampling of plant commodities, so that attribution approaches including these sources may be expanded beyond outbreak data. Limited data in the United States (USDA, 2012) suggest that contamination rates are relatively low in most of these foods. Rates likely vary among countries with different agricultural practices, and even a low rate in a commonly consumed food that is not cooked can be important.

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Table 1.

Strengths and Limitations of Source Attribution (SA) Methods

SA approach	Strengths	Limitations
Subtyping approaches Microbial subtyping	Identifies the most important reservoirs of the zoonotic agent, and therefore: is useful to prioritize interventions at production level. reduces uncertainty due to cross-contamination and the risk of attributing to an "accidental" source. is able to follow trends over time.	Limited to pathogens that are heterogeneously distributed among the reservoirs. No information on different transmission pathways from reservoirs to humans. Data intensive, requiring a collection of representative isolates from all (major) sources. Standardized subtyping methods with appropriate level of discrimination are required (methods are changing over time, and new methods are potentially too discriminatory for SA models).
Comparative exposure assessment	Attributes illness to sources taking into account the different transmission routes from the same reservoir. Once a model is developed, new data can be easily included.	Often limited by lack of data, which results in large uncertainties around the estimates.
Epidemiological studies Case–control studies (including systematic review)	Valuable tool to identify relevant risk factors for human infections, including sources of exposure, predisposing, behavioral or seasonal factors. A systematic review of published case–control studies can provide an overview of the relevant exposures and risk factors for that infection, and may detect temporal and geographical variations. Can identify a wide range of known and unknown risk factors.	Misclassification due to immunity may reduce attributable risk or even suggest protection. Most studies only explain a small fraction of all cases. Cases may reflect a mixture of possible sources of exposure, and it may be difficult to distinguish between these exposures. Statistical power to determine the importance of common exposures often requires enrollment of many participants. Misclassification of exposures due to lack of accuracy of recall may lead to an underestimation of the burden of illness attributed to specific exposures.
Analysis of data from outbreaks	Documentation that a specific pathogen was transmitted to humans via a specific food item can be available. Data may capture the effect of contamination at multiple points from the farm-to-consumption chain A wide variety of food vehicles are represented, including less frequently identified food items. Data from outbreak investigations may be the most readily available source of information for source attribution in some countries or regions.	Quality of evidence varies and food classification schemes are not harmonized. Large outbreaks, outbreaks associated with point sources, outbreaks that have short incubation periods, and outbreaks that cause serious illness are more likely to be investigated. Illnesses included in data from outbreak investigations may not be representative of all foodborne illnesses. Certain food vehicles are more likely to be associated with reported outbreaks than others, which can lead to an overestimation of the proportion of human illnesses attributed to a specific food.
Intervention studies	Allows for a direct measure of the impact of a given source on the number of human cases of infection, avoiding the account for the effect of external sources or risk factors.	Interpretation of data from "large-scale" interventions is difficult, since usually several interventions are implemented at the same time. Complex and resource demanding studies.
Expert elicitations	Useful tool when data are lacking. For some pathogens, may be the only available method for SA.	Conclusions are based on the individual experts' judgment, which may be misinformed or biased.

Table 2.

Overview of *Salmonella* Illness Source-Attribution Studies Conducted Worldwide, by Source Attribution Method

Country/region	Microbial subtyping	Analyses of outbreak data	Expert elicitation	Comparative exposure assessment	Systematic review of case–control studies[a]	References
Denmark	X					Hald *et al.* (2004)
				X		Pires (2009)
Sweden	X					Whalström *et al.* (2011)
The Netherlands	X					Valkenburgh *et al.* (2007)
			X			Havelaar *et al.* (2008)
European Union	X	X				Pires *et al.* (2011a)
Latin America and Caribbean		X				Pires *et al.* (2012)
United States	X					Guo *et al.* (2011)
		X				Painter *et al.* (2013)
						Gould *et al.* (2013)
			X			Hoffman *et al.* (2007)
Canada		X				Ravel *et al.* (2009)
			X			Ravel *et al.* (2010)
Japan	X					Toyofuku *et al.* (2011)
		X				Pires *et al.* (2011b)
New Zealand	X					Mullner *et al.* (2009)
		X				King *et al.* (2011)
			X			Lake *et al.* (2010)
Global					X	Domingues *et al.* (2012)

[a] Several case–control studies of sporadic *Salmonella* infections have been published.

Table 3.

Estimated Percentage of *Salmonella* Illnesses Attributable to Animal-Food Sources, Travel, Wildlife, Unknown Sources, and Outbreaks in Denmark, Sweden, the European Union[*] (EU), the United States (USA), New Zealand, and Japan Using a Microbial Subtyping Approach

	Denmark[a]	Sweden[b]	EU[c]	EU Eastern[c,*]	EU Northern[c,*]	EU Western[c,*]	EU Southern[c,*]	USA[d,†]	New Zealand[e]	Japan[f,‡]
Pigs	15.1	0.08	26.9	22.7	10.6	34.1	43.6	< 1	60	5.3
Cattle	0.7	0.1	—	—	—	—	—	29[*,a]	11.5	0.5
Layers	1.8	0.16	43.8	59.4	30	41.8	28.4	6[*,b]	3.2	63.3
Broilers	0.5	0.09	3.4	7.0	1.2	2.1	3.1	48	21.2	6.4
Ducks	0.1	—	—	—	—	—	—	—	—	—
Turkeys	__[#]	—	4.0	2.2	7.4	4.1	7.6	17	—	—
Lamb/mutton	—	—	—	—	—	—	—	—	1.4	—
Imported food	—	6.4	—	—	—	—	—	_	_	—
Pork	5.4	—	—	—	—	—	—	—	—	—
Beef	2.0	—	—	—	—	—	—	_	_	—
Poultry	2.5	—	—	—	—	—	—	—	—	—
Wildlife	—	0.6	—	—	—	—	—	—	—	—
Travel	46.9	82	9.2	0.8	34.5	4.8	0.7	—	__[*,c]	—
Unknown, outbreak-associated	5.1	2.9	3.6	5.4	4.0	2.2	4.2	—	—	—
Unknown, sporadic	19.8	7.7	9.0	2.5	12.4	10.9	12.5	—	—	20.8

[*] EU regions as defined by the United Nations. Eastern Europe: Czech Republic, Hungary, Poland, and Slovakia. Northern Europe: Denmark, Estonia, Finland, Ireland, Latvia, Lithuania, Sweden, and the United Kingdom. Southern Europe: Cyprus, Greece, Italy, Portugal, Slovenia, and Spain. Western Europe: Austria, Belgium, France, Germany, Luxembourg, and the Netherlands.

[a] Data from 2010, Anon., 2011;

[b] Data from 2004–2006, Whalström *et al.*, 2011;

[c] Data from 2007–2009, Pires *et al.*, 2011a;

[d] Guo *et al.*, 2011;

[e] Mullner *et al.*, 2009;

[f] Toyofuku *et al.*, 2011.

[†] Estimates are restricted to those infections estimated to be domestically acquired and sporadic.

‡ Median of estimates over 10 years (1998–2017).

*,a Sum of estimates for "ground beef" and "intact beef".

*,b Estimate for "egg products" other than intact shell eggs.

Source not included in model.

*,c Estimates are restricted to those infections estimated to be domestically acquired.

Table 4.

Percentage of Estimated Number of *Salmonella* Infections Attributed to Food Sources in European Union Regions, Japan, and the United States, as Estimated by Analyses of Outbreaks with Known Sources

	Europe						
	2007–2009[a,d]				Japan[b,d]		USA[c]
	EE	NE	SE	WE	2000–2004	2005–2009	1998–2008
Eggs	84.3	40.0	73.8	62.1	57.2	49.6	14.8
Dairy	2.7	7.1	1.5	4.0	0.5	0.4	7.2
Goat milk	0.0	0.0	0.0	0.0	0.0	0.0	—
Meat	1.8	3.0	2.1	4.4	0.1	0.4	—
Poultry	0.0	0.0	13.7	0.3	0.0	0.0	19.0
Chicken	4.1	11.8	2.1	4.0	5.3	6.4	—
Ducks	0.0	0.0	0.0	0.0	0.3	0.8	—
Turkey	0.3	1.6	0.0	0.7	0.0	0.0	—
Beef	0.7	0.2	0.4	1.4	2.0	0.8	7.3
Pork	2.4	14.0	0.0	16.6	2.0	1.2	6.2
Other meat	0.0	0.0	0.0	0.0	0.0	0.0	—
Lamb	0.0	0.0	0.0	0.3	0.0	0.0	—
Mutton	0.0	0.0	0.0	0.0	0.0	0.0	—
Horse	—	—	—	—	0.0	0.0	—
Game	0.0	0.0	0.0	0.0	0.3	0.8	0.4[e]
Fruits and nuts	0.0	1.6	0.0	0.5	0.7	0.4	13.0
Vegetables	0.6	18.5	1.4	2.1	13.2	16.8	—
Vine	—	—	—	—	—	—	20.7
Sprout	—	—	—	—	—	—	3.1
Leafy	—	—	—	—	—	—	2.9
Root	—	—	—	—	—	—	1.2
Grains and beans	1.3	1.0	0.5	0.7	11.8	12.4	2.9
Oils and sugar	1.7	0.2	0.1	0.7	0.7	0.8	0.0
Seafood	0.3	1.2	3.8	2.3	0.0	0.0	—
Mollusk	—	—	—	—	—	—	0.2

	Europe						
	2007–2009[a,d]				Japan[b,d]		USA[c]
	EE	NE	SE	WE	2000–2004	2005–2009	1998–2008
Crustacean	—	—	—	—	—	—	0.2
Shellfish	—	—	—	—	2.0	2.8	—
Finfish	—	—	—	—	3.3	5.6	0.7
Seaweed	—	—	—	—	0.5	0.2	—
Fungus	—	—	—	—	—	—	0.1
Water	0.0	0.0	1.0	0.0	0.3	0.4	—
Other	—	—	—	—	—	—	—

[a] Pires *et al.*, 2011a;

[b] Pires *et al.*, 2011b;

[c] Painter *et al.*, 2013.

[d] Illness was attributed to different hierarchical levels of the food categorization tree, on the basis of available data. Attribution to a given level (e.g., chicken) is not counted at another level in the same branch (e.g., poultry).

[e] Includes lamb and mutton.

EE, Eastern Europe; NE, Northern Europe; SE, Southern Europe; WE, Western Europe.