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Secular trends in outbreaks caused by *Salmonella* spp. serotypes, United States, 1973–2012

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Department of Epidemiology
2014

Abstract

Secular trends in outbreaks caused by *Salmonella* spp. serotypes, United States, 1973–2012

By Brendan R. Jackson

Salmonella infections cause an estimated 94 million illnesses worldwide annually and are the leading cause of hospitalization and death from US foodborne illness. Serotyping yields important information for *Salmonella* public health surveillance. Although most illnesses represent sporadic infections, surveillance of salmonellosis outbreaks provides valuable insight into transmission routes of *Salmonella* infection if a source can be implicated. The serotype distribution among all *Salmonella* laboratory isolates reflects a variety of sources and not just foodborne transmission (estimated 55–95% of illnesses). We used data from the US Foodborne Disease Outbreak Surveillance System to examine secular trends in serotype distribution specifically within foodborne salmonellosis. We calculated proportions of foodborne salmonellosis outbreaks caused by each serotype within 9 time periods from 1973–2012 with bootstrap 95% confidence intervals (CIs) and compared these with proportions of serotypes among laboratory isolates from the National *Salmonella* Surveillance System, which reflect all transmission routes. Among 3,326 salmonellosis outbreaks with a single, known serotype, 72% were caused by the 4 most common serotypes (Enteritidis, Typhimurium, Heidelberg, and Newport). Of 90 serotypes reported, 28 caused 10 outbreaks or more (94% of outbreaks). Serotype Enteritidis caused 9% (95% CI 4–13%) of outbreaks from 1973–1977, 68% (95% CI 63–73%) from 1993–1997, and 30% (95% CI 26–34%) from 2008–2012. From 1993–1997 to 2008–2012, serotypes Typhimurium (11 percentage points), Newport (9), and Javiana (3) exhibited the largest increases in proportions of outbreaks. The proportion of outbreaks caused by serotype Enteritidis was higher than the proportion of isolates that were Enteritidis in each time period (maximum difference: 70% of outbreaks vs. 26% of isolates in 1993–1997), whereas proportions of outbreaks were lower than proportions of isolates in nearly all time periods for serotypes Typhimurium, Newport, and Javiana, suggesting that non-foodborne transmission might be more common for these serotypes since they were underrepresented among foodborne disease outbreaks. Given that the overall incidence of salmonellosis has not declined in the past decade despite intensive efforts, information about these secular trends in serotypes and foodborne disease outbreaks may be useful in guiding future control and prevention strategies.

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BACKGROUND/LITERATURE REVIEW

Salmonella infection is estimated to be the leading cause of hospitalization and death from foodborne disease in the United States and to be the leading bacterial cause of US foodborne illness, causing an estimated 1.2 million illnesses annually (1). *Salmonella* infections also take an economic toll; non-typhoidal *Salmonella* infections alone cost the U.S. economy an estimated $3.3 billion each year (2). Despite intensive efforts, the reported incidence has not declined in the past decade and remains above the Healthy People 2020 goal (3). *Salmonella* spp. can be transmitted through water, animals, the environment, and person-to-person contact, but foodborne transmission is estimated to be the most common route (estimated 55–95% of illnesses caused by *Salmonella*)(4). *Salmonella* control is therefore a priority for the two federal agencies that regulate food: the U.S. Department of Agriculture (USDA)(5) and the Food and Drug Administration (FDA) (6).

Beyond the United States, salmonellosis is a substantial health problem at the global level. Worldwide, *Salmonella* spp. are responsible for an estimated 94 million illnesses (including 80 million foodborne illnesses) and 155,000 deaths annually (4).

The genus *Salmonella* is comprised of two species, *S. enterica* and *S. bongori*. *S. enterica* is divided into 6 subspecies (I, II, IIIa, IIIb, IV, and VI), and *S. enterica* subspecies are further classified into serotypes, over 2,500 of which have been described (7). A list of known *Salmonella* serotypes has been maintained since the 1930s and was last updated in 2007 (7). Most human illnesses are caused by a relatively small number of *S. enterica* subspecies I serotypes. In 2011, only 20 serotypes caused >82% of the

~40,000 serotyped human-derived *Salmonella* isolates in the United States reported to the Centers for Disease Control and Prevention (8).

US laboratory surveillance data suggest that the incidence of illness caused by some *Salmonella* serotypes has increased in recent decades while the incidence for other serotypes has decreased (8). However, the transmission source for reported human isolates is rarely known, and it is unclear to what extent changes in serotype incidence among reported isolates reflect changes in routes of transmission.

With the exception of *Salmonella* serotypes causing typhoid and paratyphoid fever, for which humans are the reservoir, the primary reservoir for *Salmonella* is non-human animals, including poultry and other birds, cattle, pigs, rodents, reptiles, and amphibians (9). Most foodborne salmonellosis results from contamination of food with animal feces at some stage of production, though *Salmonella* can also grow on plants and in the environment (9, 10). *Salmonella* serotypes differ in virulence among various animal hosts and in the level of host specificity and adaptation. For example, serotype Typhi causes disease only in humans, whereas serotype Gallinarum causes disease almost exclusively in poultry (11). On the other end of the spectrum are serotypes Enteritidis and Typhimurium, which can infect, and cause disease in, a broad range of host species (11). Despite the broad host range of serotype Enteritidis, human infections appear to result predominantly from consumption of eggs and poultry (12-14), suggesting that even serotypes with diverse hosts species can be transmitted to humans predominantly through specific food pathways.

A few serotypes that cause human disease have a specific animal reservoir (e.g., serotype Cholerasuis in pigs and serotype Dublin in cattle), and many other serotypes are

non-exclusively associated with particular animal hosts (15). Some serotypes have been linked to plant products like fruits and vegetables (e.g., serotypes Javiana, Litchfield, and Poona) (12); feed animal or reptile feces in the environment has been suspected as the source of contamination for some foodborne illnesses linked to produce (16, 17). Although information about serotypes isolated from animals can inform our understanding of *Salmonella* transmission to humans, *Salmonella* isolates from humans differ from those in animals (11). The study of human isolates and outbreaks is needed to fully understand the epidemiology of salmonellosis in humans and sources of transmission.

Foodborne disease outbreak surveillance can provide valuable insight into transmission routes of salmonellosis (18), and outbreak data have been used to link *Salmonella* serotypes to particular food categories (12). However, no published studies systematically describe secular trends in serotypes causing US foodborne salmonellosis outbreaks. The Foodborne Disease Outbreak Surveillance System (FDOSS), maintained by CDC, has collected reports of foodborne disease outbreaks since 1973. We examined changes in the distribution of *Salmonella* serotypes causing foodborne illness over time using data from this surveillance system.

METHODS

To examine secular trends in serotypes causing outbreaks, we performed a secondary analysis of outbreak data from FDOSS and made comparisons with laboratory isolate data from the National *Salmonella* Surveillance System (NSSS).

A foodborne disease outbreak is defined here as two or more cases of similar illness caused by the same *Salmonella* serotype resulting from ingestion of a common food. Our study includes outbreaks reported to FDOSS from 1973 through 2012. FDOSS data were collected by CDC through three sequential reporting systems (19). From 1973 through 1997, FDOSS collected reports of foodborne disease outbreaks from state, local, and territorial public health departments through the paper Foodborne Outbreak Reporting System (pFORS) (Figure 1). Starting in 1998 and through 2008, FDOSS collected these reports electronically through the electronic Foodborne Outbreak Reporting System (eFORS). Since 2009, reports of foodborne disease outbreaks have been collected, along with reports of non-foodborne disease outbreaks, through the National Outbreak Reporting System (NORS). FDOSS reports include data on the pathogen, the serotype when the pathogen is *Salmonella enterica*, date of outbreak onset, number of ill persons, and mode of transmission.

In NSSS, clinical diagnostic laboratories submit *Salmonella* isolates to state and territorial public health departments, which confirm the isolates as *Salmonella*, perform serotyping according to the Kauffman-White scheme, and report the isolate to CDC (20). No information is available on how patients acquired the *Salmonella* spp. infection (e.g., through food, water, animals, infected person, or environment). NSSS data from 1973

through 2011 were examined for comparison with FDOSS; NSSS data were not as yet available for 2012.

We included in the analysis foodborne disease outbreak reports of salmonellosis (1973–2012) and NSSS isolates (1973–2011) caused by a single, laboratory-confirmed serotype. We included only outbreaks reported as foodborne. We excluded outbreaks and isolates that had unknown or incomplete serotype information and outbreaks with multiple etiologies. Outbreaks etiologies and isolates reported as serotype Java were reclassified as serotype Paratyphi B to conform to updated nomenclature; data were not consistently reported to allow separate analyses of the 2 variants of this serotype. Because of changes in reporting during the study period, we reclassified outbreak etiologies and isolates reported as serotype I 4,[5],12:i:- as serotype Typhimurium (21).

FDOSS outbreaks were assigned a year according to date of the first illness in the outbreak and NSSS isolates were assigned a year according to the date of specimen collection. We grouped the 40 years of surveillance data into 9 time periods corresponding to the 3 FDOSS reporting systems: 1973–1977, 1978–1982, 1983–1987, 1988–1992, and 1993–1997 for outbreaks reported to pFORS; 1998–2000, 2001–2004, and 2005–2008 for outbreaks reported to eFORS; and 2009–2012 for outbreaks reported to NORS. The final time period for NSSS data included only the years 2009–2011. Because we constructed the time periods to avoid overlap between reporting systems, the number of years in each time period differs, ranging from 3 to 5 years (Figure 1).

For analysis, we calculated the mean number of outbreaks of salmonellosis per year for each time period and the total number of outbreaks for each serotype. To examine changes over time in the distribution of serotypes among less common

serotypes, we made 3 serotype groups (serotypes that caused 50–99 outbreaks overall, serotypes that caused 20–49 outbreaks, and serotypes that caused <20 outbreaks) for comparison to the 4 serotypes causing the largest number of outbreaks. To compare the distribution of serotypes for outbreaks and isolates over a more recent time period (1998–2011), we calculated the proportions of outbreaks caused by common serotypes and the proportions of isolates for these serotypes and reported serotypes that accounted for ≥1% of isolates.

For each time period, we calculated the proportions of outbreak etiologies and isolates of each serotype and serotype group and, for outbreaks, used bootstrapping to calculate 95% confidence intervals (CIs) around each proportion (22). Bootstrapping, which is a data-based simulation method, was chosen to calculate CIs because small numbers of outbreaks existed for some data points and the method does not require assumptions of normality in the data. SAS version 9.3 (SAS Institute, Cary, NC) was used for analysis.

To further explore changes over time in the distribution of serotypes causing outbreaks, we compared the first 20 years of the study period (1973–1992) with the latter 20 years (1993–2012). Because the total number of outbreaks reported during each period differed, we also calculated for each serotype the expected difference in number of outbreaks between the 2 periods. We did so by multiplying the difference in the number of outbreaks caused by all serotypes between each period (latter period minus earlier period) by the percentage of all outbreaks caused by each serotype. For this analysis, we reported data for serotypes in which the difference from the expected number of outbreaks between the periods was more than 5. To explore more recent changes, we

performed a similar analysis for the time periods 1998–2004 (7 years) and 2005–2012 (8 years), reporting data for serotypes in which the difference exceeded the expected by at least 2 outbreaks. The expected difference in number of outbreaks between the 2 periods was calculated to account for the fact that the number of years in each period differed.

To compare the distribution of serotypes among individual *Salmonella* cases with those causing outbreaks, we calculated proportions of serotypes among NSSS isolates.

RESULTS

During 1973–2012, 3,762 *Salmonella* spp. outbreaks were reported to FDOSS, of which 3,326 (88%) had a single, known serotype and were included in the study. The mean numbers of outbreaks reported per year were similar during the time periods from 1988 through 2012 (range 80–118 outbreaks) and the fewest mean number of outbreaks per year (32) were reported during the first time period (1973–1977) (Figure 2). The number of serotypes causing outbreaks each year ranged from 7 to 29 and the mean number of outbreaks per serotype per year ranged from 1.8 to 10.6 (Figure 3). The mean number of outbreaks per serotype was highest in the 1990s, during the time when serotype Enteritidis caused the largest proportion of outbreaks.

Ninety different serotypes caused outbreaks during the study period and twenty-eight different serotypes caused 10 outbreaks or more, accounting for 94% of outbreaks. Nearly three-quarters (72%) of outbreaks were caused by the 4 most common serotypes (serotypes Enteritidis, Typhimurium, Heidelberg, and Newport), and nearly half (43%) were caused by serotype Enteritidis alone (Figure 4).

The distribution of serotypes causing outbreaks varied substantially across the 9 time periods. Serotype Enteritidis caused 9% (95% CI 4–13%) of outbreaks during 1973–1977 but 68% (95% CI 63–73%) of outbreaks during 1993–1997 (Figure 5). During 2001–2012, serotype Enteritidis caused 30% of outbreaks (95% CI 26–34% for 2009–2012). Serotypes Typhimurium and Newport and the 3 serotype groups generally followed the opposite trend, decreasing as a proportion of outbreaks from the 1970s to the 1980s and mid-1990s, followed by increases to remain relatively steady during the final decade of the study period. For example, serotype Typhimurium caused 27% (95%

CI 20–34%) of outbreaks during 1973–1977, but only 7% (95% CI 4–9%) of outbreaks from 1993–1997 and then 18% of outbreaks from 2001–2012 (95% CI 14–21% for 2009–2012). Serotype Newport caused 1% (95% CI 0–4%) of outbreaks during 1988–1992 and 10% (95% CI 7–13%) during 2009–2012. The percentage of outbreaks caused by serotype Heidelberg varied less over time (range 6–10%).

Of the 1,440,741 *Salmonella* isolates reported to NSSS from 1973–2011, 1,328,359 (92%) had a known serotype and were included in the study. Differences existed in the distribution of serotypes across outbreaks and isolates. From 1998–2012, serotype Enteritidis caused a higher percentage of FDOSS outbreaks (34%) than did serotype Typhimurium (18%), but serotype Typhimurium comprised a larger percentage of NSSS isolates (22%) than did serotype Enteritidis (19%) (Figure 6). Among the 17 serotypes that each comprised ≥1% of isolates, serotypes Braenderup, Enteritidis, Hadar, Heidelberg, Infantis, and Thompson caused a higher percentage of FDOSS outbreaks than NSSS isolates and the remaining serotypes were more common among isolates than outbreaks, particularly serotypes Typhimurium, Newport, and Javiana.

The distribution of serotypes varied less among NSSS isolates than among FDOSS outbreaks over the 9 time periods (Figure 5). For example, serotype Enteritidis accounted for 6% of isolates and 9% of outbreaks during 1973–1977 and 26% of isolates and 70% of outbreaks during 1993–1997. For most serotypes and serotype groups, the percentage of outbreaks approximated the percentage of isolates, with the largest divergence occurring for serotypes Enteritidis and Typhimurium during 1983–2000 (Figure 5).

Comparing the number of outbreaks in the first 20 years of the study period with the last 20 years, certain serotypes caused more outbreaks than expected during the more recent period (1993–2012), including serotypes Newport, Javiana, Braenderup, and Muenchen, which each caused ≥10 more outbreaks than expected (Table 1). By contrast, other serotypes caused fewer outbreaks than expected during the more recent period, including serotypes Enteritidis, Typhi, Blockley, Reading, and Agona, which each caused ≥10 fewer outbreaks than expected. Examining more recent changes—those during the final 15 years of the study period (1998–2012)—serotypes Typhimurium, Newport, Braenderup, Javiana, Montevideo, Paratyphi B, Uganda, and Muenchen each caused ≥5 more outbreaks than expected during 2005–2012 compared with 1998–2004, whereas serotypes Enteritidis, Heidelberg, and Thompson each caused ≥5 fewer outbreaks than expected (Table 2).

DISCUSSION

The distribution of *Salmonella* spp. serotypes causing reported foodborne disease outbreaks changed significantly during the last 4 decades. In particular, serotype Enteritidis, which caused fewer than 10% of outbreaks from 1973–1977, emerged as the major cause of salmonellosis outbreaks (about two-thirds) by the late 1980s and early 1990s before declining to about one-third of outbreaks during 2001–2012. The large increases in illnesses caused by serotype Enteritidis in the 1990s were not limited to the United States, and multiple subtypes (phage types and pulsed-field electrophoresis patterns) were involved (23). Two major factors likely contributed to the tremendous increase in serotype Enteritidis infections, which has been predominantly linked to eggs (13). First, from the 1930s to the 1980s, producers markedly reduced the incidence in poultry of infections with serotypes Gallinarum and Pullorum, which cause disease in poultry but not in humans; serotype Enteritidis, which causes disease in humans but not in poultry, appears to have occupied the ecologic niche vacated by these serotypes, since infection with serotypes Gallinarum and Pullorum yields cross-immunity to serotype Enteritidis in chickens (24). Without exposure and immunity to serotypes Gallinarum and Pullorum, poultry became more susceptible to serotype Enteritidis carriage. Second, serotype Enteritidis strains can invade ovarian tissue of hens and infect eggs without harm to bird or egg; vertical transmission in the absence of observable disease likely fueled the rapid spread of this serotype in poultry and commercial eggs (23).

The factors behind the partial decline in serotype Enteritidis outbreaks have been discussed elsewhere (13). Three key interventions cited in the reduction of egg contamination were the development of quality-assurance programs on farms producing

eggs, greater refrigeration of eggs, and education of consumers and food workers about risks from eggs and proper handling (13). FDA and USDA guidance and regulations played key roles in these interventions. Our study provides more recent data (2005–2012) demonstrating that the proportion of outbreaks caused by serotype Enteritidis has remained relatively constant since the early 2000s. The large increase in mean number of outbreaks per serotype observed in Figure 3 during the 1990s closely parallels the increase in the proportion of outbreaks caused by serotype Enteritidis. Because this serotype alone caused about two-thirds of outbreaks during this decade, the mean number of outbreaks per serotype rose.

As the proportion of outbreaks caused by serotype Enteritidis declined by over 35 percentage points from the mid-1990s to the 2000s, the share caused by other serotypes rose. Serotypes Typhimurium and Newport accounted for a majority of this increase. As context, during the first years of the study, serotype Typhimurium caused many more outbreaks than serotype Enteritidis (~3-fold more in 1973–1977), but caused ~10-fold fewer during 1993–1997; since then, the proportion of outbreaks caused by serotype Typhimurium has increased by 11 percentage points while the proportion of outbreaks caused by serotype Enteritidis declined, as noted above. This increase in the proportion of outbreaks caused by serotype Typhimurium occurred even as the proportion of NSSS isolates of this serotype declined, and it is unclear whether the increase in outbreaks was related to changes in transmission routes of this serotype, food production or consumption, or outbreak investigation or reporting. There was no change in laboratory methods during time. However, in this analysis serotype I 4,[5],12:i:- was grouped together with serotype Typhimurium because of inconsistent reporting; outbreaks that

were reported to have been caused by serotype I 4,[5],12:i:- accounted for about one-quarter of the observed increase in serotype Typhimurium outbreaks from 1993–1997 to 2009–2012 (serotype I 4,[5],12:i:- was reported in no outbreaks before 1998, 0.3% of all outbreaks during 1998–2000, 1.8% during 2001–2004, 3.1% during 2005–2008, and 2.9% during 2009–2012). Similar to serotype Typhimurium, the proportion of outbreaks caused by serotype Newport increased by 9 percentage points from 1993–1997 to 2009–2012. This increase in outbreaks generally followed an upward trend in the proportion of serotype Newport isolates in NSSS. Further supporting serotype Newport as a growing cause of salmonellosis outbreaks, this serotype was one of the top 2 serotypes causing more outbreaks over time in each of the 2 binary comparisons (1973–1992 vs. 1993–2012 and 1998–2004 vs. 2005–2012).

In contrast to the other three most common serotypes (Enteritidis, Typhimurium, and Newport), serotype Heidelberg changed little in the outbreak distribution over time, even as the proportion of this serotype among NSSS isolates declined since the late 1980s. Since the early 2000s, both serotypes Enteritidis and Heidelberg changed little in the distribution of outbreak serotypes.

Beyond serotype Typhimurium and Newport, serotypes Braenderup and Javiana displayed the next largest increases in outbreaks over time in both binary comparisons. In a previous study, ≥50% of outbreaks caused by these serotypes were linked to plant-based foods (e.g., fruits and vegetables), as were 43% of outbreaks caused by serotype Newport, compared with 24% for outbreaks caused by all serotypes (12). Serotype Newport has been shown to grow better and persist longer on and in tomatoes than serotypes Enteritidis and Typhimurium (25). For these reasons, it might be relevant that

an increasing proportion of foodborne disease outbreaks have been linked to fresh fruits and vegetables (10, 18). Changes in farming practices might at least partially explain the growth in salmonellosis outbreaks linked to produce. These changes are suspected to include the use of irrigation water from sources near large confined animal operations and the application of animal wastes to agricultural soils (17). The increasing globalization of the US food supply may also play a role; for example, nearly one-third of fruits sold in the US in 2007 were estimated to have been imported (17).

In general, changes in the proportions of outbreaks paralleled the proportion of NSSS isolates for each serotype with a few notable exceptions. In the 1980s and 1990s, serotype Enteritidis caused a far larger proportion of outbreaks than it represented as a proportion of NSSS isolates. Further, the proportion of outbreaks caused by serotype Enteritidis always exceeded its proportion of isolates; this relationship was also true for serotype Heidelberg in the 1990s and after. Both of these serotypes have been previously found to have caused outbreaks predominantly (>80%) attributed to eggs and poultry (12, 18). Two possible explanations for this gap are that 1) these serotypes may be associated primarily with foodborne transmission or 2) outbreaks linked to poultry and eggs are more often detected and reported than those linked to other foods. Differential outbreak detection and reporting by state could also explain this difference, but this explanation is less likely as these serotypes have no clear geographic distribution (26). It is also possible that differences in virulence among serotypes or variations in dose ingested by food type might account for some of the discrepancy between outbreaks and isolates.

In contrast to serotypes Enteritidis and Heidleberg, the proportion of serotype Typhimurium isolates exceeded the proportion of outbreaks for all time periods.

Similarly, from 1998–2012, serotypes Typhimurium, Newport, and Javiana exhibited the largest gap between their respective proportions of NSSS isolates and outbreaks. These 3 serotypes have been associated in part with environmental or reptile reservoirs (27-29) that may lead to non-foodborne transmission, which might explain the relative dearth of foodborne disease outbreaks compared with isolates. Another possible explanation is that these serotypes have been more commonly associated with outbreaks linked to plant-based foods than serotypes Enteritidis and Heidelberg (12), and it is possible that outbreaks linked to plant-based foods might be less often detected or reported. The serotype with the next largest gap between isolates and outbreaks was Mississippi, which represented >1% (~10,000) of NSSS isolates but caused no foodborne outbreaks during the 40 year study period. Supporting the hypothesis that the gap between isolates and outbreaks results in part from non-foodborne exposures, a study in Tasmania, which reported a high incidence of serotype Mississippi infections, found that wildlife are the likely reservoir of this serotype and that human exposure likely occurs through water and the environment rather than through foodborne transmission (30).

The results of this study are subject to several limitations. Because only a small proportion (~5%) of reported salmonellosis cases are part of recognized outbreaks (31), serotypes causing foodborne disease outbreaks might not fully represent serotypes causing all salmonellosis. Further, most cases and many outbreaks go undetected; there are an estimated 29 cases of salmonellosis for every case reported in the United States (1) since only a small proportion of persons with salmonellosis seek medical attention and a fraction of those have a culture performed. Only outbreaks reported to FDOSS are included in the analysis; outbreak detection and reporting might differ by time period and

state (18). For example, FDOSS data show that Oregon (population ~4 million in 2010) reported 31 salmonellosis outbreaks during 2009–2012, excluding multistate outbreaks, whereas Texas (population ~25 million) reported 4. Salmonellosis caused by certain serotypes (e.g., Javiana and Newport) is more common in states (26) that report fewer outbreaks (32), which could account for the smaller percentage of outbreaks observed for these serotypes than among NSSS isolates. Although the various reporting systems (*i.e.*, pFORS, eFORS, or NORS) likely influenced the numbers of outbreaks reported (18), the type of reporting system would be unlikely to influence the distribution of serotypes beyond the variation in reporting by state. Because the distribution of outbreak serotypes within each time period was generally similar to the distribution of serotypes among NSSS isolates, which would be expected to be reported more evenly across states, available outbreak data may be a reliable proxy of the overall serotype distribution in outbreaks in spite of the limitations mentioned above. In this study, different numbers of years were used for some of the various study periods; however, these differences likely did not impact observed results since the study focused on the proportions of outbreaks rather than the absolute number. Finally, the relatively small number of outbreaks reported within each time period for serotypes other than Enteritidis, Typhimurium, Heidelberg, and Newport limited our ability to detect significant changes over time for some serotypes.

A better understanding of trends in serotypes causing foodborne salmonellosis can guide control measures. For example, Denmark has successfully used serotyping and other subtyping methods on *Salmonella* isolates from humans, foods, and animals to guide control interventions in poultry, pigs, cattle, and pets (33). In the United States,

serotype data have been used for foodborne salmonellosis source attribution to determine the relative contribution of various animal products to human disease (34). Future data collection by NORS will shed further insight into serotypes causing both foodborne and non-foodborne outbreaks.

In summary, this study found significant differences in the serotype distribution in foodborne salmonellosis outbreaks over time. As outbreaks caused by serotype Enteriditis have declined since the 1990s, other serotypes, particularly serotypes Typhimurium, Newport, Javiana, and Braenderup, have emerged (or, in the case of serotype Typhimurium, reemerged) as more common etiologies. Information about secular trends in *Salmonella* serotypes and outbreaks will be helpful to foodborne disease investigators, regulatory agencies, and researchers examining foodborne transmission of *Salmonella* in the context of a changing food environment.

FUTURE DIRECTIONS

Serotyping has provided and will continue to provide valuable information about various *Salmonella* subtypes and their relative role in human salmonellosis. Adaptation of surveillance systems to collect additional information on *Salmonella* subtypes using pulsed-field gel electrophoresis and eventually whole-genome sequencing, combined with NORS collection of outbreak transmission sources other than foodborne, will further elucidate relationships between *Salmonella* subtypes and various transmission routes, leading to improved control measures. More study is needed to understand the rise in the United States of certain serotypes, particularly Newport, Javiana, Braenderup, and I 4,[5],12:i:-; these serotypes demonstrate evidence of foodborne and non-foodborne transmission. Finally, invasive non-typhoidal *Salmonella* infections have been identified as a significant problem in many low-income countries (35), and more work is needed to understand the distribution of serotypes in these countries and sources of transmission to implement prevention and control measures.

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TABLES

Table 1. Difference in number of *Salmonella enterica* outbreaks in 1993–2012 compared to 1973–1992 for serotypes with >5 or <-5 outbreaks deviation from expected, Foodborne Disease Outbreak Surveillance System, United States, 1998–2012

	1973–1992 (period 1)	1993–2012 (period 2)	Difference (period 2 – period 1)	% change	% of outbreaks (1973–2012)	Expected increase[a]	Difference from expected
Newport	34	148	114	335.3%	5.5%	47.0	67.0
Javiana	10	51	41	410.0%	1.8%	15.7	25.3
Braenderup	12	47	35	291.7%	1.8%	15.2	19.8
Muenchen	6	34	28	466.7%	1.2%	10.3	17.7
Hartford	0	12	12	Inf.	0.4%	3.1	8.9
Uganda	1	12	11	1100.0%	0.4%	3.4	7.6
Montevideo	25	52	27	108.0%	2.3%	19.9	7.1
Miami	0	8	8	Inf.	0.2%	2.1	5.9
Paratyphi B	3	13	10	333.3%	0.5%	4.1	5.9
Stanley	1	9	8	800.0%	0.3%	2.6	5.4
Berta	6	17	11	183.3%	0.7%	5.9	5.1
Ohio	6	3	-3	-50.0%	0.3%	2.3	-5.3
Chester	7	4	-3	-42.9%	0.3%	2.8	-5.8
Dublin	6	2	-4	-66.7%	0.2%	2.1	-6.1
Bredeney	7	1	-6	-85.7%	0.2%	2.1	-8.1
Infantis	29	38	9	31.0%	2.0%	17.3	-8.3
Typhimurium	198	323	125	63.1%	15.7%	134.4	-9.4
Agona	20	20	0	0.0%	1.2%	10.3	-10.3
Reading	13	7	-6	-46.2%	0.6%	5.2	-11.2
Blockley	14	3	-11	-78.6%	0.5%	4.4	-15.4
Typhi	19	7	-12	-63.2%	0.8%	6.7	-18.7
Enteritidis	577	841	264	45.8%	42.6%	365.8	-101.8
Total	1234	2092	858	69.5%	100%	858.0	0.0

[a]Expected increase calculated by multiplying the 858 outbreak difference (period 2 – period 1) for all serotypes by percentage of outbreaks caused by each serotype during the 40 year study period. Although both study periods were of equal duration (20 years), more outbreaks were reported in 1993–2012 than 1973–1992.

Table 2. Difference in number of *Salmonella enterica* outbreaks in 2005–2012 compared to 1998–2004 for serotypes with >2 or <-2 outbreaks deviation from expected, Foodborne Disease Outbreak Surveillance System, United States, 1998–2012

	1998–2004 (period 1)[a]	2005–2012 (period 2)[b]	Difference (period 2 – period 1)	% change	% of outbreaks (1998–2012)	Expected increase[a]	Difference from expected
Typhimurium	123	173	50	40.7%	17.5%	16.3	33.7
Newport	57	84	27	47.4%	8.3%	7.8	19.2
Braenderup	13	28	15	115.4%	2.4%	2.3	12.7
Javiana	18	30	12	66.7%	2.8%	2.6	9.4
Montevideo	17	27	10	58.8%	2.6%	2.4	7.6
Paratyphi B	2	10	8	400.0%	0.7%	0.7	7.3
Uganda	3	9	6	200.0%	0.7%	0.7	5.3
Muenchen	13	20	7	53.8%	2.0%	1.8	5.2
Litchfield	2	7	5	250.0%	0.5%	0.5	4.5
Blockley	0	3	3	Inf.	0.2%	0.2	2.8
Bareilly	1	4	3	300.0%	0.3%	0.3	2.7
Miami	2	5	3	150.0%	0.4%	0.4	2.6
Agona	7	10	3	42.9%	1.0%	0.9	2.1
Johannesburg	2	0	-2	-100.0%	0.1%	0.1	-2.1
Reading	3	1	-2	-66.7%	0.2%	0.2	-2.2
Typhi	4	2	-2	-50.0%	0.4%	0.3	-2.3
London	3	0	-3	-100.0%	0.2%	0.2	-3.2
Saintpaul	15	13	-2	-13.3%	1.7%	1.5	-3.5
Poona	6	3	-3	-50.0%	0.5%	0.5	-3.5
Anatum	9	6	-3	-33.3%	0.9%	0.8	-3.8
Brandenburg	5	1	-4	-80.0%	0.4%	0.3	-4.3
Thompson	16	12	-4	-25.0%	1.7%	1.5	-5.5
Heidelberg	73	68	-5	-6.8%	8.3%	7.8	-12.8
Enteritidis	308	260	-48	-15.6%	33.6%	31.2	-79.2
All serotypes	799	892	93	11.6%	100%	93	0

[a] Number of outbreaks in period 1 (1998–2004), which encompasses 7 years

[b] Number of outbreaks in period 2 (2005–2012), which encompasses 8 years

Expected increase calculated by multiplying the 93 outbreak difference (period 2 – period 1) for all serotypes by percentage of outbreaks caused by each serotype during the 15 year period (the 1998–2004 period includes 7 years, the 2005–2012 period includes 8 years).

FIGURES

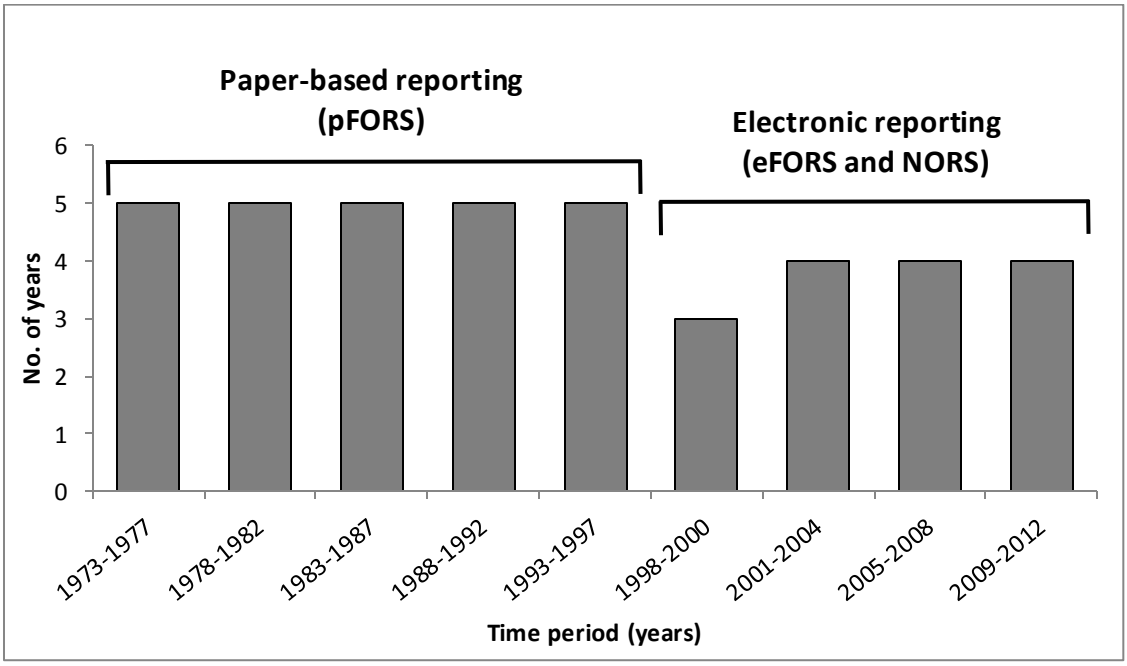


Figure 1. Number of years in each of the 9 study time periods, 1973–2012.
Abbreviations: pFORS, paper Foodborne Disease Reporting System; eFORS, electronic Foodborne Disease Reporting System; NORS, National Outbreak Reporting System.

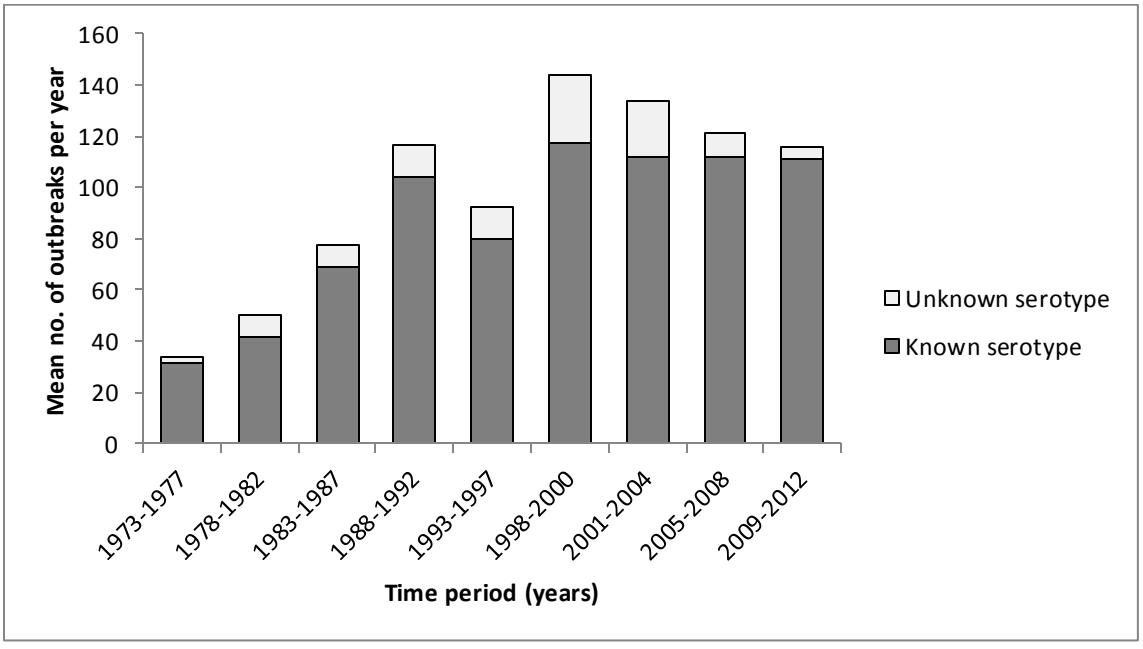


Figure 2. Mean number of *Salmonella* spp. outbreaks reported per year with known and unknown serotypes for 9 time periods, Foodborne Disease Outbreak Surveillance System, United States, 1973–2012

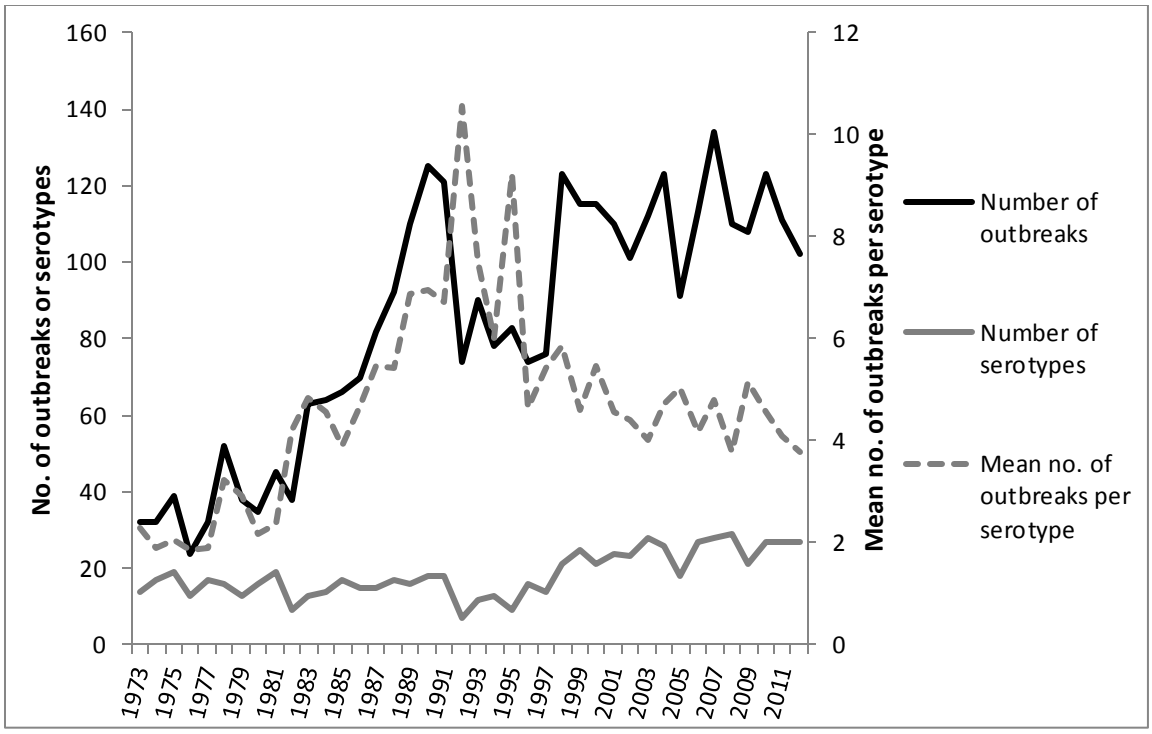


Figure 3. Number of annual reported outbreaks caused by *Salmonella* spp., number of serotypes causing outbreaks, and mean number of outbreaks per serotype, Foodborne Disease Outbreak Surveillance System, United States, 1973–2012.

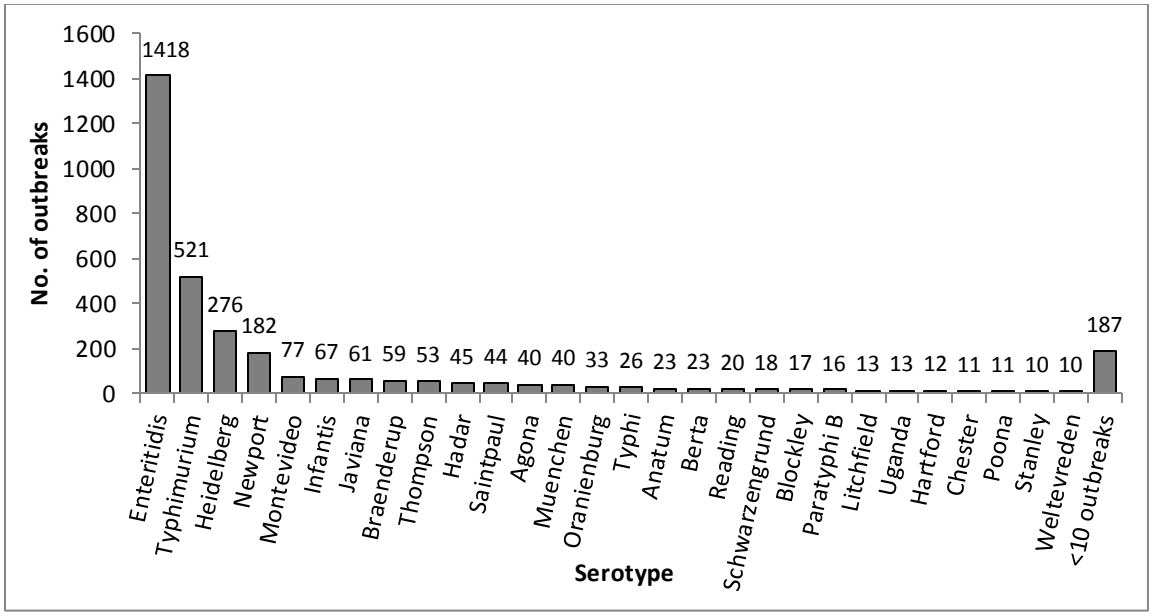


Figure 4. Number of outbreaks caused by *Salmonella* spp. serotypes over 40 year study period, Foodborne Disease Outbreak Surveillance System, United States, 1973–2012

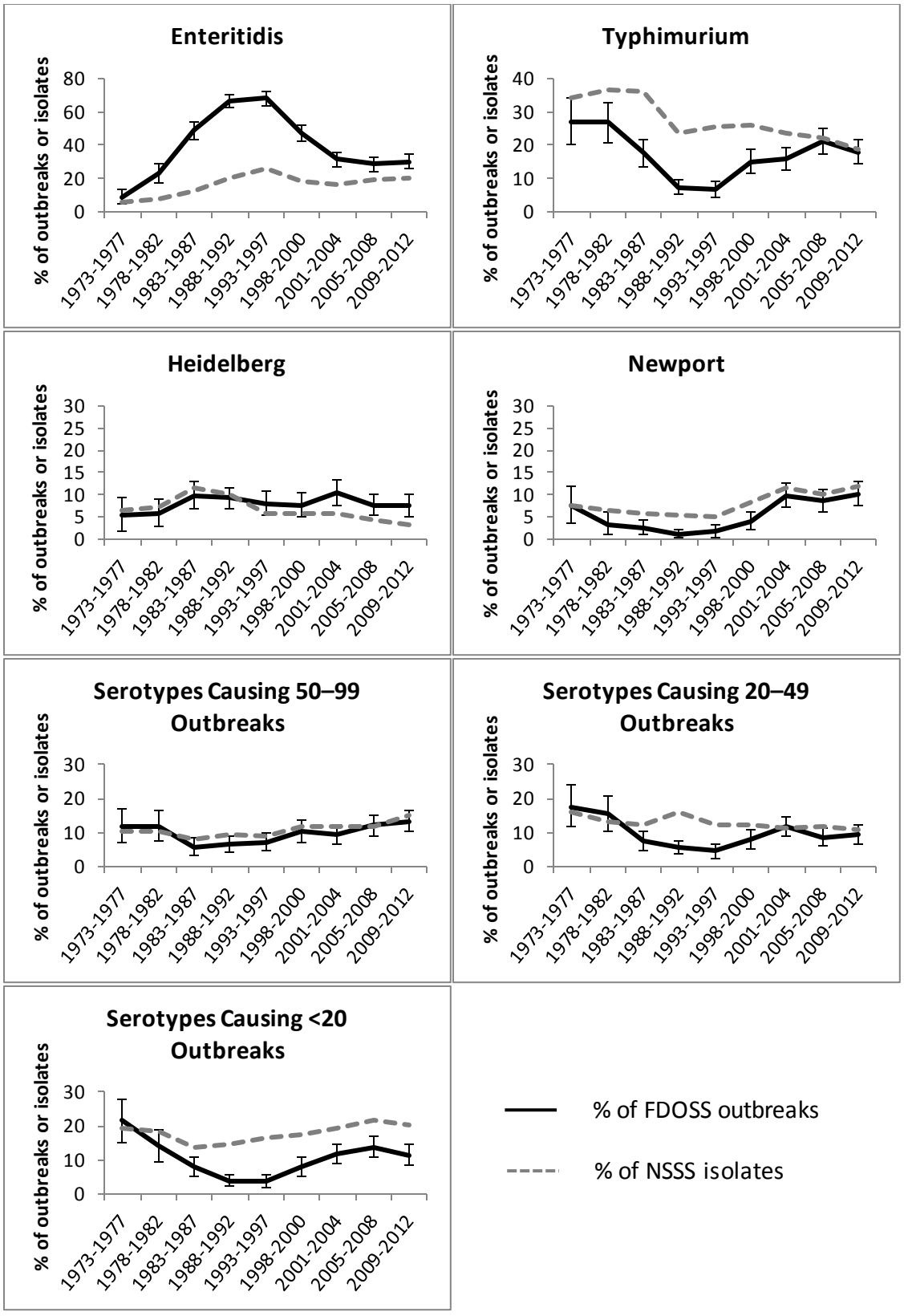


Figure 5. Percentage of outbreaks and isolates per time period caused by 3 serotype groups and *Salmonella* spp. serotypes Enteritidis, Typhimurium, Heidelberg, and Newport with 95%

bootstrap confidence intervals, Foodborne Disease Outbreak Surveillance System (FDOSS) and National *Salmonella* Surveillance System (NSSS), United States, 1973–2012.

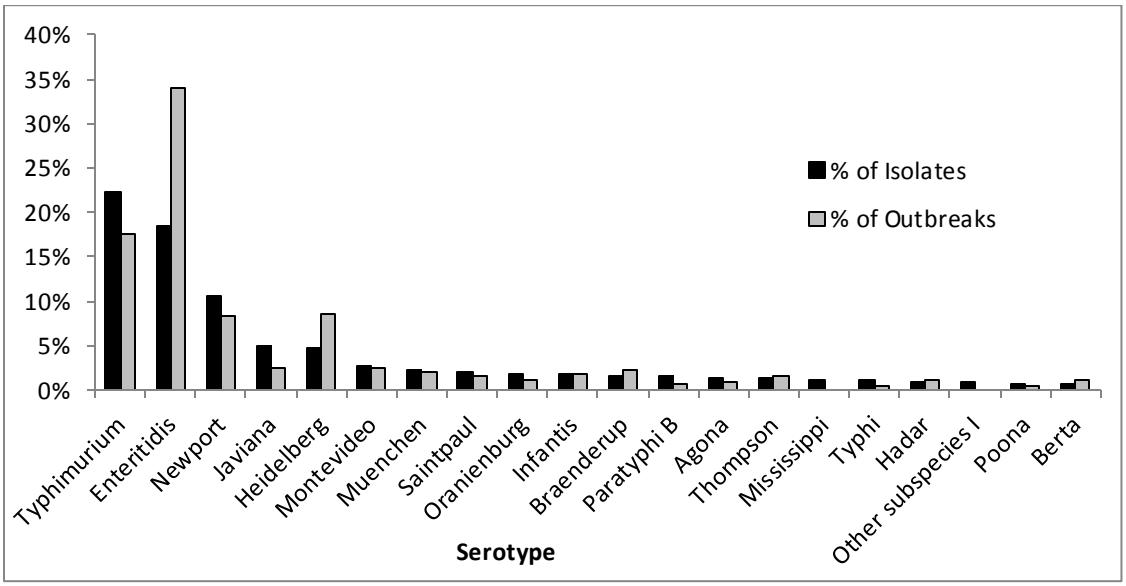
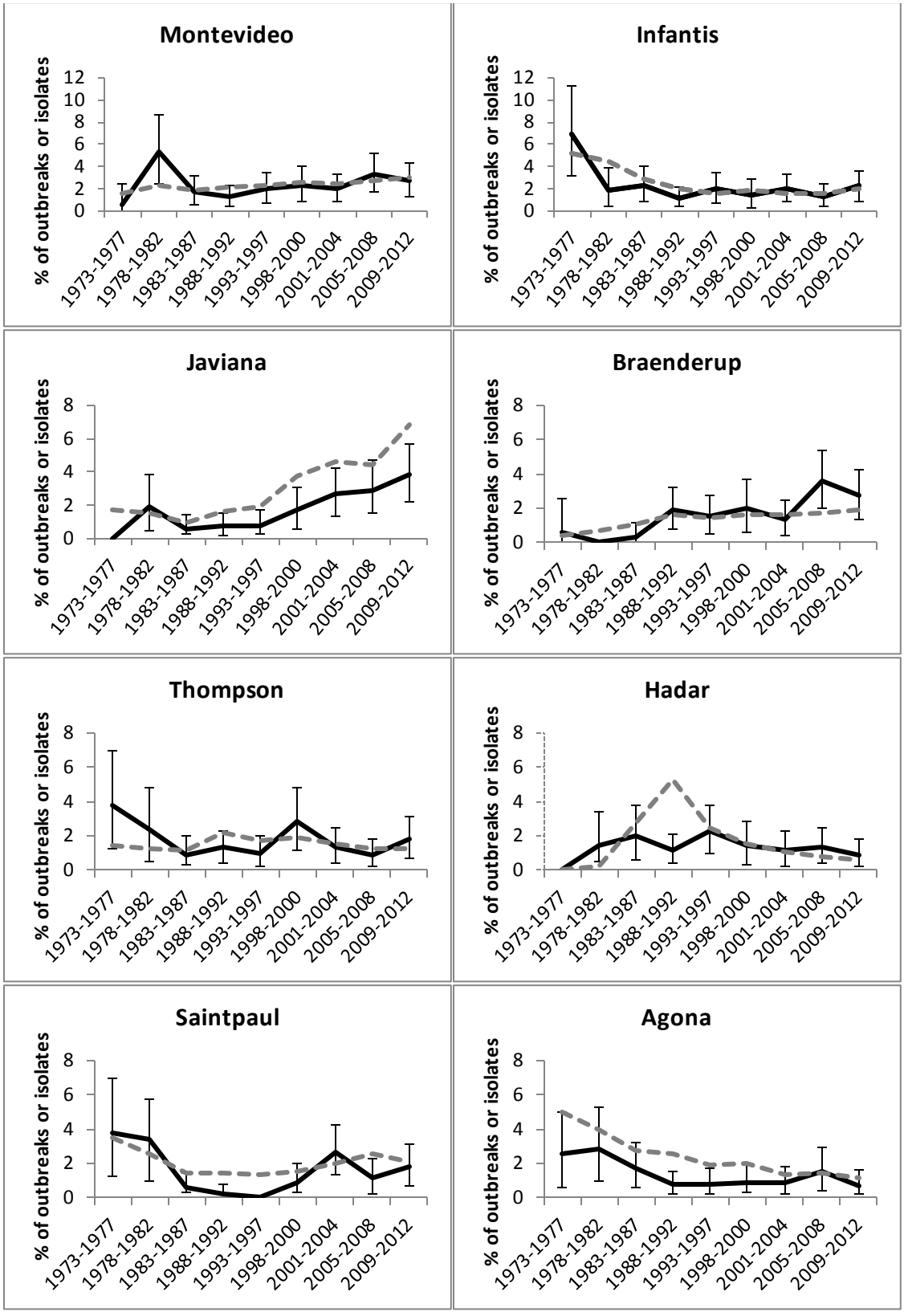
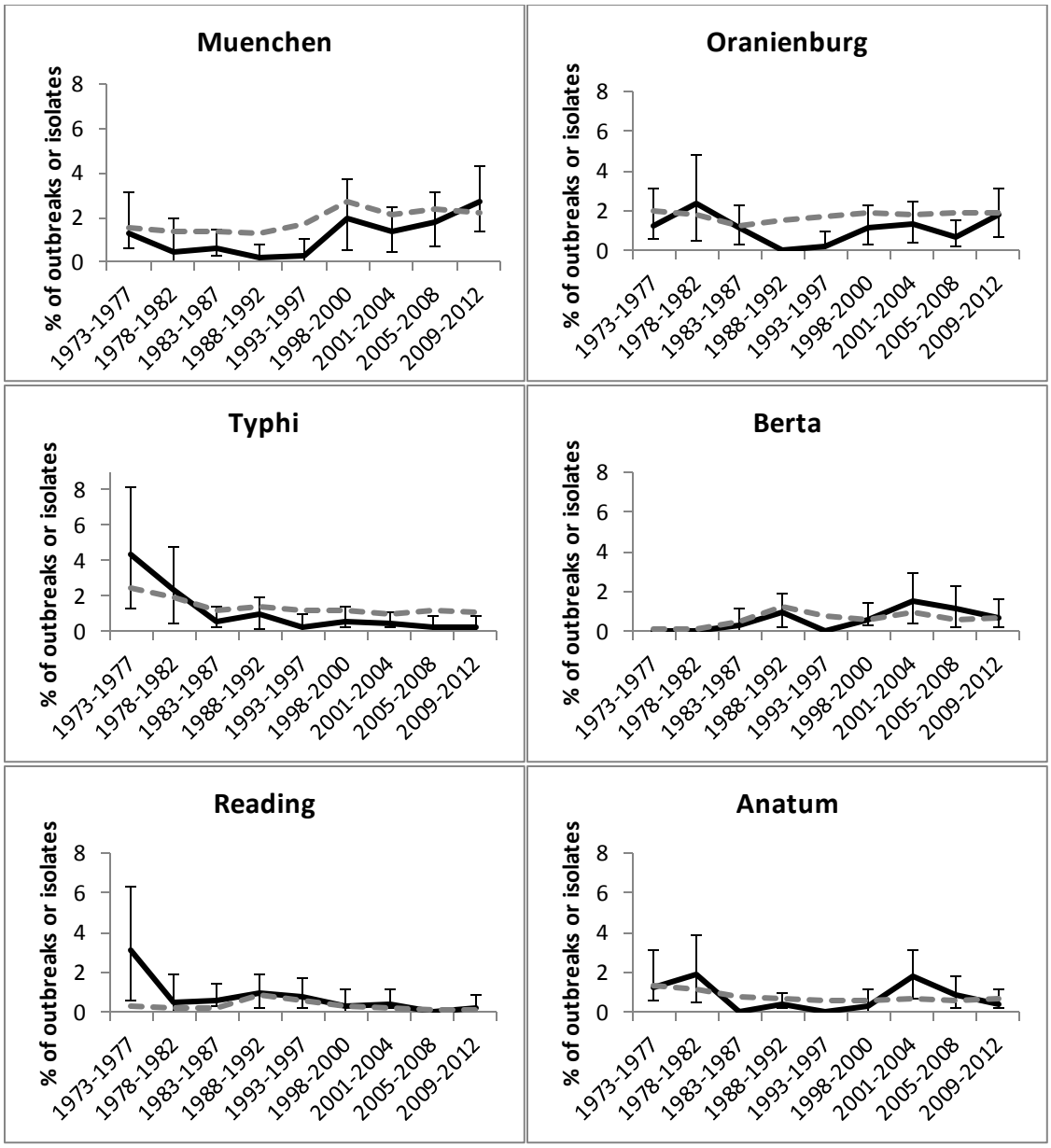


Figure 6. Percentage of the 20 most common *Salmonella* spp. serotypes among all *Salmonella* spp. isolates reported to the National *Salmonella* Surveillance System compared with the percentage of *Salmonella* spp. outbreaks caused by these serotypes in the Foodborne Disease Outbreak Surveillance System, 1998–2011

Supplemental Figures




Muenchen
Oranienburg
Typhi
Berta
Reading
Anatum
% of outbreaks or isolates
0
2
4
6
8
1973-1977
1978-1982
1983-1987
1988-1992
1993-1997
1998-2000
2001-2004
2005-2008
2009-2012
% of FDOSS outbreaks
% of NSSS isolates