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Trends in Vibriosis Transmission among the Top Four Vibrio Species, United States, 1988-2012

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Trends in Vibriosis Transmission among the Top Four *Vibrio* Species, United States, 1988-2012

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Abstract

Background

Vibrio infection (vibriosis) results from consuming contaminated seafood or exposing skin directly to marine waters or raw seafood. The Centers for Disease Control and Prevention (CDC) estimates that 80,000 illnesses occur each year in the United States. Four species, *V. parahaemolyticus, V. vulnificus, V. alginolyticus,* and *V. cholerae* (excluding toxigenic O1 and O139), are responsible for most cases. Understanding foodborne and non-foodborne transmission routes is important for describing epidemiological trends and for directing prevention efforts.

Methods

Demographic, clinical, and epidemiological data for cases reported between 1988 and 2012 were extracted from CDC's Cholera and Other Vibrio Illness Surveillance System (COVIS). Outcomes and seasonal trends were described by species and transmission route.

Results

A total of 10,173 domestically acquired, non-toxigenic cases of vibriosis were reported, including 4,224 (41.5%) *V. parahaemolyticus* cases, 1,998 (19.6%) *V. vulnificus* cases, 1,267 (12.5%) *V. alginolyticus* cases, and 963 (9.5%) *V. cholerae* cases. There were 4,026 hospitalizations and 795 deaths reported. When categorized by transmission route, 5,775 (56.8%) cases were foodborne and 3,317 (32.6%) were non-foodborne.. Most (52.4%) cases occurred during the summer months with peaks in July and August. Only 140 cases were reported from eight states in 1988 compared to 907 cases reported by 42 states in 2012. The overall crude incidence in 2011 was 0.26 cases per 100,000 population.

Discussion

The number of reported cases of vibriosis has been increasing steadily since 1988. Increased prevention efforts, including safer seafood products and consumer education, are needed. These efforts should focus on specific populations and transmission routes for each of the top four species that cause most vibriosis cases in the United States.

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CHAPTER I
INTRODUCTION

1.1 Background

Members of the family *Vibrionacae, Vibrio spp.* are gram-negative, rod shaped bacteria that occur naturally in marine and estuarine environments (1). Generally, vibrios can be found living in a variety of seafood and concentrated in filter-feeding shellfish, such as oysters and clams (2). Numbers of bacteria are highest during the summer months when waters are warmest (1, 2). Humans become exposed to vibrios via seafood consumption, exposure of skin to marine or estuarine waters, and exposure of the skin to raw seafood or drippings from raw seafood (3).With the exception of *V. cholerae* and *V. mimicus* all other species are halophilic, requiring salt water to survive. The species *V. cholerae* can also be present in food or water that has been contaminated from human feces.

There are a number of *Vibrio* species that are pathogenic to humans and cause multiple types of infections. The disease cholera is defined as illness resulting from infection with toxigenic *Vibrio* species *cholerae* serogroup O1 or O139 (3). Cholera is an acute illness characterized by watery diarrhea that can lead to dehydration and death in severe cases. *V. cholerae* O1 and O139 are responsible for cholera epidemics around the world. Human illnesses from infection with any other pathogenic *Vibrio* species are known as vibriosis. The clinical manifestations of vibriosis include watery diarrhea, primary septicemia, and skin or soft tissue infections (3).

The Centers for Disease Control and Prevention (CDC) estimates that *Vibrio* species cause 80,000 domestically-acquired illnesses annually (4). The Cholera and Other *Vibrio* Illness Surveillance System (COVIS) and the Foodborne Diseases Active Surveillance Network (FoodNet) at CDC track reported cases of vibriosis in the United States. FoodNet active surveillance captures information in 10 geographic sites covering approximately 15% of the U.S. population. COVIS collects passive surveillance data for the whole country. Between 1996 and 2010 an increase in reported cases of vibriosis in the United States was observed in both COVIS and FoodNet (5). In 2012, FoodNet reported that the rate of vibriosis had increased 43% compared to the years 2006-2008 (6).

1.2 Purpose of Study

Building upon previous research, this thesis focuses on the four species of *Vibrio* that are responsible for the largest numbers of vibriosis cases reported to COVIS. Those species are *Vibrio parahaemolyticus*, *V. vulnificus*, *V. alginolyticus*, and *V. cholerae* (excluding toxigenic O1 and O139). Surveillance data collected by COVIS from 1988 through 2012 from all reporting sites were used for the analysis. The epidemiology of infections with these species, including demographic and clinical characteristics, is described. Specimen source and exposure data were used to determine transmission route trends in vibriosis overall and within each of the four species. Crude incidence rates were calculated to estimate the increase in vibriosis from 1988-2012. The goal of this analysis is to provide a better understanding of the majority of vibriosis cases reported in the United States.

CHAPTER II
REVIEW OF THE LITERATURE

2.1 Microbiology

Vibrios are a member of the family *Vibrionaceae,* which are made up of eight genera. Recently, taxonomic changes have reclassified the species *V. hollisae* into a new genus known as *Grimontia*. *V. damselae* was also reassigned to the genus *Photobacterium* and is now known as *Photobacterium damselae* subsp. *damselae* (3).

Fourteen species in three genera are known to cause illness in humans (7). Toxin-producing strains of *V. cholerae* O1 and O139 are the serogroups responsible for cholera, an acute diarrheal illness that can cause epidemics (1, 7, 8). Strains of the O1 and O139 serogroups can also be non-toxigenic. Although *V.cholerae* serogroups reported as non-O1 and non-O139 can produce an enterotoxin that is similar to the toxin that produces cholera, most non-O1 strains in the United States do not have this toxin gene (8).

Most *Vibrio* species are halophilic, requiring salt water to survive. They freely inhabit marine coastal waters and estuarine environments; occasionally they have been found in brackish water (1). The presence of *Vibrio* species in water does not indicate fecal contamination (1, 7). *Vibrio spp.* are more abundant in the environment when waters are warmest (7). Vibriosis can occur throughout the year. However, incidence is higher between

April and October and peaks in the summer months; non-foodborne vibriosis has been known to peak in August (7, 21).

2.2 Clinical Presentation

Gastroenteritis is the most common presentation of *Vibrio* infection from consumption of contaminated seafood (14). Onset of symptoms typically occurs within seven days of exposure. In a study of *Vibrio* gastroenteritis in the U.S. Gulf of Mexico region, 90% of patients' onsets occurred within three days of seafood consumption (14). Primary symptoms of *Vibrio* gastroenteritis include nausea, vomiting, diarrhea, abdominal cramps, fever, and bloody diarrhea. Persons infected with *V. parahaemolyticus* are more likely to have gastroenteritis than persons infected with other species (14, 15).

Vibrio spp can cause skin and soft tissue infections, ocular and ear infections, and septicemia (7, 16). Some symptoms of skin infections may be similar for those with gastroenteritis, but cellulitis and bullae also can occur. Depending on severity, these infections can lead to surgical debridement or amputation. Pre-existing illnesses can increase risk and severity of vibriosis after seafood consumption or direct skin exposures. Persons with liver disease, certain immunodeficiencies, and other chronic conditions are more likely to have septicemia after infection with *V. vulnificus,* and are more likely to die from infection than otherwise healthy persons (17, 18).

2.3 Exposure/Risk Factors

Seafood consumption

Although human illness can occur after consumption of cooked or raw seafood, consumption of raw seafood increases the risk for vibriosis. Because *Vibrios* can be

concentrated in the tissues of filter-feeding, bi-valve mollusks like oysters, clams, and mussels they are frequently reported as vehicles for vibriosis (7). In a recent study on vibriosis and clam consumption, *V. parahaemolyticus* was the most commonly isolated species in patients that reported only consuming clams prior to illness onset (19). Gulf coast oysters harbor relatively high concentrations of *V. vulnificus,* and can be particularly risky when waters are warmest during the summer months (20). Oysters are the most commonly reported vehicle for *V. vulnificus* infection, which causes the most deaths associated with consuming raw oysters (20). Crustaceans (shrimp, crab, lobster, and crawfish) and finfish are also important vehicles.

Direct skin contact

Direct contact with marine or estuarine water or raw seafood products or drippings can result in a variety of infections. Exposing an existing wound to marine or estuarine waters can increase risk of infection in the skin and soft tissue. *V. alginolyticus* primarily causes infections of the skin and soft tissue as well as inner ear infections. Patients with non-foodborne infections from *V. alginolyticus* are younger (median age of 30 years) than patients with *V. vulnificus* (63 years) and *V. parahaemolyticus* (43 years) infections (21). The Gulf Coast and Pacific regions of the United States report the most cases of *V. alginolyticus* annually (21).

2.4 Surveillance

Cases of cholera have been nationally notifiable since 1944. Surveillance for vibriosis other than cholera in the United States began in 1988 as a joint effort between the CDC, the U.S. Food and Drug Administration (FDA), and the Gulf Coast states of Florida, Georgia, Mississippi, Louisiana, and Texas. By the late 1990's, most states were reporting voluntarily to what is now known as the Cholera and Other *Vibrio* Illness Surveillance System (COVIS) (9). In 2007, a Council of State and Territorial Epidemiologists position statement made vibriosis nationally notifiable. Information on cases of vibriosis is collected on a standardized COVIS case report form. The type of data collected includes demographic, isolate, and clinical characteristics as well as exposure and seafood investigation. This information is used to identify commonalities between foods consumed, host, and environmental risk factors.

The Foodborne Diseases Active Surveillance Network (FoodNet), a collaboration between 10 state health departments and CDC, FDA, and the U.S. Department of Agriculture (USDA), has also been performing *Vibrio* surveillance in the United States since 1996 (6). FoodNet is an active, population-based surveillance system that collects data on laboratory-confirmed infections with a variety of pathogens commonly transmitted by food. The geographic network of state health departments captures about 15% of the U.S. population. Ensuring that all laboratory-confirmed cases are reported increases the completeness of surveillance data because it is not subject to under-reporting; however data is still subject to

under-diagnosis as many patients may not seek medical attention. FoodNet collects data on demographic, clinical characteristics, and epidemiologic information, travel, and outbreak status (5).

2.5 Burden of *Vibrio* illness in the United States

In a 2011 report, CDC estimated that *Vibrio* causes approximately 80,000 illnesses in the United States each year; those illnesses result in an estimated 500 hospitalizations and 100 deaths annually (2). The estimates relied on the concept of a "burden of illness pyramid," which is a model used to represent diagnosis and reporting of foodborne illnesses. The model shows all persons exposed to a particular organism at the bottom of the pyramid. Some persons become ill, and fewer may seek medical attention. Some may then have a specimen collected and submitted to a laboratory, where fewer specimens may be cultured for a specific pathogen. When the pathogen is detected by culture, the case is considered laboratory-confirmed. Finally, at the top of the pyramid, some cases will be reported to a public health department. This model helps to understand that not all cases will be diagnosed or reported, and why estimated numbers of vibriosis cases are actually much larger than the numbers of cases reported to both COVIS and FoodNet. For example, the types of culture media necessary for isolating *Vibrio* species are specialized based on individual species. If appropriate media are not used, lower rates of detection and ultimately underreporting can result (22).

Between 1996 and 2010, 7,700 illnesses, 2,925 hospitalizations, and 570 deaths were reported to COVIS (5). *V. vulnificus* illnesses contributed to over half of the annual deaths

attributed to *Vibrio* infection and 81% of all deaths reported to COVIS (2, 3). Incidence of infection with *Vibrio* was highest among persons age 60 years or older; 68 % of reported illnesses are among males (5, 11). A relatively low overall incidence of vibriosis has been observed in FoodNet (0.41 per 100,000) (6). However, case fatality ratios observed by FoodNet are high at 5.8% (44 of 762) cases from any site of isolation and when *Vibrio* was isolated from a sterile site, such as blood, the case fatality ratio increased to 35.3% (36 of 102) cases (10).

Overall, *V. parahaemolyticus* is the most commonly reported species causing vibriosis in the United States. *V. vulnificus* is second most commonly reported species, but is the most commonly reported by the Gulf Coast states (5, 12). *V. vulnificus* is the most deadly of the species contributing to 462 out of 570 deaths reported between the years of 1996-2010 (5, 13). *V. alginolyticus*, the third most commonly reported species, contributes to the highest number of non-foodborne infections in the United States (12). *V. cholerae* non-O1 non-O139 is the fourth most commonly reported (12). Coastal states report the most cases annually. In 2011, only 14% of cases were reported by non-coastal states (12).

2.6 Prevention strategies

Understanding transmission types for vibriosis infections whether foodborne or non-foodborne is important for directing prevention efforts. Current prevention strategies for vibriosis have focused heavily on education of consumers and food establishments, including warnings about the consumption of raw seafood on menus. For exposures to marine or estuarine water exposures current prevention efforts focus education and warnings to avoid

exposure waters when one has a wound or other underlying health conditions (13). Cooking shellfish correctly and avoiding cross-contamination can also reduce the risk of vibriosis (15). Educating persons with underlying conditions to avoid consuming raw seafood has been prioritized for prevention of severe infections and *Vibrio*-associated deaths (17).

U.S. Food and Drug Administration (FDA) has reviewed a variety of oyster post-harvest processing methods (23). The purpose of these methods is to reduce levels of *V. vulnificus* and *V. parahaemolyticus* to non-detectible levels, defined as less than 30 MPN/g. In 2003, California passed a law restricting the sale of Gulf Coast oysters during the period of April 1 through October 31 unless the oysters were proven to have been through a post-harvest process that would reduce the amount of *V. vulnificus* contamination to non-detectable levels (24). Since the law was established, California has seen a significant reduction in cases and deaths (24).

FDA published the results of the first systematic survey of post-harvest processing for *V. vulnificus* and *V. parahaemolyticus* in the United States in 2009. Samples were collected from both processors and retail, and had been treated by one of three different methods: high hydrostatic pressure (HHP), individual quick freezing (IQF), and mild heat treatment. HHP reduces microorganisms by applying high amounts of pressure (35,000 to 40,000 psi) to shucked or half-shell oysters for a short period of time (3 to 5 minutes). The IQF method works by rapidly freezing oysters cryogenically and storing them frozen for an extended period of time. Mild heat treatment immerses whole oysters in the shell for 24 minutes and then cools them for 15 minutes. The report found that HHP and mild heat

treatment significantly reduced *V. vulnificus* and *V. parahaemolyticus* levels. IQF did not reduce levels of *V. vulnificus* to 30 MPN/g or lower (23, 25).

Understanding foodborne and non-foodborne transmission routes is important for describing epidemiological trends and for directing prevention efforts. Specifically, describing the differences in transmission routes for the four species that cause the highest number of infections; will provide the greatest impact for reduction of cases. Understanding species-specific exposure types can also aid in prioritizing prevention measures with limited resource availability. Together, these data can be used to evaluate the appropriateness and effectiveness of prevention strategies.

Chapter III

METHODOLOGY

3.1 Data Sources

For this thesis, data were extracted from the Cholera and Other *Vibrio* Illness Surveillance system (COVIS) database at CDC. State and local health officials report cases to COVIS using a case report form to collect data on patient demographics, specimen source information, clinical characteristics and exposures. If seafood is consumed, product traceback information is collected. Forms are submitted to CDC in electronic or paper format, and then entered into the COVIS database. Table 1 summarizes the types of information collected on the case report form.

Table 1: Summary of data collected through the COVIS system*

Exposure data	Demographic data	Isolate data	Clinical data	Seafood traceback
Travel	Age	Species	Symptoms	Type of seafood
Seafood consumption	Sex	Specimen source	Hospitalization	Where consumed/purchased
Recreational water exposure	Race/ethnicity	Date of specimen collection	Sequelae	Harvest information
	State	*Vibrio* species confirmed at state lab	Death	Results of inspection
	Occupation	Other organism	Antibiotic treatment	
			Preexisting conditions	
			Medications taken prior to illness	

*Case report form: http://www.cdc.gov/nationalsurveillance/PDFs/cdc5279-covis-vibriosis-508c.pdf

3.2 Transmission Route Categorization

Exposures

Based on exposures reported on the COVIS form, patients were classified as being exposed to seafood, marine or estuarine water, or both. Marine or estuarine contact includes skin contact with bodies of water, marine or estuarine life, and seafood drippings from raw or live seafood. If a patient reported more than one exposure category, such as swimming and eating oysters, the patient is considered to have multiple exposures; otherwise the patient is considered to have a single exposure to one of the categories listed above. When exposure information is not provided on the case report form is it considered an unknown exposure.

Table 2. Exposure category and description

Exposure category	Exposure description
Seafood consumption	Ingestion of seafood raw or cooked in the 7 days before illness onset
Marine/estuarine contact	Skin contact with bodies of water or marine/estuarine life, or contact with seafood drippings in the 7 days before illness onset
Unknown	Exposure information not provided on the case report form

Specimen sites

Based on the site of specimen collection for etiologic testing and confirmation, specimen site data were categorized into five types: gastrointestinal, blood or other normally sterile site, skin or soft tissue, other/non-sterile site, and unknown site. Unknown site is chosen when a specimen site is not reported on the case report form. Table 3 shows examples of specimen sites that could be reported, but is not exhaustive of all possible sites. Similar to the exposure

categories, if more than one specimen site from different categories is indicated then the specimen site category is considered multiple.

Table 3. Specimen site category and example sources

Specimen site category	Specimen source examples
Gastrointestinal (GI)	Stool, bile, appendix, rectum, gall bladder, colon
Blood or other normally sterile site (Sterile)	Blood, CSF, peritoneal fluid, lumbar disc fluid, lymph node, bullae
Skin or soft tissue (SST)	Wound, ear (not including otitis media and middle ear), appendage, tissue
Other, non-sterile (ONS)	Urine, sputum, aspirate, bronchial washing, eye, otitis media, middle ear, placenta
Unknown	No specimen site reported or site not specified for "other"

Transmission categories

Using the exposure and specimen site classifications previously described, cases were categorized into transmission routes using a hierarchy (Figure 1). Cases with a single exposure of seafood consumption and *Vibrio* isolated from a gastrointestinal (GI) site (or from multiple sites, but at least one was GI) were classified as a confirmed foodborne case. A probable foodborne case was classified when seafood consumption was reported and *Vibrio* was isolated only from skin or soft tissue (SST), other, non-sterile site (ONS) or unknown sites (or multiple sites that do not include GI). Conversely, cases in which *Vibrio* was isolated from SST, blood or other normally sterile site (sterile), or from multiple specimen site categories, and was only exposed to marine or estuarine water, were considered a confirmed non-foodborne case. A probable non-foodborne case was classified when the specimen site is only GI, ONS, or unknown or multiple specimen sites that do not include SST, and exposure is only to marine or estuarine water.

It was possible for cases to have multiple exposures (e.g., a patient eats oysters and swims in the ocean). For cases with multiple exposures, it was necessary to categorize them

using the specimen site categories alone. A case was considered confirmed foodborne if the specimen site was only GI, or there were multiple specimen site categories with GI included and without SST. A case with multiple exposures was considered probable non-foodborne when the specimen site was only SST, or there were multiple specimen sites that include SST but there was not a site from GI. The third category for multiple exposures was unknown, which happens when the specimen sites are only from sterile, ONS, or an unknown site, when there are multiple specimen site categories, including GI and SST, or if the multiple sites do not include GI and SST. Unknown or no reported exposures were classified the same as those cases with multiple exposures.

3.4 Analysis

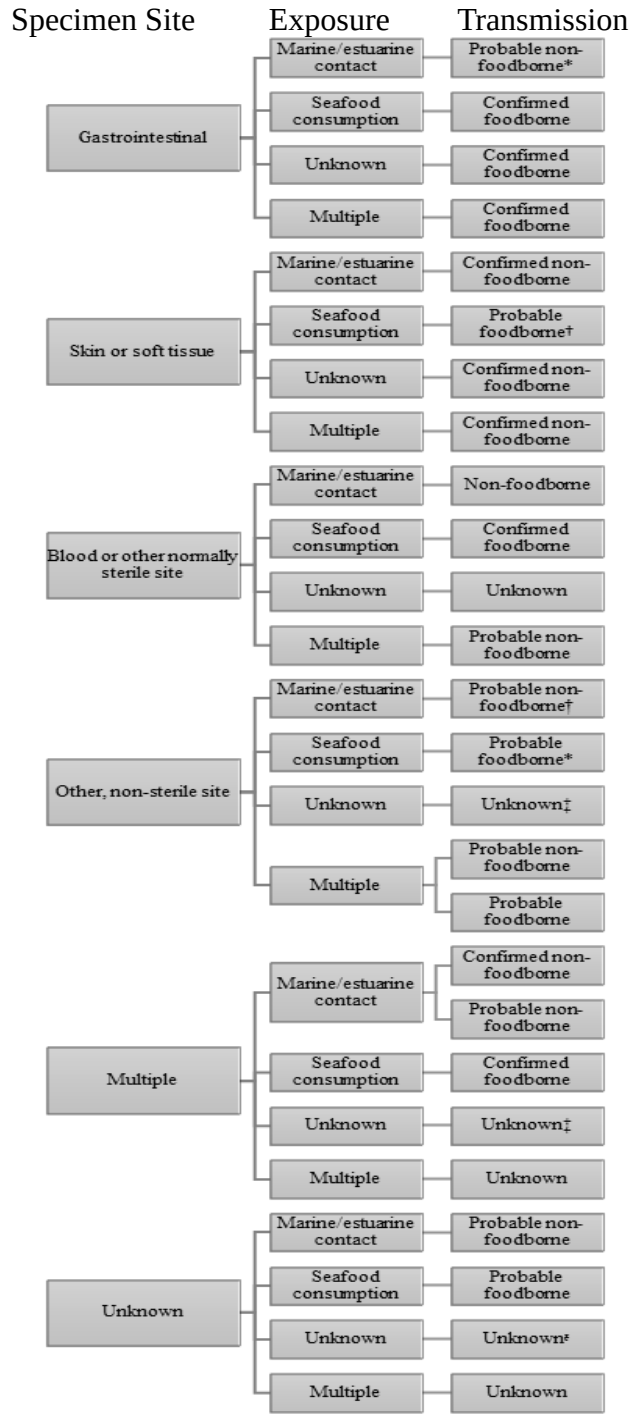
For the purposes of this analysis, all cases reported to COVIS from 1988 through 2012 were used; cases that reported international travel in the 30 days prior to illness onset were excluded from the analysis. In addition, all toxigenic *V. cholerae* O1 and O139 cases were excluded from this analysis. *V. cholerae* serogroups that were non-toxigenic were included in the analysis and were combined into a single category, referred to as *V. cholerae.*

Basic epidemiologic information on demographics, clinical characteristics, and exposures were analyzed as frequencies. Chi-squared tests were used to assess the significance of observed differences in selected categorical data. For most questions, the case report form provides three options for a response: yes, no, or unknown. For hospitalizations and deaths if the question was answered as unknown it was coded as missing. If a question was not answered on the case report form it was also coded as missing. Missing data were not included in the results. Until 2007, Hispanic ethnicity was reported on the case report form as a category of race. The form was changed to separate race and ethnicity questions. To avoid double counting and maintain

consistency across the study period, Hispanics of all races were reported as Hispanic ethnicity and unknown race.

To understand changes in reported vibriosis from 1988-2011, crude incidence rates were calculated for all *Vibrio* species and individually for *V. parahaemolyticus*, *V. vulnificus*, *V. alginolyticus*, and *V. cholerae.* Population data for the denominator was available through the year 2011; consequently, all incidence rates were calculated through the year 2011. Incidence rates were calculated by dividing the number of cases reported to COVIS each year by the total population of the reporting area for that year. A state's population was included in the denominator the first year a case was reported and continuously each year subsequently. Data was analyzed using *SAS version* 9.3 (SAS Institute, Cary, NC).

Figure 1. Transmission categories



†Probable foodborne cases are classified when a specimen is isolated from multiple specimen sites that do not include gastrointestinal.
*Probable non-foodborne cases are classified when a specimen is isolated from multiple specimen categories not including skin or soft tissue.
‡Unknown cases are classified when a specimen is isolated from multiple specimen site categories including gastrointestinal or skin or soft tissue, or neither gastrointestinal or skin or soft tissue.
§ Unknown cases are classified when a specimen is isolated from multiple specimen site categories including gastrointestinal or skin or soft tissue, or neither gastrointestinal or skin or soft tissue.

Chapter IV

RESULTS

4.1 Species Results

A total of 10,173 domestically acquired, non-toxigenic cases of vibriosis, 4,026 hospitalizations, and 795 deaths were reported to COVIS between the years of 1988 and 2012. The top four species contributed 8452 cases or 83.9% of all cases. *V. parahaemolyticus* contributed to the most reported cases with 4,224 (41.5%), followed by 1,998 *V. vulnificus* cases (19.6%), 1,267 *V. alginolyticus* cases (12.5%), and 963 *V. cholerae* cases (9.5%). Initial analysis showed few demographic differences when comparing confirmed and probable foodborne and non-foodborne cases. Among the top four species there were 4414 (52.2%) confirmed foodborne cases, 276 (3.36%) probable foodborne cases, 2669 (31.6%) confirmed non-foodborne cases, and 214 (2.53%) probable non-foodborne cases. For subsequent analyses, cases of confirmed and probable foodborne transmission routes were combined into one category called foodborne; confirmed and probable non-foodborne cases were combined into another category called non-foodborne. Cases with unknown transmission are presented separately in the results.

Figure 2 shows the number of cases reported to COVIS annually since 1988. Overall, the number of cases reported increased over time. In 1988 140 cases were reported and in 2012 there were 907 cases reported. The number of reporting jurisdictions has also increased (Figure 3). In 1988, eight states reported to COVIS. In 2012, 42 states had reported to COVIS.

Figure 2. Number of cases reported to COVIS, by species, 1988-2012

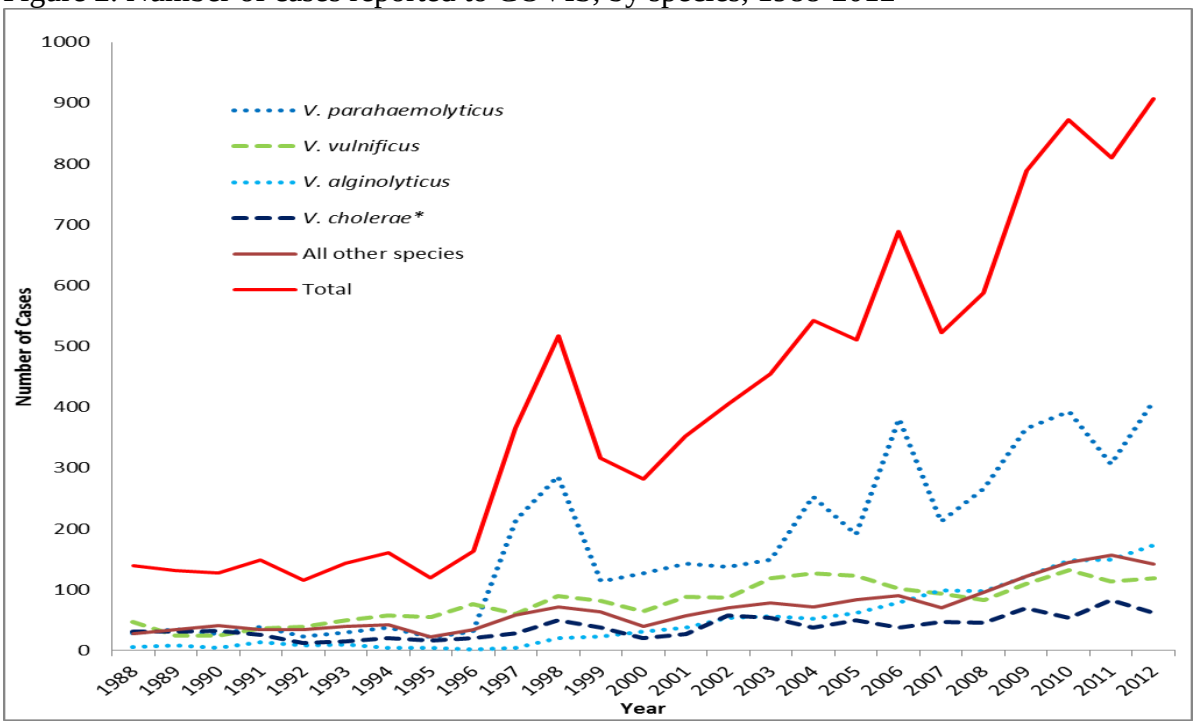
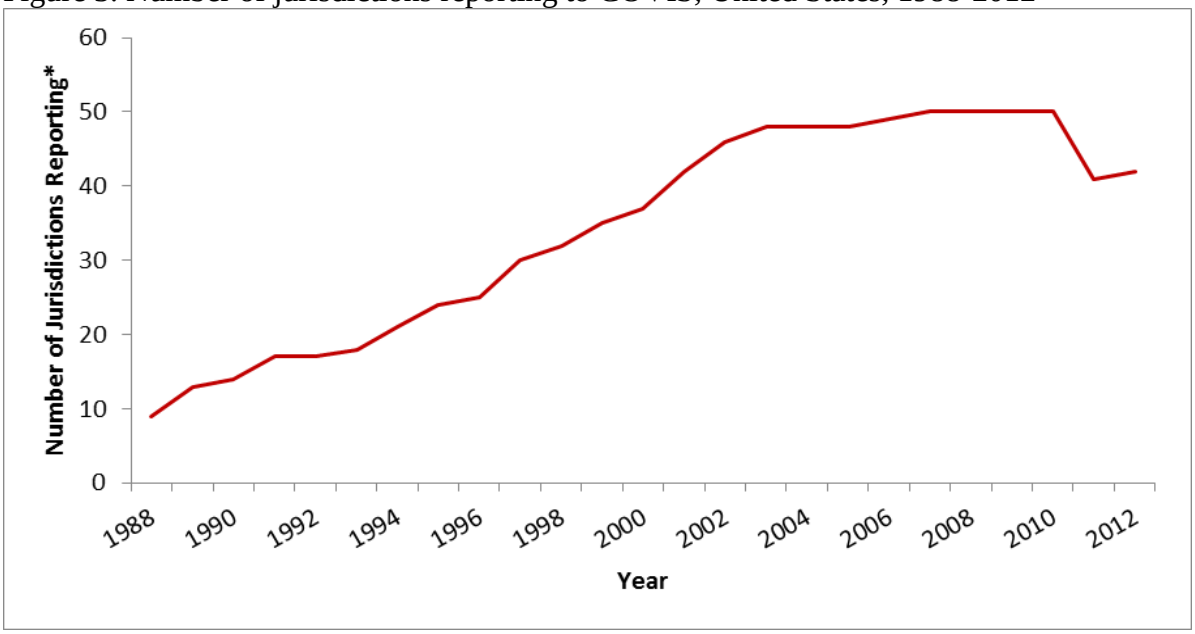


Figure 3. Number of jurisdictions reporting to COVIS, United States, 1988-2012



Demographics and clinical characteristics

Over 60% of cases of each species occurred among males (Table 4). Most (85.8%) *V. vulnificus* patients were male. The median age varied from 32 to 58 years. *V. alginolyticus* patients had the lowest median age (32 years), while the median age of patients with *V. vulnificus* infection was 58 years. Most cases were among Whites, accounting for at least 65% among each of the four species.

Table 4. Demographics by species, 1988-2012

	V. parahaemolyticus N=4,224	*V. vulnificus* N=1,998	*V. alginolyticus* N=1,267	*V. cholerae* N=963
	n(%)	n(%)	n(%)	n(%)
Sex (N)	4,140	1,977	1,244	944
Male	2,755 (66.6)	1,697 (85.8)	872 (70.1)	612 (64.8)
Age (N)	4,076	1,959	1,212	929
Median(Range)	44 (1-94)	58 (0-96)	32 (0-92)	44 (0-96)
Race/Ethnicity (N)	3,612	1,866	1,082	851
White	2,554 (70.7)	1,425 (76.4)	752 (69.5)	558 (65.6)
Black or African American	286 (7.9)	150 (8.0)	59 (5.5)	107 (12.6)
Hispanic*	373 (10.3)	186 (9.9)	88 (8.1)	103 (12.1)
Asian	196 (5.4)	70 (3.8)	73 (6.7)	51 (6.0)
American Indian/Alaska Native	16 (0.4)	3 (0.2)	3 (0.3)	4 (0.5)
Native Hawaiian or other Pacific Islander	8 (0.2)	3(0.2)	10 (0.9)	2 (0.2)
Other	17 (0.5)	5 (0.3)	7 (0.6)	3 (0.4)
Unknown	162 (4.5)	24 (1.3)	90 (8.3)	23 (2.7)

*Hispanics of all races were only counted as Hispanic ethnicity.

The most common symptoms of infection with *V. parahaemolyticus* were diarrhea (79.9%), abdominal cramps (62.9%), nausea (47.7%), and vomiting (32.2%) (Table 5). Fever (61.5%) and cellulitis (55.7%) were the most common clinical characteristics of infection with *V. vulnificus*. Cellulitis was the most common clinical presentation in *V. alginolyticus* cases reported by 29.8%. *V. cholerae* cases reported diarrhea (73.6%), abdominal cramps (55.6%) and nausea (50.2%) most frequently. All clinical symptoms listed in Table 5, frequencies differed significantly among the top four species (X^2=4690, d.f.=21, $p<0.0001$).

Table 5. Clinical symptoms and presentations of infection by species, 1988-2012

	Clinical Characteristic							
	Fever	Diarrhea	Abdominal Cramps	Nausea	Vomiting	Bloody Diarrhea	Cellulitis	Bullous lesions
Species (N)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
V. parahaemolyticus (4224)	1,148 (27.2)	3,122 (73.9)	2,657 (62.9)	2,013 (47.7)	1,358 (32.2)	501 (11.9)	447 (10.6)	75 (1.8)
V. vulnificus (1998)	1,229 (61.5)	557 (27.9)	493 (24.7)	717 (35.9)	595 (29.8)	94 (4.7)	1,113 (55.7)	535 (26.8)
V. alginolyticus (1267)	189 (14.9)	86 (6.8)	77 (6.1)	84 (6.6)	61 (4.8)	16 (1.3)	376 (29.8)	71 (5.6)
V. cholerae (963)	355 (36.9)	709 (73.6)	535 (55.6)	483 (50.2)	358 (37.2)	93 (9.7)	83 (8.6)	22 (2.3)

Outcomes

V. parahaemolyticus was the most commonly reported species, but only 1.2% of cases resulted in death compared to 31.6% of cases of *V. vulnificus* (Table 6). Hospitalization was most common among *V. vulnificus* cases (85.0%) and *V. cholerae* cases (45.9%). Hospitalization and death were least commonly reported for *V. alginolyticus* cases at less than one percent.

Table 6. Hospitalizations and deaths reported to COVIS, by species, 1988-2012

	Total Cases	Hospitalizations	Deaths
Species	N (%)*	n(%)	n(%)
V. parahaemolyticus	4,224 (41.5)	949 (22.5)	46 (1.2)
V. vulnificus	1,998 (19.6)	1,699 (85.0)	631 (31.6)
V. alginolyticus	1,267 (12.5)	216 (17.0)	12 (<1)
*V. cholerae**	963 (9.6)	442 (45.9)	51 (5.3)
All other species	1,721 (125)	720 (41.8)	55 (3.2)
Total	10173	4026	795

*Percent of total cases reported

Specimen site and exposures

The most common site of specimen isolation for *V. parahaemolyticus* and *V. cholerae* cases was GI (Table 7). Isolation from sterile sites were most common for *V. vulnificus* cases. *V. alginolyticus* was isolated from SST in 82.7% of cases. Multiple specimen sites were common among *V. vulnificus* cases (11.5%). For GI, sterile, and SST specimen sites, frequencies differed significantly among the top 4 species (X^2=6,438.3, d.f.=6, $p<0.0001$).

Table 7. Specimen site category by species, 1988-2012*

		Specimen site category					
Species	Species Total N	Gastrointestinal (GI) n(%)	Blood or other normally sterile (Sterile) n(%)	Skin or soft tissue (SST) n(%)	Other, non-sterile (ONS) n(%)	Unknown n(%)	Multiple n(%)
V. parahaemolyticus	4,224	3,261 (77.2)	113 (2.3)	609 (14.4)	33 (0.8)	177 (4.2)	31 (0.7)†
V. vulnificus	1,998	87 (4.4)	1,123 (56.2)	492 (24.6)	28 (1.4)	38 (1.9)	230 (11.5)‡
V. alginolyticus	1,267	56 (4.4)	50 (39)	1,048 (82.7)	59 (4.7)	49 (3.8)	5 (0.4)§
V. cholerae	963	566 (58.8)	171 (17.8)	108 (11.2)	58 (6.0)	37 (3.8)	23 (2.4)¶

*For specific specimen sources please refer to the methods section.
†Sterile and GI (7); sterile and SST (14); sterile and ONS (1); sterile and unknown (1); GI and SST (5); GI and ONS (2); SST or other (1)
‡ Sterile, GI and unknown (1); sterile and GI (12); sterile and SST (195); sterile and ONS (2); sterile, SST, and GI (1); sterile and unknown (3); GI and SST (5); SST and ONS (2)
§ Sterile, GI, SST, and other (1); sterile and GI (11); sterile and SST (8); sterile and ONS (2); GI and SST (1)
¶ Sterile and SST (2); sterile and ONS (2); SST and other (1)

Seafood consumption was reported more often among *V. parahaemolyticus* (76.6%) and *V. cholerae* patients(60.3%) (Table 8). Marine or estuarine contact was reported most often *V.vulnificus* (60.4%) and *V. algnolyticus* (62.6%) patients. Many patients reported both seafood consumption and marine or estuarine exposure.

Table 8. Exposures by species, 1988-2012

	Seafood Consumption			Marine/Estuarine Contact*		
	Yes	No	Unknown	Yes	No	Unknown
Species	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
V. parahaemolyticus	3,067 (72.6)	407 (9.6)	750 (17.8)	1,418 (33.6)	1,926 (45.6)	880 (20.8)
V. vulnificus	1,100 (55.1)	406 (20.3)	492 (24.6)	1,206 (60.4)	445 (22.3)	347 (17.4)
V. alginolyticus	236 (18.6)	435 (34.3)	596 (47.0)	793 (62.6)	227 (17.9)	247 (19.5)
V. cholerae	581 (60.3)	170 (17.7)	212 (22.0)	364 (37.8)	407 (42.3)	192 (19.9)

*Marine/Estuarine contact includes contact with a body of water, seafood drippings, or any marine wildlife.

4.2 Transmission Categories

Foodborne transmission represented the largest number of cases (n=5,775, 56.8%) followed by non-foodborne (n=3,317, 32.6%) and unknown (n=1,081, 10.6%) (Table 9). Foodborne *V. parahaemolyticus* had the largest number of cases among all species and transmission categories, accounting for 33% of all reported vibriosis cases. *V. vulnificus* cases represented the most cases in the unknown transmission category (n=514, 25.7%). *V. alginolyticus* had the highest number of non-foodborne cases (n=1,080). For foodborne and non-foodborne, frequencies differed significantly among the top four species (X^2=2,528.1, d.f.=3, $p<0.0001$).

Table 9. Species by transmission category, 1988-2012

Species	Foodborne n(%)	Non-foodborne n(%)	Unknown n(%)	Species Total N
V. parahaemolyticus	3,361 (79.6)	723 (17.1)	140 (3.3)	4,224
V. vulnificus	596 (29.8)	888 (44.4)	514 (25.7)	1,998
V. alginolyticus	98 (7.7)	1,080 (85.2)	89 (7.0)	1,267
V. cholerae	635 (65.9)	194 (20.2)	134 (13.9)	963
All other species	1,085 (63.0)	432 (25.1)	204 (11.9)	1,721
Grand Total	5,775 (56.8)	3,317 (32.6)	1,081 (10.6)	10,173

Demographics and clinical characteristics

Demographics varied by species and transmission (Tables 10-13). The median age of non-foodborne *V. parahaemolyticus* patients was 42 years old and over 80% were White. The median age for all *V. vulnificus* patients was higher compared to all other species and transmission categories; non-foodborne *V. vulnificus* patients have the highest median age of 61 years. Non-foodborne *V. vulnificus* also had the highest percentage of White patients (86.9%). Foodborne *V. alginolyticus* and *V. cholerae* had the highest percentage of females (38.8% and 39.2%, respectively). Non-foodborne *V. alginolyticus* and *V. cholerae* had the lowest median age at 28 years for both species.

Table 10. Demographics of *V. parahaemolyticus* cases, by transmission, 1988-2012

	Foodborne N=3,361	Non-foodborne N=723	Unknown N=140
	n(%)	n(%)	n(%)
Sex	3,298	709	131
Male	2,131 (64.6)	538 (75.9)	86 (65.7)
Age	3,243	704	129
Median(Range)	44 (1-94)	42 (1-92)	48 (1-92)
Race/Ethnicity*	2,868	636	108
White	1,966 (68.5)	515 (81.1)	72 (66.7)
Black or African American	235 (8.2)	39 (6.1)	12 (11.1)
Hispanic†	330 (11.5)	30 (4.7)	13 (12.0)
Asian	168 (5.9)	24 (3.8)	4 (3.7)
American Indian/Alaska Native	15 (0.5)	1 (0.2)	0 (0)
Native Hawaiian or other Pacific Islander	8 (0.3)	0 (0)	0 (0)
Other	12 (0.4)	4 (0.6)	0 (0)
Unknown	134 (4.7)	21 (3.3)	7 (6.5)

* For foodborne and non-foodborne, frequencies differed significantly among Whites, Blacks/African Americans, Hispanics, and Asians (X^2=41.13, d.f.=3, p<0.0001).

† Hispanics of all races were only counted as Hispanic ethnicity.

Table 11. Demographics of *V. vulnificus* cases, by transmission, 1988-2012

	Foodborne N=596	Non-foodborne N=888	Unknown N=514
	n(%)	n(%)	n(%)
Sex	589	877	511
Male	491 (83.4)	776 (88.5)	430 (84.2)
Age	589	863	507
Median(Range)	55 (0-93)	61 (1-94)	56 (0-96)
Race/Ethnicity*	561	822	483
White	378 (67.4)	700 (85.2)	347 (71.8)
Black or African American	42 (7.5)	56 (6.8)	52 (10.8)
Hispanic†	101 (18.0)	34 (4.1)	51 (10.6)
Asian	31 (5.5)	16 (1.9)	23 (4.8)
American Indian/Alaska Native	1 (0.2)	2 (0.2)	0 (0)
Native Hawaiian or other Pacific Islander	1 (0.2)	1 (0.1)	1 (0.2)
Other	1 (0.2)	1 (0.1)	3 (0.6)
Unknown	6 (1.1)	12 (1.5)	6 (1.2)

* For foodborne and non-foodborne, frequencies differed significantly among Whites, Blacks/African Americans, Hispanics, and Asians (X^2=91.9, d.f.=3, p<0.0001).

† Hispanics of all races were only counted as Hispanic ethnicity.

Table 12. Demographics of *V. alginolyticus* cases, by transmission, 1988-2012

	Foodborne N=98	Non-foodborne N=1,080	Unknown N=89
	n(%)	n(%)	n(%)
Sex	98	1,058	86
Male	60 (61.2)	752 (71.2)	60 (69.8)
Age	97	1,031	84
Median(Range)	48 (0-92)	28 (0-89)	43 (0-86)
Race/Ethnicity*	91	919	72
White	63 (69.2)	647 (70.4)	42 (58.3)
Black or African American	9 (9.9)	40 (4.4)	10 (13.9)
Hispanic†	7 (7.7)	76 (8.3)	5 (6.9)
Asian	7 (7.7)	64 (6.9)	2 (2.8)
American Indian/Alaska Native	1 (1.1)	2 (0.2)	0 (0)
Native Hawaiian or other Pacific Islander	2 (2.2)	8 (0.9)	0 (0)
Other	1 (1.1)	5 (0.5)	1 (1.4)
Unknown	1 (1.1)	77 (8.4)	12 (16.7)

* For foodborne and non-foodborne, frequencies did not differ significantly among Whites, Blacks/African Americans, Hispanics, and Asians (X^2=4.96, d.f.=3, p=0.1747).

† Hispanics of all races were only counted as Hispanic ethnicity.

Table 13. Demographics of *V. cholerae* cases, by transmission, 1988-2012

	Foodborne N=635	Non-foodborne N=194	Unknown N=134
	n(%)	n(%)	n(%)
N	635	194	134
Sex	622	189	133
Male	378 (60.8)	135 (71.4)	99 (74.4)
Age	609	189	131
Median(Range)	46 (0-96)	28 (0-93)	52 (0-95)
Race/Ethnicity*	566	170	115
White	377 (66.6)	111 (65.3)	70 (60.9)
Black or African American	81 (14.3)	14 (8.2)	12 (10.4)
Hispanic†	59 (10.4)	22 (12.9)	22 (19.1)
Asian	32 (5.7)	11 (6.5)	8 (6.9)
American Indian/Alaska Native	1 (0.2)	3 (1.8)	0 (0)
Native Hawaiian or other Pacific Islander	2 (0.4)	0 (0)	0 (0)
Other	2 (0.4)	1 (0.6)	0 (0)
Unknown	12 (2.1)	8 (4.7)	3 (2.6)

* For foodborne and non-foodborne, frequencies did not differ significantly among Whites, Blacks/African Americans, Hispanics, and Asians (X^2=4.56, d.f.=3, p=0.207).

† Hispanics of all races were only counted as Hispanic ethnicity.

Clinical characteristics of each species varied by transmission category (Tables 14-17). Diarrhea and abdominal cramps were most common in foodborne V. *parahaemolyticus* and foodborne *V. cholerae* patients. Over 70% of *V. vulnificus* cases in all transmission categories reported fever. Cellulitis was reported by more patients with (86.7%) non-foodborne *V. vulnificus* and non-foodborne *V. alginolyticus* (40.7%). Bullous lesions were reported less frequently and but were most common among non-foodborne *V. vulnificus* (44.0%).

Table 14. Clinical characteristics of *V. parahaemolyticus* cases, by transmission, 1988-2012*

	Foodborne	Non-foodborne	Unknown
Clinical Characteristic*	n(%)	n(%)	n(%)
Fever	893 (33.6)	211 (37.6)	44 (52.4)
Diarrhea	2,985 (97.0/)	92 (16.3)	45 (51.1)
Abdominal Cramps	2,538 (84.14)	79 (14.3)	40 (45.9)
Nausea	1,871 (63.8)	107 (18.9)	35 (41.7)
Vomiting	1,267 (43.17)	65 (11.6)	26 (30.2)
Bloody Diarrhea	478 (18.2)	13 (2.4)	10 (12.7)
Cellulitis	41 (1.5)	386 (65.4)	20 (25.3)
Bullous lesions	21 (0.8)	49 (10.2)	5 (6.9)

* For foodborne and non-foodbornetransmission frequencies differed significantly for all clinical characteristics among *V. parahaemolyticus* cases (X^2=4230 d.f.=7, p<0.0001).

Table 15. Clinical characteristics of *V. vulnificus* cases, by transmission, 1988-2012*

	Foodborne	Non-foodborne	Unknown
Clinical Characteristic*	n(%)	n(%)	n(%)
Fever	391 (78.7)	539 (72.2)	299 (77.3)
Diarrhea	287 (59.9)	126 (18.2)	144 (40.7)
Abdominal Cramps	83 (12.4)	120 (36.1)	290 (61.6)
Nausea	290 (61.6)	249 (35.1)	178 (50.0)
Vomiting	266 (54.9)	173 (24.6)	156 (42.6)
Bloody Diarrhea	51 (13.8)	16 (2.5)	27 (8.8)
Cellulitis	207 (48.8)	676 (86.7)	230 (64.3)
Bullous lesions	144 (37.4)	273 (44.0)	118 (39.7)

* For foodborne and non-foodborne transmission frequencies differed significantly for all clinical characteristics among *V. vulnificus* cases (X^2=376 d.f.=7, p<0.0001).

Table 16. Clinical characteristics of *V. alginolyticus* cases, by transmission, 1988-2012*

Clinical Characteristic*	Foodborne n(%)	Non-foodborne n(%)	Unknown n(%)
Fever	26 (31.3)	145 (17.6)	18 (39.1)
Diarrhea	44 (53.7)	37 (4.5)	5 (11.1)
Abdominal Cramps	35 (43.2)	36 (4.5)	6 (13.3)
Nausea	27 (33.8)	50 (6.1)	7 (15.9)
Vomiting	22 (27.2)	31 (3.8)	8 (18.2)
Bloody Diarrhea	11 (14.3)	4 (0.5)	1 (2.3)
Cellulitis	21 (28.0)	345 (40.7)	10 (22.7)
Bullous lesions	6 (8.7)	64 (8.6)	1 (2.6)

* For foodborne and non-foodborne transmission frequencies differed significantly for all clinical characteristics among *V. alginolyticus* cases (X^2=196 d.f.=7, p<0.0001).

Table 17. Clinical characteristics of *V. cholerae* cases, by transmission, 1988-2012*

Clinical Characteristic*	Foodborne n(%)	Non-foodborne n(%)	Unknown n(%)
Fever	232 (44.9)	60 (42.6)	63 (64.3)
Diarrhea	539 (90.6)	59 (38.3)	40 (42.6)
Abdominal Cramps	428 (78.7)	53 (35.6)	54 (56.3)
Nausea	378 (67.4)	57 (37.3)	48 (50.0)
Vomiting	279 (49.6)	41 (26.9)	38 (41.3)
Bloody Diarrhea	73 (14.8)	7 (4.9)	13 (15.3)
Cellulitis	15 (3.1)	52 (35.4)	16 (18.8)
Bullous lesions	7 (1.5)	9 (6.9)	6 (7.3)

* For foodborne and non-foodborne transmission frequencies differed significantly for all clinical characteristics among *V. cholerae* cases (X^2=261 d.f.=7, p<0.0001).

Outcomes

Outcomes varied by species and transmission (Table 18). Nearly two-thirds (64.4%) of *V. parahaemolyticus* hospitalizations were among cases with foodborne transmission. Deaths from *V. parahaemolyticus* among patients with foodborne transmission were common (41.3%). *V. vulnificus* hospitalizations were highest among patients with non-foodborne transmission (42.8%); deaths were highest in foodborne patients (44.06%). *V. alginolyticus* patients had the lowest number of deaths among all

species and transmission categories (<1%) and the lowest number of hospitalizations among foodborne (11.1%) and unknown transmission (12.0%) patients.

Table 18. Number of cases, hospitalizations, and deaths reported to COVIS by transmission category and species, 1988-2012

	Foodborne	Non-foodborne	Unknown	Total
Species	n(%)	n(%)	n(%)	N
V. parahaemolyticus	3,361 (79.6)	723 (17.1)	140 (3.3)	4224
Hospitalizations	611 (64.4)	288 (30.3)	50 (5.3)	949
Deaths	19 (41.3)	13 (28.3)	14 (30.4)	46
V. vulnificus	596 (29.8)	888 (44.4)	514 (25.7)	1998
Hospitalizations	527 (31.0)	727 (42.8)	445 (26.2)	1699
Deaths	278 (44.1)	142 (22.5)	211 (33.4)	631
V. alginolyticus	98 (7.7)	1,080 (85.2)	89 (7.0)	1267
Hospitalizations	24 (11.1)	166 (76.9)	26 (12.0)	216
Deaths	1 (8.3)	7 (58.3)	4 (33.3)	12
V. cholerae	635 (65.9)	194 (20.2)	134 (13.9)	963
Hospitalizations	279 (63.1)	75 (16.9)	88 (19.1)	442
Deaths	18 (35.3)	10 (19.6)	23 (45.9)	51
All other species	1085 (63.0)	432 (25.1)	204 (11.9)	1721
Hospitalizations	443 (61.5)	186 (25.8)	91 (12.6)	720
Deaths	20 (2.1)	13 (3.5)	22 (13.9)	55
All Cases				
Hospitalizations	1,884 (34.5)	1,442 (47.8)	700 (77.8)	4026
Deaths	336 (42.3)	185 (23.3)	274 (34.5)	795
Total	5,775 (56.8)	3,317 (32.6)	1,081 (10.6)	10173

Almost 76% of foodborne *V. parahaemolyticus* cases were from a gastrointestinal specimen site, compared to 1.35% of non-foodborne *V. parahaemolyticus* cases (Table 19). More than half (56.2%) of all *V. vulnificus* infections were isolated from blood or other normally sterile sites. Most (79.7%) *V. alginolyticus* cases were non-foodborne transmission from a skin or soft tissue specimen site. Gastrointestinal specimens from foodborne *V. cholerae* represented the largest specimen site category of all *V. cholerae* cases (58.78%).

Table 19. Specimen site categories for reported cases by species and transmission*

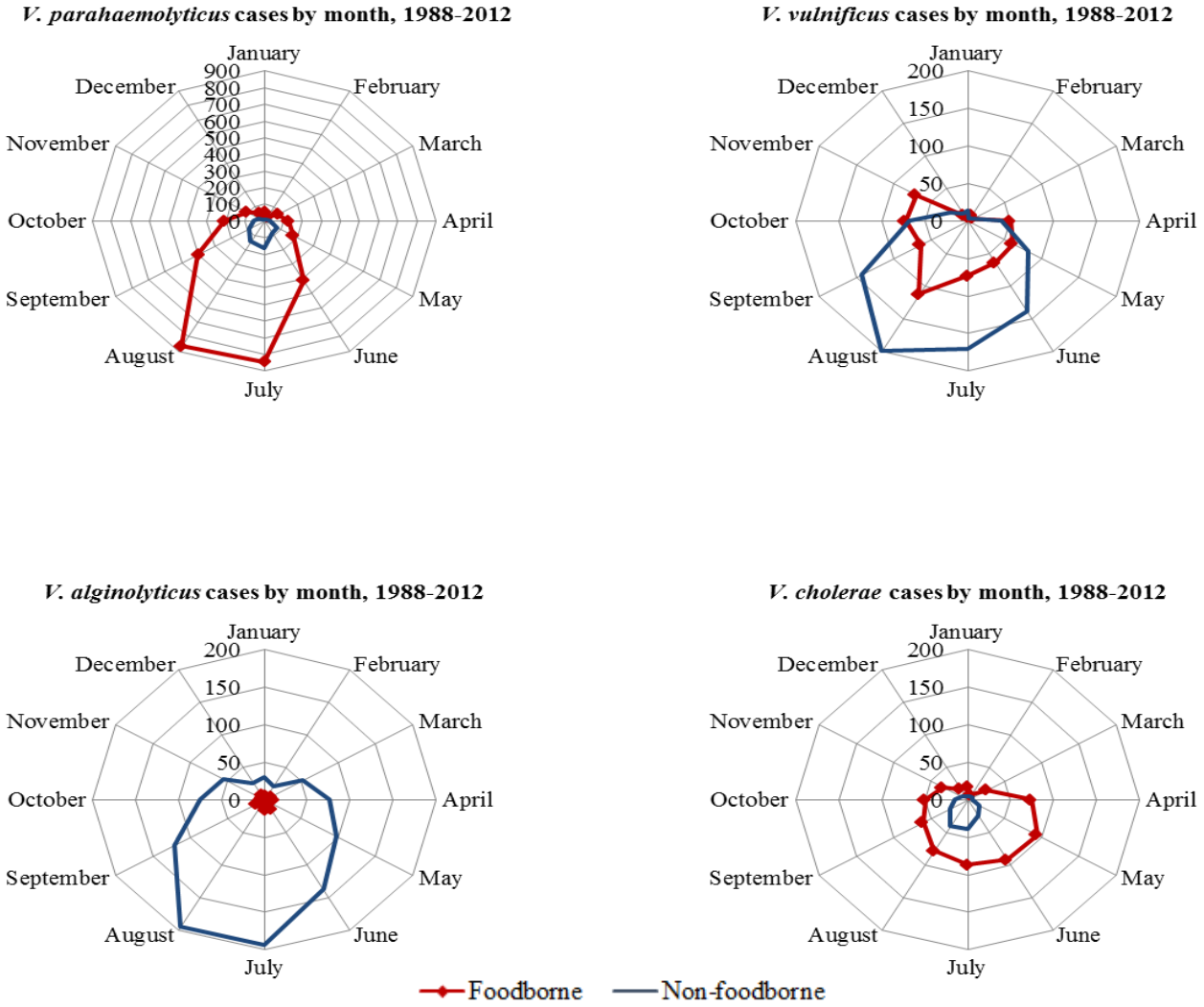
	Foodborne	Non-foodborne	Unknown	Species Total
	n(%)	n(%)	n(%)	N(%)
V. parahaemolyticus	3,361 (79.6)	723 (17.1)	140 (3.3)	4,224 (100)
Gastrointestinal (GI)	3,204 (95.3)	57 (7.9)	0 (0)	3,261 (77.2)
Blood or other normally sterile (Sterile)	38 (1.1)	32 (4.4)	43 (30.7)	113 (2.9)
Skin or soft tissue (SST)	13 (0.4)	596 (82.4)	0 (0)	609 (14.4)
Other, non-sterile (ONS)	8 (0.2)	9 (1.2)	16 (11.4)	33 (0.8)
Unknown	89 (2.7)	12 (1.7)	79 (54.3)	177 (4.2)
Multiple†	9 (0.3)	17 (2.4)	5 (3.6)	31 (0.7)
V. vulnificus	596 (29.8)	888 (44.4)	514 (25.70	1,998 (100)
Gastrointestinal (GI)	85 (14.3)	2 (0.2)	0 (0)	87 (4.4)
Blood or other normally sterile (Sterile)	404 (67.8)	252 (28.4)	467 (90.9)	1123 (56.2)
Skin or soft tissue (SST)	33 (5.5)	459 (51.7)	0 (0)	492 (24.6)
Other, non-sterile (ONS)	2 (0.3)	11 (1.2)	15 (2.9)	28 (1.4)
Unknown	14 (2.4)	6 (0.7)	18 (3.5)	38 (1.9)
Multiple‡	58 (9.7)	158 (17.8)	14 (2.7)	230 (11.5)
V. alginolyticus	98 (7.7)	1,080 (85.2)	89 (7.0)	1,267 (100)
Gastrointestinal (GI)	49 (50.0)	7 (0.6)	0 (0)	56 (4.4)
Blood or other normally sterile (Sterile)	4 (4.1)	19 (1.8)	27 (30.3)	50 (3.9)
Skin or soft tissue (SST)	38 (38.8)	1,010 (93.5)	0 (0)	1,048 (82.7)
Other, non-sterile (ONS)	4 (4.1)	29 (2.7)	26 (29.2)	59 (4.7)
Unknown	2 (2.0)	12 (1.1)	35 (39.3)	49 (3.8)
Multiple§	1 (1.0)	3 (0.3)	1 (1.1)	5 (0.4)
V. cholerae	635 (65.9)	194 (20.2)	134 (13.9)	963 (100)
Gastrointestinal (GI)	532 (83.8)	34 (17.5)	0 (0)	566 (58.8)
Blood or other normally sterile (Sterile)	64 (10.1)	18 (9.3)	89 (66.4)	171 (17.8)
Skin or soft tissue (SST)	7 (1.1)	101 (52.1)	0 (0)	108 (11.2)
Other, non-sterile (ONS)	8 (1.3)	29 (14.9)	21 (15.8)	58 (6.0)
Unknown	10 (1.8)	5 (2.6)	22 (16.4)	37 (3.8)
Multiple¶	14 (2.2)	7 (3.6)	2 (1.5)	23 (2.4)
All other species	1,085 (63.0)	432 (25.1)	204 (11.9)	1,721 (100)
Gastrointestinal (GI)	959 (88.4)	22 (5.1)	0 (0)	981 (57.0)
Blood or other normally sterile (Sterile)	33 (3.0)	21 (4.9)	55 (26.9)	109 (6.3)
Skin or soft tissue (SST)	17 (1.8)	344 (79.6)	0 (0)	361 (20.9)
Other, non-sterile (ONS)	19 (1.8)	12 (2.8)	58 (58.4)	89 (5.2)
Unknown	46 (4.2)	15 (3.5)	86 (42.2)	147 (8.5)
Multiple**	11 (1.0)	18 (4.2)	5 (2.5)	34 (1.9)
Grand Total	5,775 (56.8)	3,317 (32.6)	1,081 (10.6)	10,173

*For specific specimen sources please refer to the methods section.
†Sterile and GI (7); Sterile and SST (14); sterile and ONS (1); sterile and unknown (1); GI and SST(5); GI and ONS (2); SST and other (1)
‡Sterile, GI and unknown (1); sterile and GI (12); sterile and SST (195); sterile and ONS (2); sterile, SST, and GI (1); sterile and unknown (3); GI and SST (5); SST and ONS (2)
§Sterile, GI, SST, other (1); sterile and GI (11); sterile and SST (8); sterile and ONS (2); GI and SST (1)
¶Sterile and SST (2); Sterile and ONS (2); SST and other (1)
**Sterile and GI (7)

Geography

Coastal states reported the most cases to COVIS. California has reported 1,054 foodborne cases since their first report in 1988 followed by Florida (544) andWashington (464). Among the California foodborne cases, most (91%) were *V. parahaemolyticus*. Florida reported the most non-foodborne cases (1,013) followed by Texas (406) and Hawaii (242). *V.alginolyticus* was the most commonly reported non-foodborne species among Florida cases (39%). Florida also had the most cases with unknown transmission routes (206); 67% of those cases were *V.vulnificus*.

Figure 4. Cases by month and transmission, 1988-2012



Seasonality

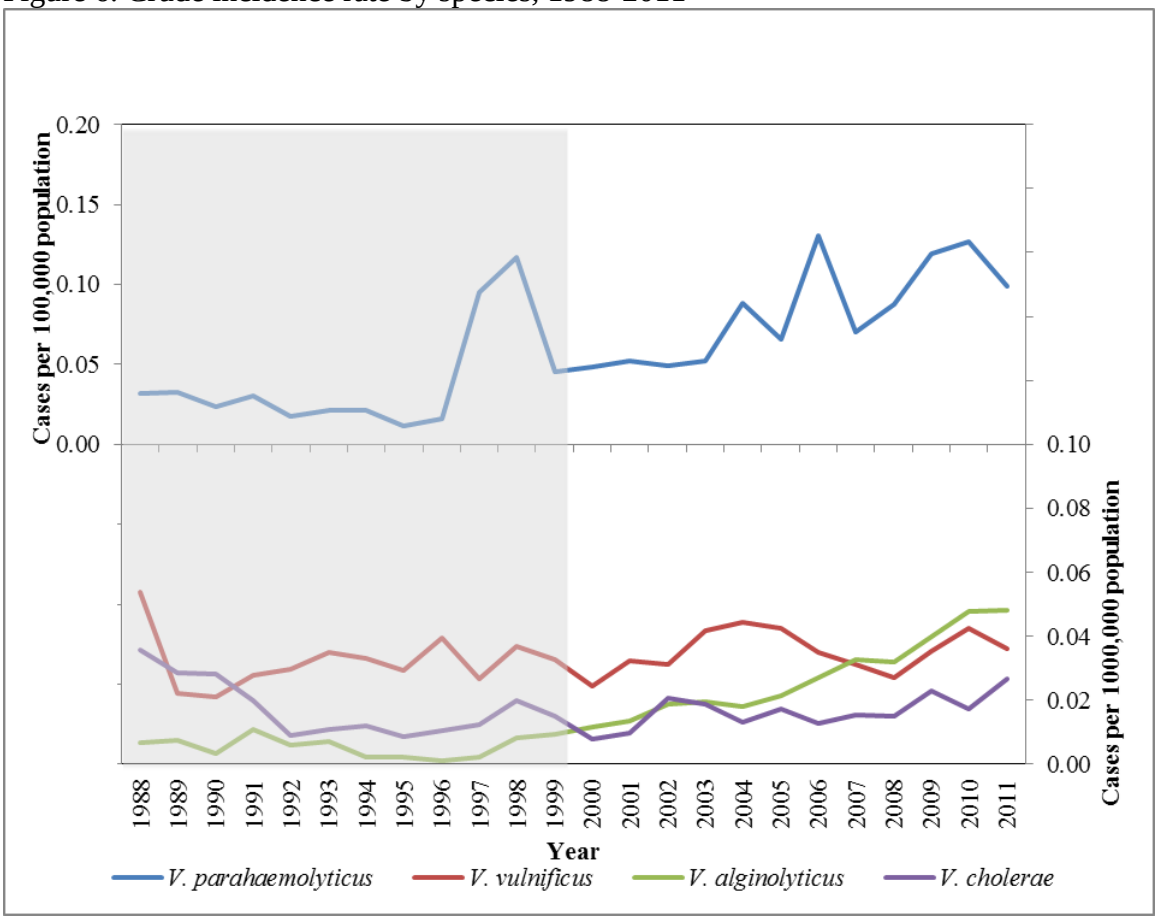
Radar plots demonstrate the seasonality of infections by species and transmission (Figure 4).The number of foodborne and non-foodborne cases by month and species. The axis for *V. parahaemolyticus* is greater than those for the other three species because the number of cases reported is higher. The majority of cases occurred during the summer months among all species (52.4%). Foodborne *V. parahaemolyticus* cases peaked in July and August; non-foodborne cases peaked in July. Foodborne *V. vulnificus* rose sharply from June to peak in August and declined again sharply in September. By comparison, non-foodborne *V. vulnificus* cases gradually increased through the spring and summer months to a peak in August. Non-foodborne *V. alginolyticus* cases peaked in July and August. Foodborne *V. cholerae* cases were highest in the month of May but remained high through June and July.

4.3 Crude Incidence Rates

Figure 5 shows the crude incidence rate of *Vibrio* infections in the United States since surveillance began in 1988. Incidence has increased 62.5% between 1988 and 2011 from 0.16 cases per 100,000 population to 0.26 cases per 100,000 population. Reporting rates of states have been most consistent since 2000, making the data more reliable from 2000 onward. Rates for *V. parahaemolyticus* shown in Figure 6 have been increasing since 1988, from 0.032 per million in 1988 to 0.098 per million in 2011. The highest rate of *V. parahaemolyticus* occurred in 2006 at 0.13 per million population. Rates have increased steadily for V. alginolyticus and in 2011, were 0.048 per 100,000 population. The crude incidence of *V. cholerae* has had little change over time (Figure 6).

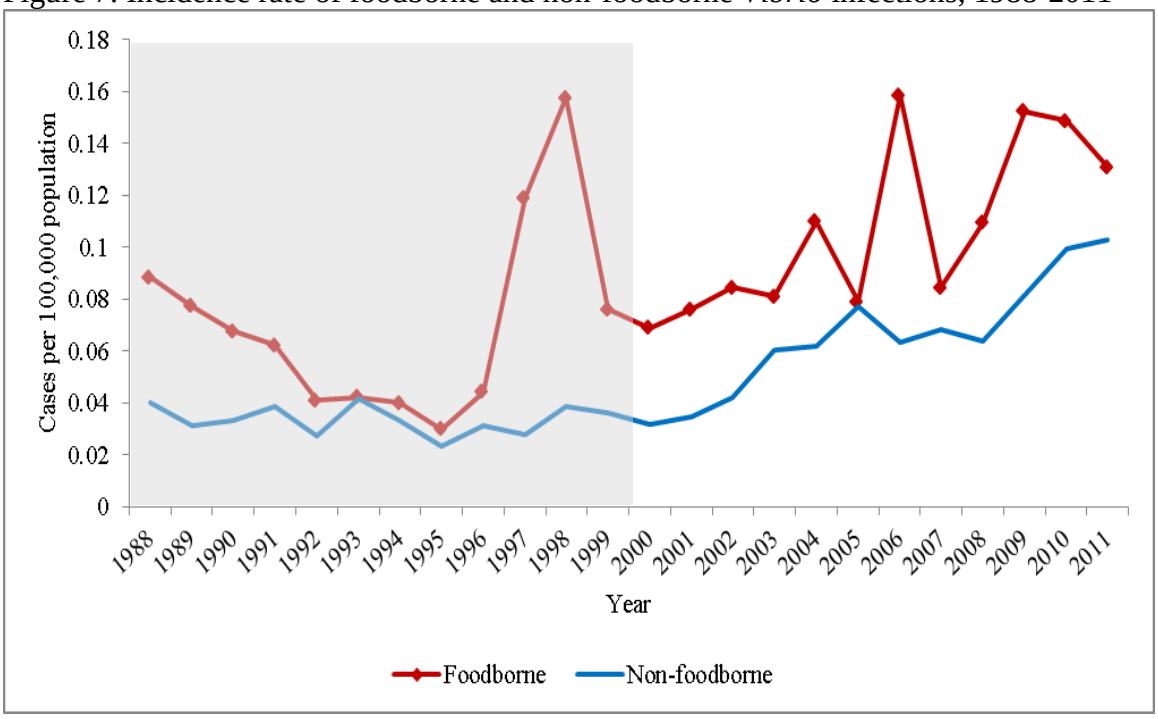
Figure 5. Crude incidence rate of *Vibrio* infections, all species, 1988-2011

Figure 6. Crude incidence rate by species, 1988-2011



Incidence rates among foodborne and non-foodborne transmission cases have fluctuated over time (Figure 7). Like the rates for overall incidence and for each of the four species, reporting rates were most consistent beginning in the year 2000. In 2011, rates of foodborne *Vibrio* infections were 0.13 cases per 100,000 population; non-foodborne infections were 0.10 cases per 100,000 population.

Figure 7. Incidence rate of foodborne and non-foodborne *Vibrio* infections, 1988-2011



Incidence rates for the top four species vary by transmission (Figures 8-11). Incidence rates of foodborne *V. parahaemolyticus* have increased since 1988. In 2011, the crude rate for foodborne *V. parahaemolyticus* was 0.075 cases per 100,000 population. Non-foodborne cases have also increased and in 2011 the crude rate was .02 per 100,000 population. Rates of foodborne and non-foodborne *V. vulnificus* infections have varied over time and non-foodborne rates have remained highest. In 2011, the crude rate for non-foodborne *V. vulnificus* infections was 0.017 per 100,000 population. The crude rate for non-foodborne *V. alginolyticus* cases has increased steadily since 2000 (0.01 per 100,000) and in 2011 was 0.04 per 100,000 population. The crude rates for *V. cholerae* infections have remained stable for both foodborne and non-foodborne cases. However, the highest rates are among foodborne cases; in 2011 the crude rate was 0.015 per 100,000 population.

Figure 8. Crude incidence rate of *V. parahaemolyticus* cases by transmission, 1988–2011

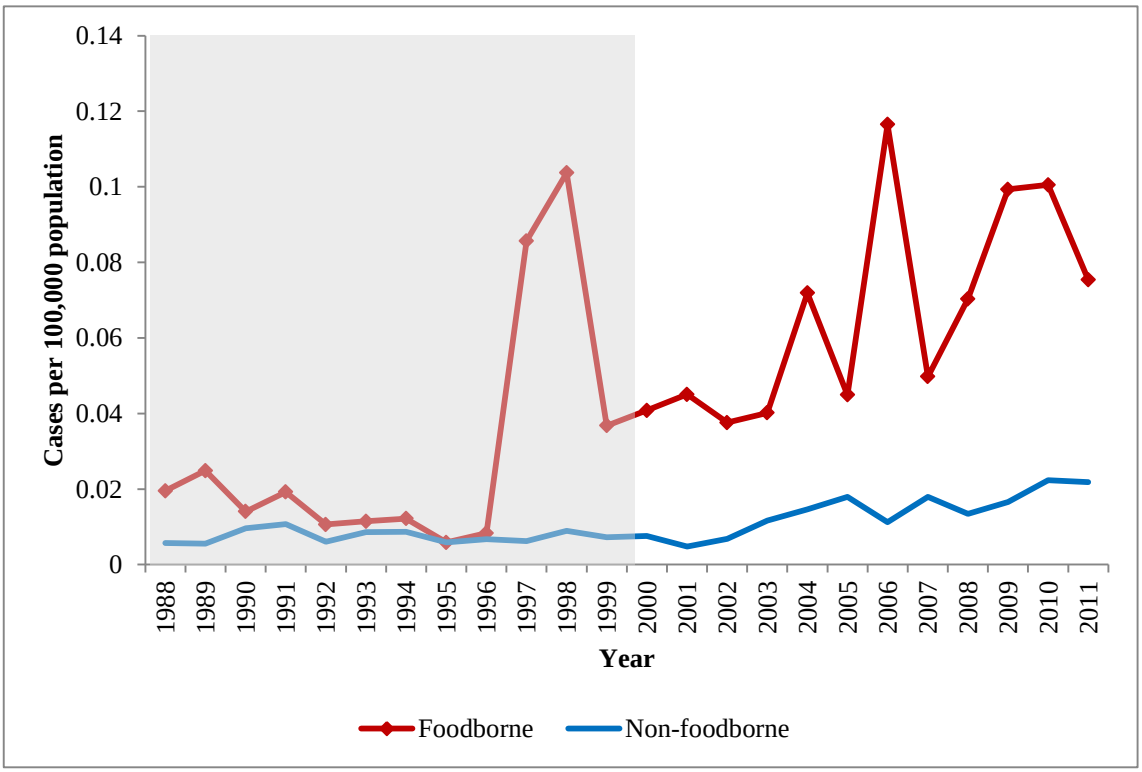


Figure 9. Crude incidence rate of *V. vulnificus* cases by transmission, 1988–2011

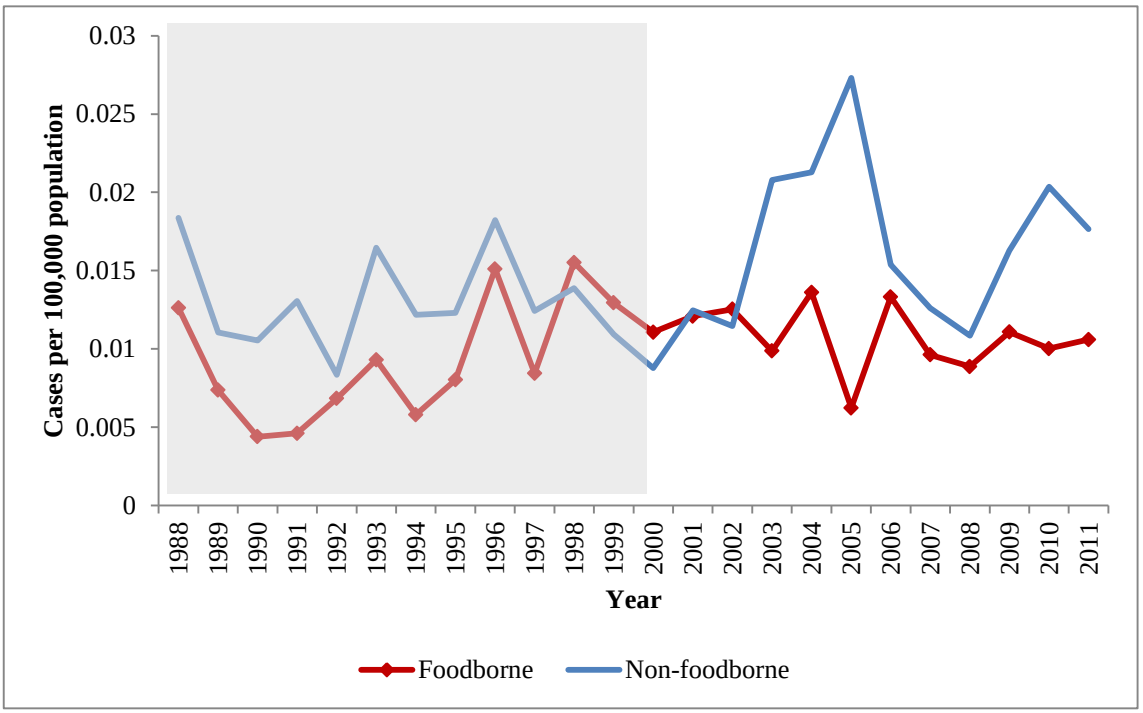


Figure 10. Crude incidence rate of *V. alginolyticus* cases by transmission, 1988–2011

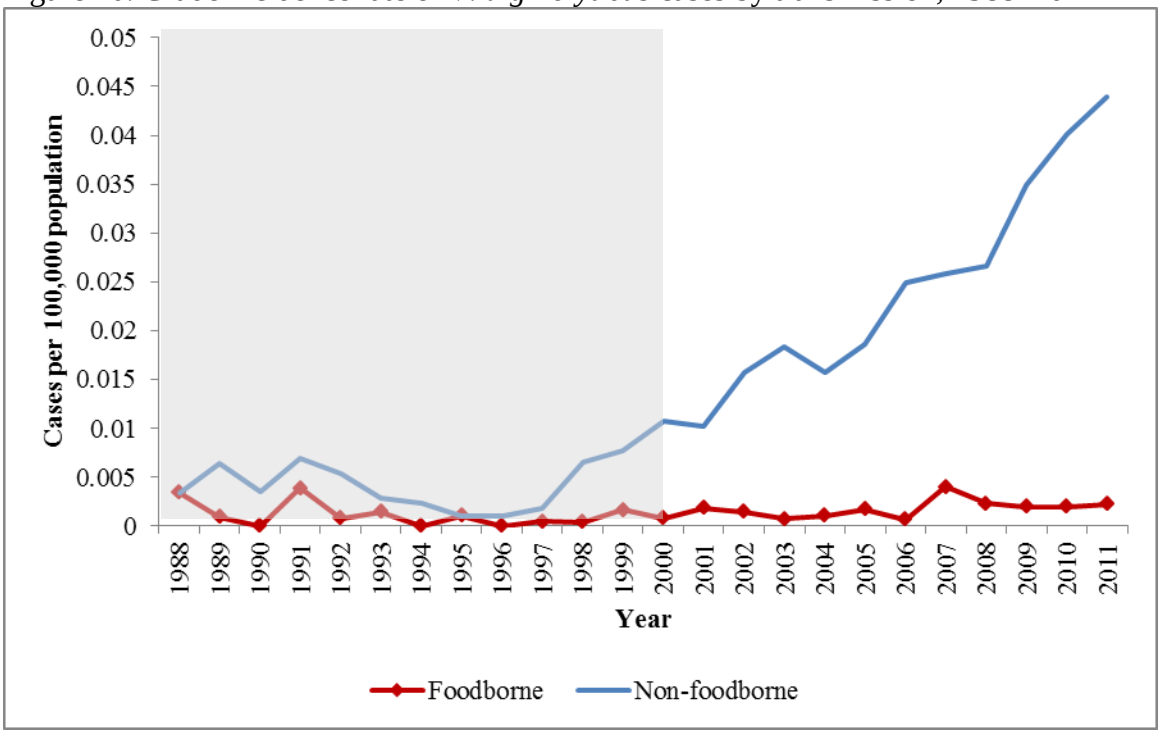
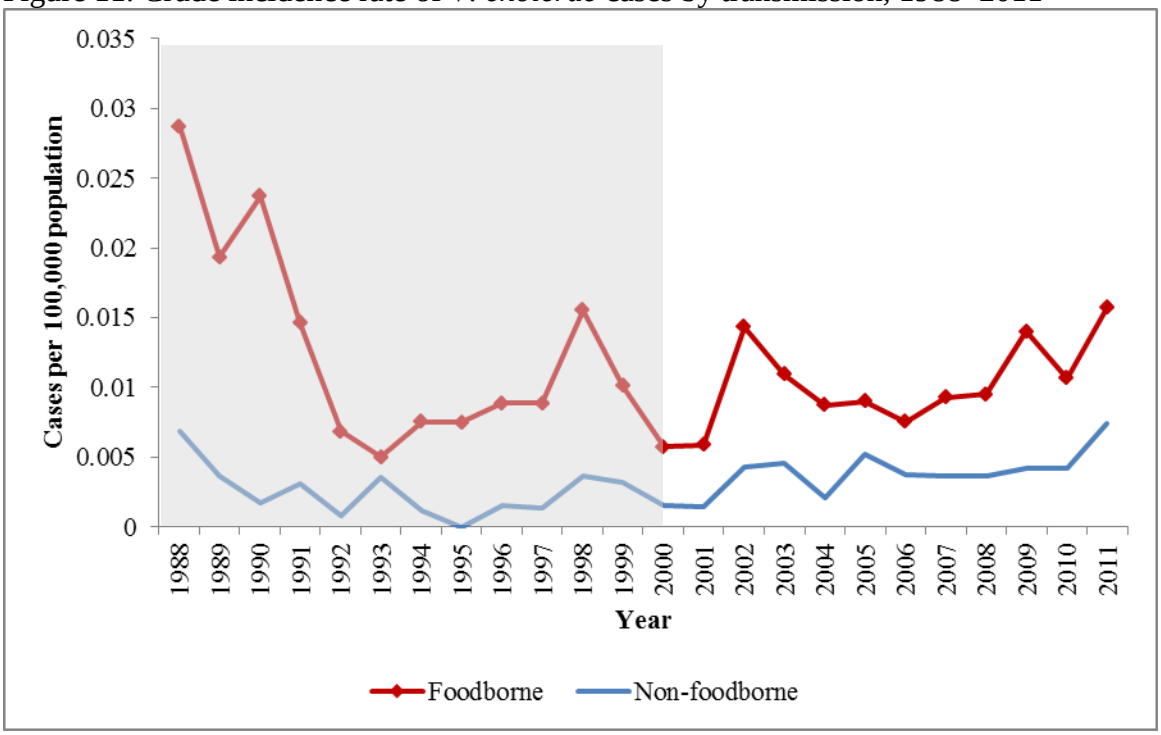


Figure 11. Crude incidence rate of *V. cholerae* cases by transmission, 1988–2011



Chapter V

DISCUSSION AND CONCLUSION

5.1 Discussion

Vibriosis is an important public health problem in the United States that affects an estimated 80,000 persons annually (4). *V. parahaemolyticus*, *V. vulnificus*, *V. alginolyticus*, and *V. cholerae* are the species most reported to COVIS and together contribute to 83.9% of the total reported cases. Between 1988 and 2012, 10,173 cases of these top four species and 4,026 hospitalizations and 795 deaths were reported to COVIS. Reporting of vibriosis has increased since 1988 when the Gulf Coast states first began surveillance for vibrios other than *V. cholerae* O1 and O139. In 1988 only 140 cases were reported from eight states. In 2012, 907 cases were reported from 42 states. Not only has the reporting population increased, incidence rates have also increased over time to 0.26 cases per 100,000 population in 2011.

This analysis showed that understanding differences of foodborne and non-foodborne transmission routes overall and among *Vibrio spp.* are important for characterizing epidemiological trends. Both routes play significant roles in infection in the United States (14, 21). All of the top four species are transmitted through both foodborne and non-foodborne routes, though for some species the proportion of infections transmitted through food may be much smaller than those transmitted through non-foodborne exposures. For example, foodborne *V. alginolyticus* represents only 7.8% of all *V. alginolyticus* cases, but 85.2% of cases are non-foodborne. Differences in

outcomes suggest that the foodborne transmission contributes to the highest burden of infection and deaths, but that non-foodborne infections should be considered equally as important (21). Incidence rates of foodborne infections are highest among all species reported to COVIS. In 2011, the crude rate of foodborne cases was 0.13 per 100,000 population. Rates of non-foodborne vibriosis were 0.10 per 100,000 population in 2011.

V. parahaemolyticus contributed the largest number of cases in COVIS (4,224). Gastroenteritis was the most commonly reported result of infection in *V. parahaemolyticus*, as seen in other studies (15). However, septicemia also occurred among patients (14, 15). Incidence rates of both foodborne and non-foodborne *V. parahaemolyticus* cases have been increasing. However, foodborne rates remained higher and were 0.075 per 100,000 population in 2011. High rates of *V. parahaemolyticus* have also been observed in FoodNet and among individual states (4, 13, 29).

Outbreaks may be a significant contributor to high rates of foodborne *V. parahaemolyticus* cases (26, 27) and may play an important role in the increase of vibriosis. The Foodborne Outbreak Online Database (FOOD) is a tool created for users to view information about outbreaks reported to the National Outbreak Reporting System (NORS) at CDC. The database shows that a number of outbreaks seafood-related happen annually in the United States; the majority of those outbreaks are attributed to *V. parahaemolyticus* (26). A single outbreak of *V. parahaemolyticus* linked to oysters from Oyster Bay Harbor in 2012, resulted in 28 cases from nine states. Prior to this outbreak the strain responsible had only been found in the Pacific Northwest (27). Reducing the number of infections from *V. parahaemolyticus* would have a strong effect on the

reduction of vibriosis overall. Prevention of foodborne cases should be of primary concern.

V. vulnificus was the second most common species reported to COVIS since 1988. *V. vulnificus* cases are the most severe and result in the highest number of hospitalizations and deaths (18, 20). Gulf coast oysters have been attributed to causing the majority of foodborne *V. vulnificus* infections and targeted prevention efforts have focused on reducing *V. vulnificus* in oysters (28). As a result, incidence rates may be less dramatic due to the use of post-harvest processing methods to reduce contamination of raw oysters in the seafood industry (24, 25). California has seen a significant reduction in infections and deaths as a result of restricting the sale of Gulf Coast oysters harvested between April 1 and October 31 (24). *V. vulnificus* cases had the largest number with unknown transmission route (n=514, 25.7%), possibly due to inability to correctly classify cases based on exposure (e.g., patients ate seafood and swam in the water). Therefore, prevention efforts to reduce *V. vulnificus* cases should be directed towards both foodborne and non-foodborne transmission because infections can be severe and deadly especially among patients with pre-existing conditions (18).

Incidence rates for non-foodborne *V. alginolyticus* cases have been increasing steadily and were 0.04 per 100,000 population in 2011. The majority of infections with *V. alginolyticus* resulted in skin and soft tissue infections, including otitis media (13, 21). For states like Florida, the season for water exposures is longer due warmer water and air temperatures putting higher numbers of persons at risk for infection (13). Patients were on average younger than those with infections from the other three species (21).

Consequently, the focus of *V. alginolyticus* prevention should be towards educating persons at risk and parents about water exposures, especially those with existing wounds.

V. cholerae was the species with the lowest number of cases reported. When categorized by transmission, more cases were foodborne (65.9%) and most cases presented with gastroenteritis. Previous research has shown that the case fatality rate of infection is high (2). However, it was observed in this thesis that *V. cholerae* cases had a high proportion of hospitalization (45.9%) but few (5.3%) resulted in death. This could be due to efforts to reduce contamination in shellfish targeted towards other species that also may have had an effect on the reduction of *V. cholerae*. The seasonality of *V. cholerae* infections differed compared to the other species; notably foodborne cases peaked in May. Incidence rates have remained steady. *V. cholerae* cases can be severe as indicated by the high number of hospitalizations prevention efforts should focus on reducing foodborne transmitted infections.

The information presented in this thesis describes the relationships between *Vibrio spp.*, transmission routes, and their role in incidence of vibriosis in the United States. The differences in incidence rates by transmission provide a clearer picture of the burden of illness. Most notably, the increasing rates among foodborne *V. parahaemolyticus* and non-foodborne *V. alginolyticus* cases. This thesis has also confirmed that accurately determining transmission route using specimen site and exposure data can be successful when data is available for each patient. Thus, signifying the importance for complete case report forms for accurate surveillance.

5.2 Study Limitations

There were several limitations to this thesis related to reporting. As with all passive surveillance systems, there is underreporting. Whether this is due to under-diagnosis or lack of clinical awareness of vibriosis is unknown. Persons with vibriosis may or may not seek medical attention. It is likely that only the most severe cases seek medical attention. Persons with gastrointestinal symptoms may not have a stool culture performed and thus will never be reported. Lack of healthcare provider awareness of the clinical presentation of vibriosis also may contribute to under-diagnosis, making the number of cases reported a fraction of what is actually occurring. Estimates of illness from the CDC corrected data for under-reporting and counts were doubled to account for under-diagnosis of infections to address this issue (4).

Reporting rates for vibriosis have varied over time. In the initial years of surveillance, reporting varied by state. Since 2007, when reporting for vibriosis became nationally notifiable, it is assumed that states reporting no cases did not have any laboratory-confirmed cases. It is difficult to determine whether some cases are not being diagnosed and reported or whether cases are just not occurring in certain states before 2007. It is also difficult to determine before their first reported cases what the true burden of illness was for those states that started reporting later. It is also possible that there is differential diagnostic suspicion by state. For instance, awareness of the impact of vibriosis in their population may be greater in coastal states.

Incomplete data was another limitation to this thesis. The absence of information on the case report form can significantly affect data. Forms may be incomplete or patients

lost to follow-up and unavailable for interview. Some data are especially important for understanding of vibriosis (e.g., information on pre-existing conditions, where seafood was consumed, and location of skin exposure). Incomplete data also made it difficult to categorize cases by transmission and contributed to a higher rate of cases with unknown transmission. Inability to validate exposure or specimen site categories can lead to misclassification of transmission route and is a weakness of the data.

5.4 Conclusion

Vibriosis is a significant public health problem and reported infections are increasing. Outcomes associated with vibriosis are an indicator of importance for reducing the burden of illness in the United States. Transmission routes are central to understanding trends in infection and for directing prevention efforts.

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