Epidemiologic Summary of Shiga Toxin-producing *Escherichia coli* (STEC) Infections and Hemolytic Uremic Syndrome (HUS) in California, 2013 - 2019

Key Findings

Shiga toxin-producing *E. coli* (STEC) infection is caused by certain *E. coli* bacteria that live in the intestines and feces (poop) of many animals, especially farm animals such as cows and goats. STEC bacteria make toxins that can make people very sick with bloody diarrhea, stomach cramps, vomiting, and fever. Some people with STEC infection can develop hemolytic uremic syndrome (HUS), which is a blood disorder that includes damage to the kidneys and can be deadly. Young children and older adults are more likely to get very sick with STEC and HUS. People can get infected with STEC in many ways, such as by eating or drinking something that has been contaminated with animal poop, and having contact with infected animals, animal areas, or other people infected with STEC.

STEC and HUS in California from 2013 through 2019

Total Cases: There were a total of 9,489 new STEC cases and 398 HUS cases from 2013 through 2019. This is an average of 1,356 STEC and 57 HUS cases each year.

Rate: The average annual rate of new STEC cases during 2013-2019 was about 4 cases per 100,000 people in California. The average annual rate of new HUS cases was less than 1 case per 100,000 people. Annual rates of both STEC and HUS in California increased over time.

- **By County**: Of the 36 counties that had at least one STEC case each year, Marin (about 10 cases per 100,000 people), Glenn (9 cases per 100,000 people), and Sonoma (about 7 cases per 100,000 people) had the highest average rates. Of the 4 counties that had at least one HUS case each year, Sacramento and Alameda (both with less than 1 case per 100,000 people) had the highest average rates.
- **By Sex:** The average rate of STEC was higher in females (about 4 cases per 100,000 people) than in males (about 3 cases per 100,000 people). The average rate of HUS for both females and males was less than 1 case per 100,000 people, but females made up almost 60% of all new HUS cases.
- **By Age Group**: The average rates of STEC were highest in children aged 1 to 4 years (about 16 cases per 100,000 people in this age group) and children aged less than 1 year (about 8 cases per 100,000 people in this age group). Nearly 70% of HUS cases were in children aged 12 years and younger. The average annual rates of HUS were highest in children aged 1 to 4 years (about 1 case per 100,000 people in this age group) and 5 to 14 years (less than 1 case per 100,000 people in this age group).
- **By Race/Ethnicity**: For cases where race and ethnicity information was available, the highest percentage of both STEC and HUS cases was in people who reported non-Hispanic White race/ethnicity (about 45% for STEC and about 56% for HUS).

To help prevent STEC infections and HUS, people should follow food safety guidelines when preparing food, especially by cooking food to the right temperature and refrigerating food right away to prevent bacteria from growing. It is also important for people to wash their hands with

soap and water before preparing or eating food, after using the toilet or changing a diaper, and after touching animals (especially farm animals) or being in areas where animals live. People should also avoid swallowing water when swimming or playing in rivers, lakes, and pools because STEC bacteria can also be in untreated water.

For more information about STEC in California, please visit the CDPH STEC webpage. For details about key infectious diseases in California, please visit the CDPH Surveillance and Statistics Section webpage.

Background

Shiga toxin-producing *Escherichia coli* (STEC) are important enteric bacterial pathogens in the United States, causing an estimated 265,000 infections, 3,600 hospitalizations, and 30 deaths each year. In 2019, the overall U.S. incidence rate of STEC infection was 5.2 new cases per 100,000 population.[1]

STEC produce Shiga toxin 1 and/or Shiga toxin 2, potent toxins responsible for many of the pathogenic effects of STEC infection. The most widely recognized serogroup among STEC is STEC O157, which causes an estimated 95,000 infections in the U.S. annually. However, numerous other STEC serogroups, which are often grouped together as STEC non-O157, may cause illness similar to O157 and account for an estimated 170,000 infections nationwide each year.[2, 3] The six most common non-O157 serogroups in the U.S. are O26, O103, O111, O121, O145, and O45.[4] The national *Healthy People 2020* target objective for STEC O157 infections was to have an incidence rate lower than 0.6 cases per 100,000 population.[5]

STEC commonly colonize the intestines of ruminant animals, including cows, deer, sheep, pigs, and goats. STEC is transmitted by exposure to the feces of a shedding animal or infected human. Raw and improperly cooked or handled foods of animal origin such as beef and dairy products are the most common sources of STEC infection, but transmission has also occurred through the consumption of contaminated produce such as lettuce and other leafy greens. Illness can also result from waterborne transmission by ingesting contaminated water (e.g., through swimming in a lake), direct contact with shedding animals or their contaminated environments (e.g., through a farm or petting zoo), or direct exposure to infected people or their personal items.[3, 6]

Acute illness, usually gastroenteritis, typically occurs after an incubation period of 3 to 4 days but may occur anywhere from 1 to 10 days after exposure. Illness may be more severe in young children and older patients. Overall, STEC O157 appears to be more likely to cause severe illness than STEC non-O157, though illness severity is also affected by the virulence characteristics of the infecting strain.[3] About 5-10% of STEC case-patients develop hemolytic uremic syndrome (HUS), a potentially life-threatening complication of a STEC infection. HUS is a disease characterized by hemolytic anemia, acute kidney failure, and often a low platelet count, and is the leading cause of short-term acute renal failure in U.S. children.[7] Progression to HUS occurs on average 7 days after symptom onset, and may be delayed until after the STEC infection has cleared.[3] Most cases of HUS are caused by STEC O157, but STEC non-O157 can also cause HUS.[8] For surveillance purposes, post-diarrheal HUS cases without laboratory evidence of an STEC infection are presumed to be related to an undetected STEC infection. The national *Healthy People 2020* target objective for HUS was to have an incidence rate lower than 1 case per 100,000 children aged less than 5 years.[5]

This report describes the epidemiology of confirmed and probable STEC infections in California from 2013 through 2019. The epidemiology of HUS from 2013 through 2019 is also described, including HUS cases in which STEC was identified and post-diarrheal HUS cases without laboratory evidence of an STEC infection. Due to multiple factors that can contribute to underreporting, data in this report are likely underestimates of actual disease incidence. For a complete discussion of the definitions, methods, and limitations associated with this report, please refer to the *Technical Notes*.[9] The epidemiologic description of STEC and HUS for earlier surveillance periods can be found in the *Epidemiologic Summary of Shiga toxin-producing Escherichia coli (STEC) Infections and Hemolytic Uremic Syndrome (HUS) in California, 2001-2008 and 2009-2012*.[10, 11]

California Reporting Requirements and Surveillance Case Definitions

California Code of Regulations (CCR), Title 17, Section 2500 requires health care providers to report suspected cases of STEC infection to their local health department (LHD) within one working day of identification or immediately by telephone if an outbreak of STEC or case of post-diarrheal HUS is suspected.[12] Per CCR, Title 17, Section 2505, laboratories are required to report laboratory testing results suggestive of STEC infection to either the California Reportable Disease Information Exchange (CalREDIE) via electronic laboratory reporting or the LHD; reporting must occur within one working day after the health care provider has been notified.[13] Also per CCR, Title 17, Section 2505, STEC isolates, including O157 and non-O157 strains, or Shiga toxin-positive fecal broths, must be submitted to a local public health laboratory or California Department of Public Health (CDPH) Microbial Diseases Laboratory for serotyping and molecular subtyping.[14]

California regulations require cases of STEC infection and post-diarrheal HUS to be reported to CDPH. CDPH counted cases that satisfied the U.S. Centers for Disease Control and Prevention/Council of State and Territorial Epidemiologists surveillance case definition (per year of case onset) of a confirmed or probable case.[15, 16]

During the surveillance period (2013-2019), the case definition of an STEC infection was as follows:

- A confirmed case of STEC was defined as an illness with laboratory-confirmed infection with STEC or *E. coli* O157:H7. Serotype O157:H7 isolates were assumed to be Shiga toxin-producing, while for all other serotypes, evidence of toxin production or the presence of Shiga toxin genes was required.
- From 2013 through 2017, a probable case of STEC was defined as an illness with laboratory-confirmed infection with *E. coli* O157 without confirmation of H7 antigen or Shiga toxin production; or as a clinically compatible case that either was epidemiologically linked to a confirmed or probable case or was a member of a defined risk group during an outbreak; or had an elevated antibody titer to a known STEC serotype. Beginning in 2018, a probable case of STEC could also be defined as an illness with detection via culture-independent diagnostic testing (CIDT) of Shiga toxin or Shiga toxin genes in the absence of *Shigella* isolation; or with detection via CIDT of *E. coli* O157, STEC, or Enterohemorrhagic *E. coli* (EHEC).

During the surveillance period (2013-2019), the case definition of HUS was as follows:

- A confirmed case of HUS was defined as an illness with anemia with microangiopathic changes and renal injury that began within three weeks of onset of acute or bloody diarrhea.
- A probable case of HUS was defined as an illness with laboratory evidence of HUS but an unclear history of diarrhea; or as an illness that met all criteria for a confirmed case but did not have confirmed microangiopathic changes.

Epidemiology of STEC Infections and HUS in California, 2013-2019

STEC Infections

CDPH received reports of 9,489 cases of STEC infection with estimated symptom onset dates from 2013 through 2019. This corresponds to an average of 1,355.6 cases per year and an average annual incidence rate of 3.5 cases per 100,000 population. Overall, annual incidence rates increased by 318.8%, from 1.6 per 100,000 (631 cases) in 2013 to 6.7 per 100,000 (2,680 cases) in 2019, with large increases during 2018-2019 [Figure 1]. A total of 2,839 (29.9%) STEC case-patients were hospitalized. Deaths were reported for 33 (0.3%) STEC case-patients by the time of case report; of these 33 STEC patients, 13 (39.4%) had infections that had progressed to HUS.

There were 36 California counties in which at least one case of STEC infection occurred every year during 2013-2019. Of these counties, Marin (9.6 per 100,000; 175 cases), Glenn (9.0 per 100,000; 18 cases), Sonoma (7.4 per 100,000, 260 cases), Placer (6.5 per 100,000, 172 cases), and Santa Clara (6.1 per 100,000, 826 cases) had the highest average annual incidence rates. Los Angeles County had the highest number of STEC cases during the surveillance period with 1,823 total cases and an average annual incidence rate of 2.6 per 100,000 population [Figure 2]. By region (see *Technical Notes*), average incidence rates were twice as high in Northern California (4.8 per 100,000; 5,757 cases) than in Southern California (2.4 per 100,000; 3,732 cases).

From 2013 through 2019, the average annual incidence rate was higher among females (3.6 per 100,000; 4,965 cases) than among males (3.3 per 100,000; 4,515 cases); 52.4% of STEC case-patients were female and 47.6% were male.

Average annual incidence rates for STEC infection during the surveillance period were highest among children aged 1 to 4 years (15.8 per 100,000; 2,186 cases) and children less than 1 year (7.5 per 100,000; 255 cases). The marked increase in STEC infections in 2018 and 2019 was reflected in higher incidence rates in most age groups during those two years [Figure 3].

For STEC cases with complete race/ethnicity information (see *Technical Notes*), cases reported non-Hispanic White race/ethnicity (45.3%) more frequently and non-Hispanic Asian/Pacific Islander race/ethnicity (8.2%) less frequently than would be expected compared to the percentage of these groups in California during the same time period (38.0% and 14.8%, respectively) [Figure 4].

Of all STEC infections during 2013-2019, laboratory stool culture identified a serogroup for 6,655 (70.1%) cases; of these 6,655 cases, 37.1% were STEC O157 (average annual rate of 0.9 per 100,000; 2,468 cases) and 62.9% were STEC non-O157 (average annual rate of 1.5 per 100,000; 4,187 cases) serogroups. STEC O157 yearly incidence rates remained fairly

stable during the surveillance period [Figure 5]. Yearly incidence rates of STEC non-O157 serogroup infections increased by 228.6% from 2013 (0.7 per 100,000; 267 cases) through 2019 (2.3 per 100,000; 924 cases). The most common STEC non-O157 serogroups identified were O26, O111, and O103. Of the 2,834 STEC cases for which a serogroup was not identified by a laboratory stool culture, 89.9% (2,549) occurred in 2018-2019.

Each year during 2013 through 2019, the incidence rate of STEC O157 was greater than the national *Healthy People 2020* target objective of 0.6 cases per 100,000 population. There was no *Healthy People 2020* target objective for STEC non-O157.

A total of 339 (3.6%) STEC infections progressed to HUS by the time of case report [Figure 6]. Of 2,441 STEC case-patients aged less than 5 years,158 (6.5%) developed HUS (not shown).

HUS

CDPH received reports of 398 patients with HUS with estimated symptom onset dates from 2013 through 2019. This corresponds to an average of 56.9 cases per year and an average annual incidence rate of 0.14 cases per 100,000 population in California. Overall, yearly incidence rates increased by 13.7% from 2013 through 2019 [Figure 7]. A total of 380 (95.5%) HUS case-patients were reported to be hospitalized. Deaths were reported for 17 (4.3%) HUS case-patients by the time of case report.

Of HUS diagnoses, the majority, 327 cases (82.2%), were associated with an STEC infection; 242 (74.0%) of the 327 cases were associated with an STEC O157 infection. The remaining 71 (17.8%) HUS case-patients did not have laboratory evidence of an STEC infection [Figure 6].

There were 4 counties in which at least one HUS case occurred each year during 2013 through 2019: Sacramento, Alameda, San Diego, and Los Angeles. Of these counties, Sacramento (0.2 per 100,000; 23 cases) and Alameda (0.2 per 100,000; 21 cases) had the highest rates of HUS. By region (see *Technical Notes*), the average annual incidence rate for HUS for the surveillance period was 4.2 times higher in Northern California (0.3 per 100,000; 298 cases) than in Southern California (0.1 per 100,000; 100 cases) [Figure 8].

From 2013 through 2019, the average annual incidence rate of HUS was higher among females (0.2 per 100,000; 234 cases) than among males (0.1 per 100,000; 164 cases); 58.8% of HUS case-patients were female and 41.2% were male.

Of total HUS cases, 69.3% were among children aged 12 years and under. Average annual HUS incidence rates were highest among children aged 1 to 4 years (1.3 per 100,000; 180 cases) and children aged 5 to 14 years (0.3 per 100,000; 99 cases). Only in 2015 (0.8 per 100,000; 21 cases) was the incidence rate in children aged less than 5 years lower than the national *Healthy People 2020* target objective of 1 case per 100,000 population in this age group.

For HUS cases with complete race/ethnicity information (see *Technical Notes*), cases reported non-Hispanic White race/ethnicity (55.6%) much more frequently than would be expected compared to the percentage of this group in California during the same time period (38.0%) [Figure 9].

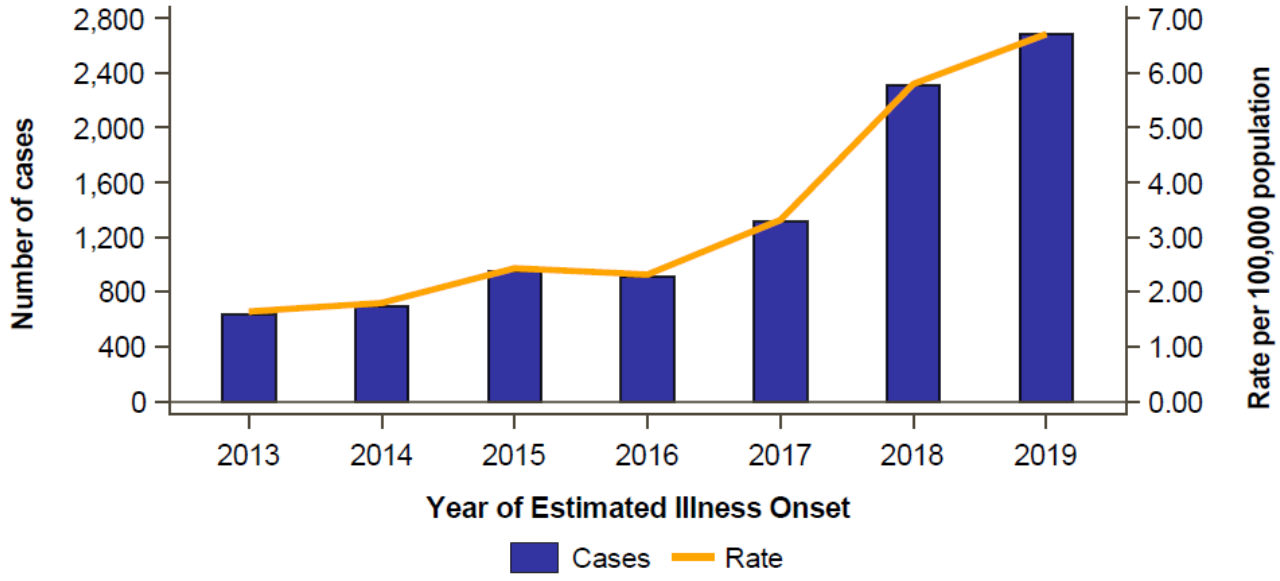
STEC Outbreaks

From 2013 through 2019, there were 49 foodborne outbreaks of STEC involving more than 664 California case-patients; the greatest number of outbreaks occurred in 2018 with 13 (26.5%). Thirty-four (69.4%) outbreaks were caused by STEC O157, 12 (24.5%) outbreaks were caused by STEC non-O157, and 3 (6.1%) outbreaks involved case-patients infected with both STEC O157 and non-O157. STEC O26 was the most common STEC non-O157 serogroup involved in outbreaks. Thirty-six (73.5%) outbreaks involved patients exposed in multiple states[17] and were primarily due to widely distributed food products.

Some notable multi-state STEC outbreaks involving California residents that led to food recalls included: 2018 and 2019 STEC O157 outbreaks associated with romaine lettuce (210 cases in the U.S., with 49 from California in 2018; 167 cases in U.S., with 8 from California in 2019); a 2017 STEC O157 outbreak associated with I.M. Healthy brand SoyNut Butter (32 cases in U.S., with 5 from California), and a 2016 outbreak of both STEC O121 and O26 associated with General Mills flour (63 cases in U.S., with 3 from California). There were also multi-state STEC outbreaks linked to other foods including sprouts, beef, and other leafy greens.

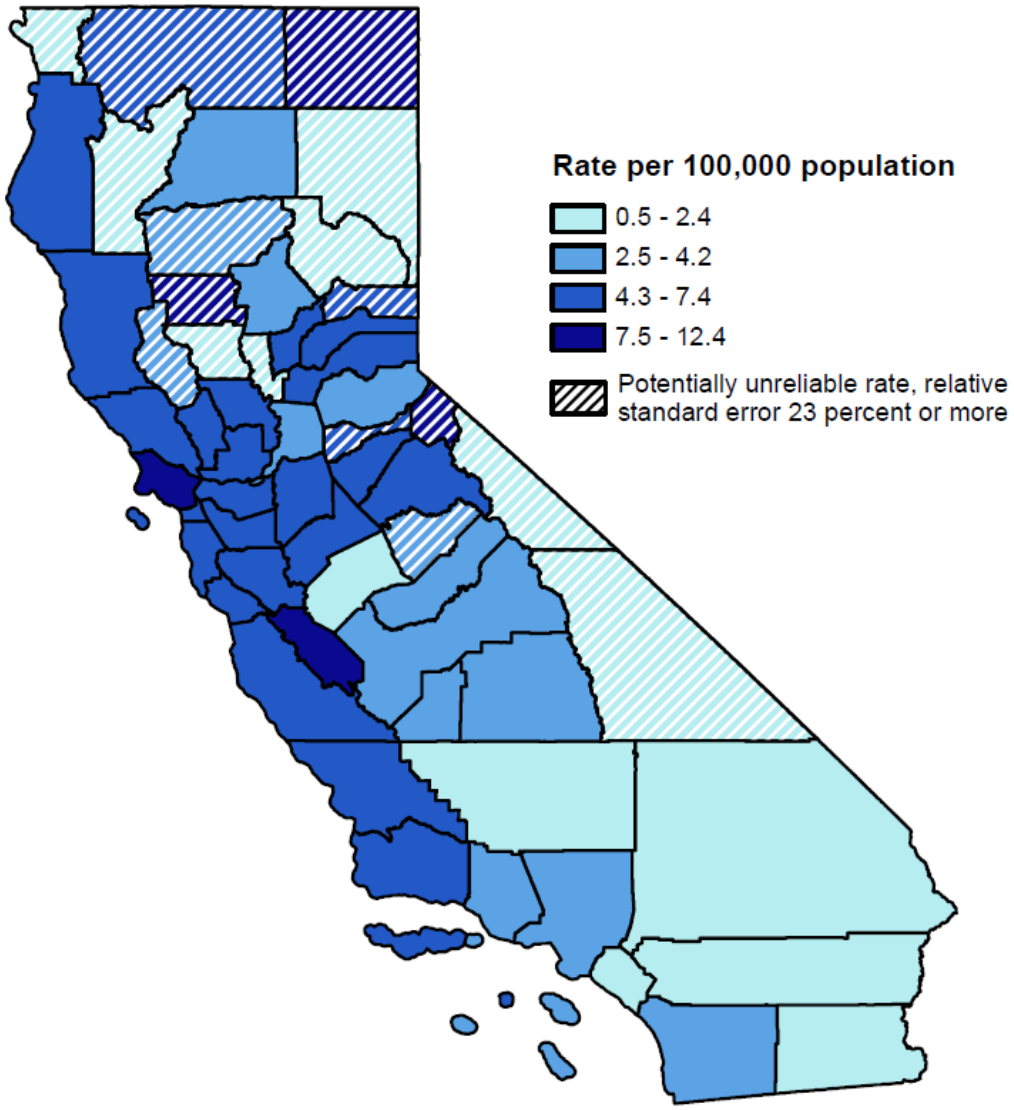
The largest STEC outbreak within California, which involved both STEC O157 and O26 infections, occurred in 2017 and involved 244 recruits at a Marine Corps Recruit Depot in San Diego. Thirty case-patients were hospitalized and 15 had HUS.[17, 18]

Figure 1. Shiga Toxin-producing *E. coli* (STEC) Cases and Incidence Rates by Year of Estimated Illness Onset, California, 2013-2019 *



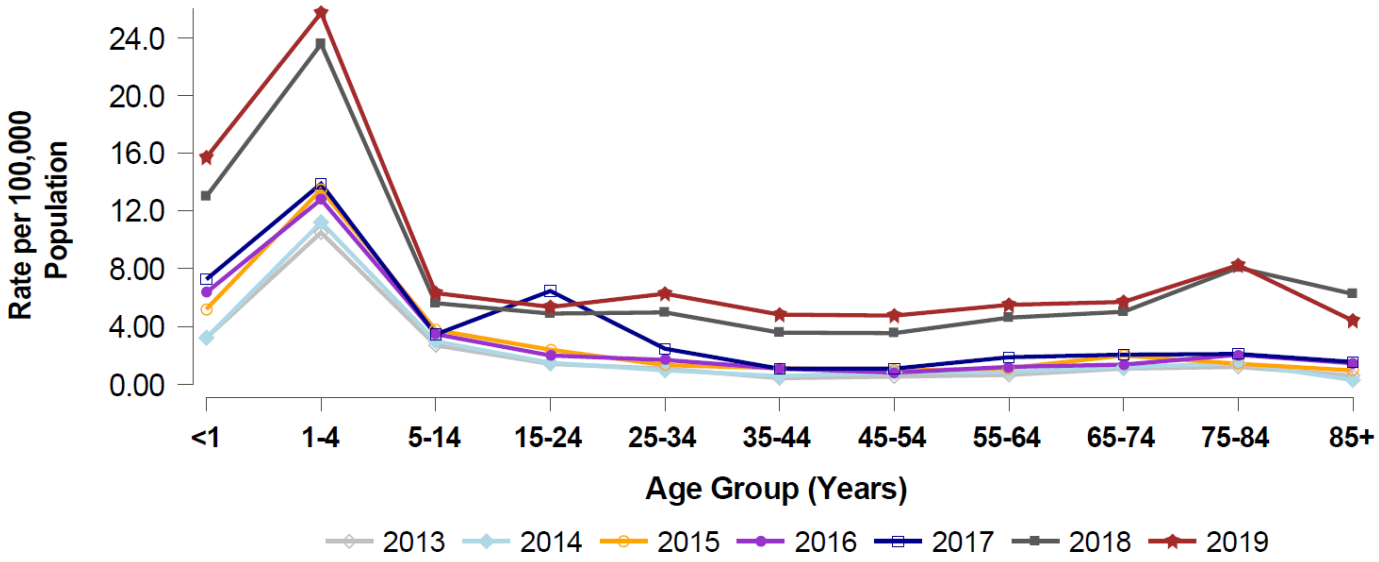
*Includes all reported cases of STEC, both with and without hemolytic uremic syndrome (HUS).

Figure 2. Shiga Toxin-producing *E. coli* (STEC) Average Annual Incidence Rates by County, California, 2013-2019 *



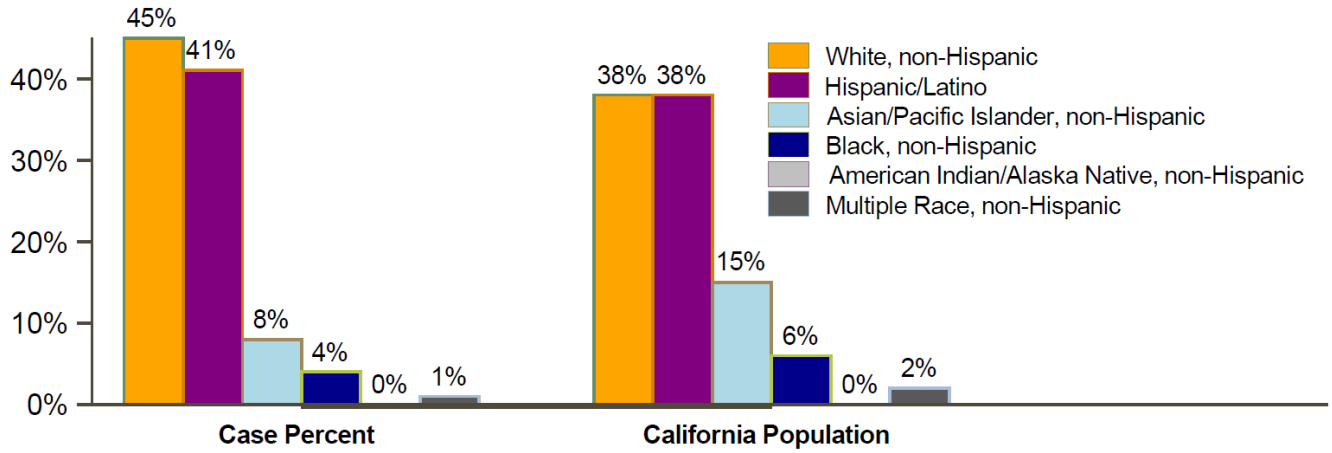
*Includes all reported cases of STEC, both with and without hemolytic uremic syndrome (HUS).

Figure 3. Shiga Toxin-producing *E. coli* (STEC) Incidence Rates by Age Group and Year of Estimated Illness Onset, California, 2013-2019 *



*Includes all reported cases of STEC, both with and without hemolytic uremic syndrome (HUS).

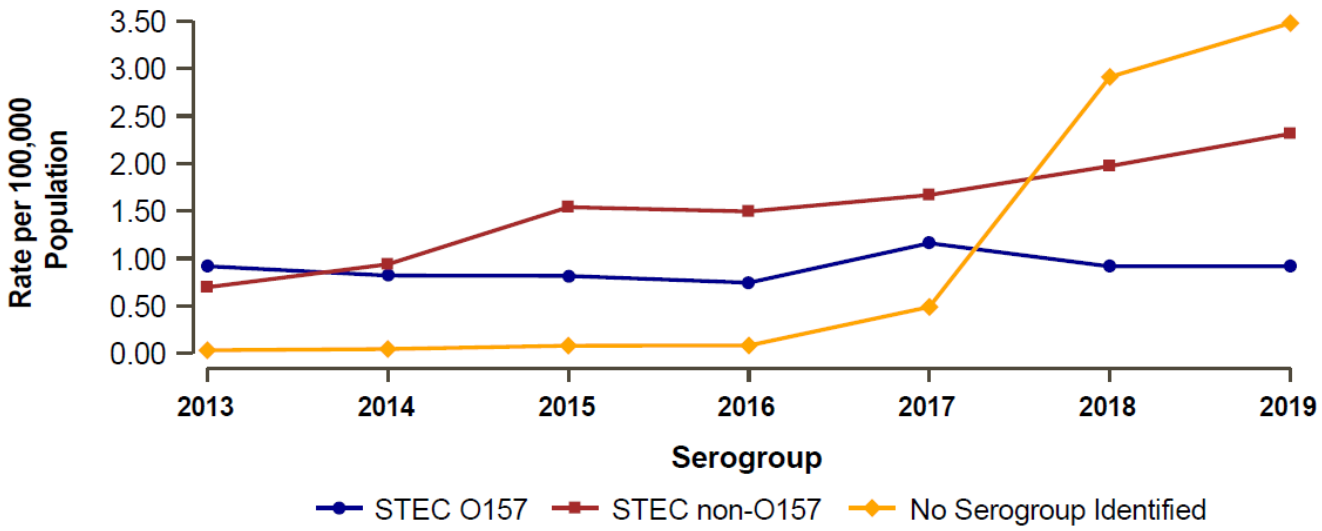
Figure 4. Shiga Toxin-producing *E. coli* (STEC) Cases and Population by Race/Ethnicity, California, 2013-2019 *



16.3% (n=1545) of reported incidents of Shiga toxin-producing E. coli (STEC) did not identify race/ethnicity and 4.4% (n=421) of incidents identified as 'Other' race/ethnicity and are not included in the Case Percent calculation. Information presented with a large percentage of missing data should be interpreted with caution.

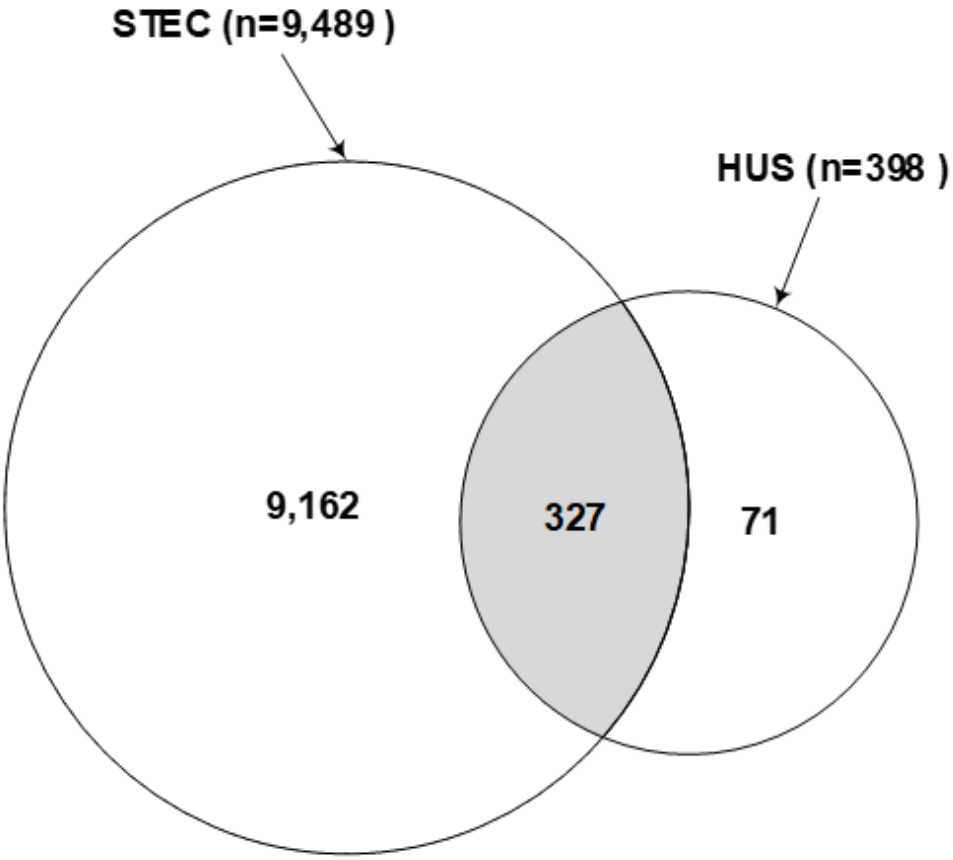
*Includes all reported cases of STEC, both with and without hemolytic uremic syndrome (HUS).

Figure 5. Shiga Toxin-producing *E. coli* (STEC) Incidence Rates by Serogroup and Year of Estimated Illness Onset, California, 2013-2019 *



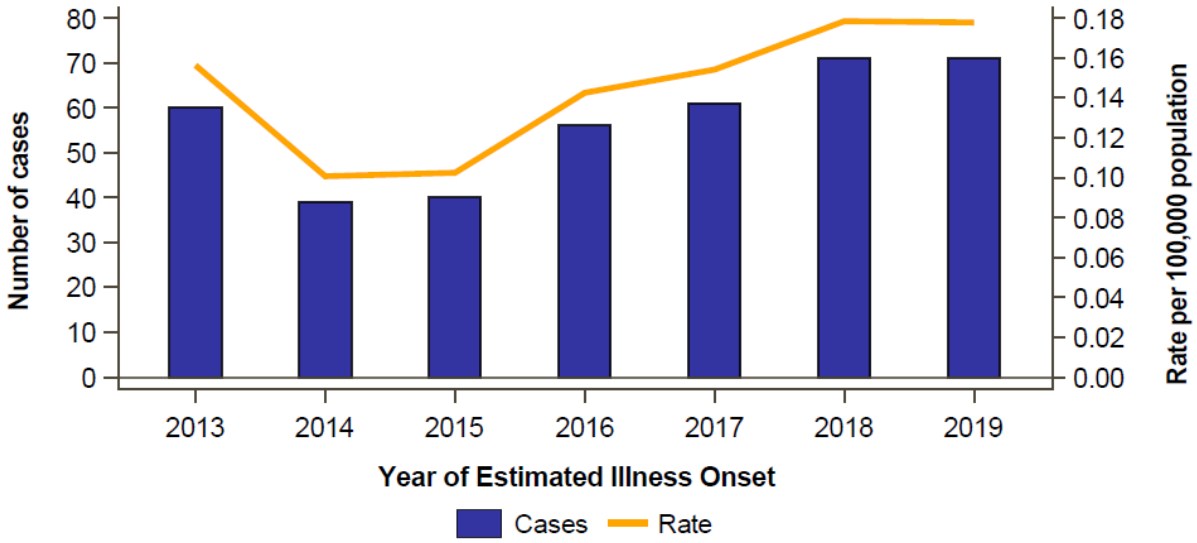
*'STEC O157' and 'STEC non-O157' include reported cases of STEC for which a laboratory (stool) culture identified a STEC serogroup. 'No Serogroup Identified' includes STEC cases that either were not cultured, or the culture did not identify an STEC serogroup. Beginning in 2018, reported probable STEC cases included those identified via culture-independent diagnostic test (CIDT).

Figure 6. Venn Diagram of California Cases of Shiga Toxin-producing *E. coli* (STEC) Infection and Hemolytic Uremic Syndrome (HUS), 2013-2019 *



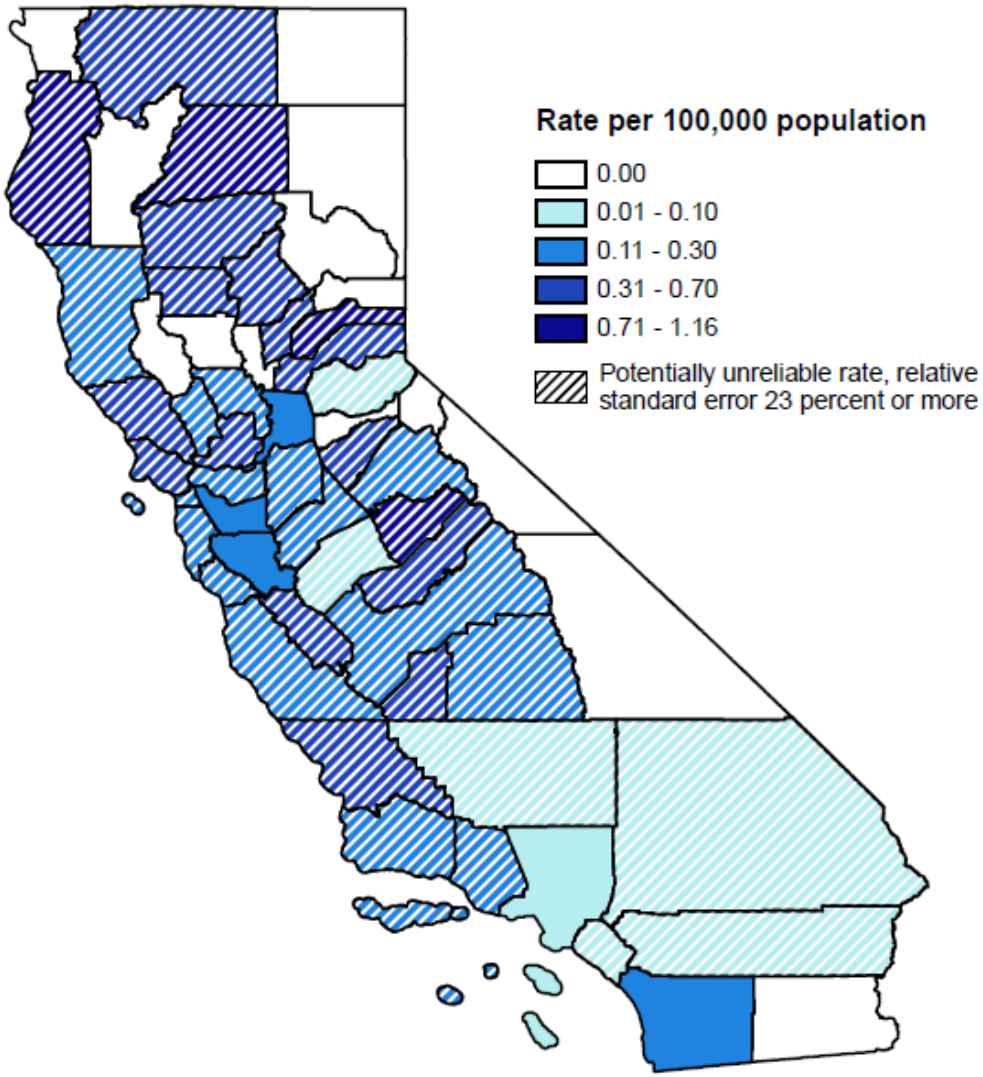
* Drawing not to scale

Figure 7. Hemolytic Uremic Syndrome (HUS) Cases and Incidence Rates by Year of Estimated Illness Onset, California, 2013-2019 *



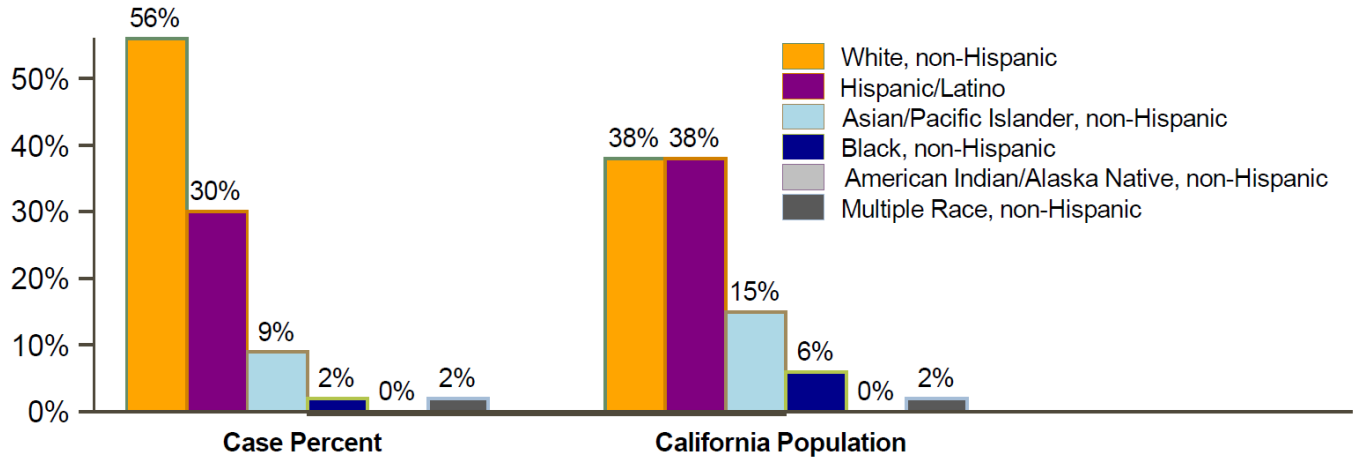
*Includes all reported cases of HUS, both with and without evidence of Shiga toxin-producing *E. coli* (STEC).

Figure 8. Hemolytic Uremic Syndrome (HUS) Average Annual Incidence Rates by County, California, 2013-2019 *



*Includes all reported cases of HUS, both with and without evidence of Shiga toxin-producing *E. coli* (STEC).

Figure 9. Hemolytic Uremic Syndrome (HUS) Cases and Population by Race/Ethnicity, California, 2013-2019 *



14.1% (n=56) of reported incidents of Hemolytic Uremic Syndrome (HUS) did not identify race/ethnicity and 5.5% (n=22) of incidents identified as 'Other' race/ethnicity and are not included in the Case Percent calculation. Information presented with a large percentage of missing data should be interpreted with caution.

*Includes all reported cases of HUS, both with and without evidence of Shiga toxin-producing *E. coli* (STEC).

Comments

From 2013 through 2019, incidence rates of reported STEC infection in California increased more than four-fold, most of the increase in 2018 and 2019. The statewide average annual incidence rate of STEC infection during 2013-2019 (3.5 per 100,000 population) was similar to that reported nationally.[2, 19, 20, 21, 22] Similarly, STEC incidence rates in the U.S. increased during 2018-2019.[2] The change in the surveillance case definition in 2018 for probable cases to include CIDT results likely contributed to the substantial rate increase during 2018-2019 in California STEC cases overall and STEC cases with no serogroup identified.

Reported infections caused specifically by STEC non-O157 serogroups also increased during recent years in both California and the U.S.[23, 24] This increase may be influenced by several factors, including increased use of Shiga toxin testing by clinical laboratories, growing awareness of reporting requirements for STEC non-O157, and increasing numbers of Shiga toxin-positive specimens forwarded to a public health laboratory for culture and identification. The rise in incidence may also be due to a true increase in STEC infections, due to yet undefined demographic and environmental risk factors.

HUS incidence rates in California were somewhat variable but increased slightly overall from 2013 to 2019, with an average incidence rate of 0.14 cases per 100,000. Fewer STEC infections progressed to HUS during 2013-2019 (3.6%) than did during the 2009-2012 surveillance period (nearly 10%).[11] As in the U.S. overall, the majority of post-diarrheal HUS diagnoses in California were associated with an STEC infection.[1, 7, 25] Also similar to national trends, California children aged 1 to 4 years experienced the highest rates of STEC infection, as well as of HUS.[2,19-22, 25]

In order to capture the burden of STEC infections in California and to develop a comprehensive public health response, it is crucial that clinical laboratories routinely test all stool specimens collected from patients with symptoms consistent with acute bacterial enteritis for the presence of Shiga toxin and attempt to culture STEC. Suspect STEC specimens must be sent to a public health laboratory for serogrouping and subtyping. Better adherence to these stool culture recommendations can improve surveillance estimates of O157 and non-O157 STEC infections and improve assessment of true disease burden in California.

Avoiding contamination and cross-contamination during the production and processing of foods, including beef and fresh fruits and vegetables, combined with consumer education may provide the best opportunities for preventing and controlling STEC infections and HUS. To help prevent STEC infections and HUS, persons should follow food safety guidelines when preparing food, especially by cooking food thoroughly and promptly refrigerating perishable food to inhibit bacterial growth. Persons should also wash their hands with soap and water before preparing or eating food, after using the toilet or changing a diaper, and after touching animals (especially farm animals) or being in animal environments. Persons should also avoid swallowing water when swimming or recreating in rivers, lakes, and pools because STEC bacteria can also be present in untreated water. Persons with STEC infections who develop symptoms of HUS, which can include decreased frequency of urination, fatigue, and pallor, should immediately consult their healthcare provider.

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