A Multistate Outbreak of *E Coli* O157: H7 Infections Linked to Soy Nut Butter

Rashida Hassan, MSPH,[a,b] Sharon Seelman, MS, MBA,[c] Vi Peralta, MPH,[d,k] Hillary Booth, MPH,[e] Mackenzie Tewell, MA, MPH, CPH,[f] Beth Melius, RN, MN, MPH,[g] Brooke Whitney, PhD,[c] Rosemary Sexton, BS,[c] Asha Dwarka, BS,[c] Duc Vugia, MD, MPH,[d,k] Jeff Vidanes, BS,[d,k] David Kiang, PhD,[d,k] Elysia Gonzales, RN, MPH,[h] Natasha Dowell, MPH,[a,i] Samantha M. Olson, MPH,[a,j] Lori M. Gladney, MS,[a] Michael A. Jhung, MD,[a] Karen P. Neil, MD, MSPH[a]

abstract

BACKGROUND: In 2017, we conducted a multistate investigation to determine the source of an outbreak of Shiga toxin-producing *Escherichia coli* (STEC) O157:H7 infections, which occurred primarily in children.

METHODS: We defined a case as infection with an outbreak strain of STEC O157:H7 with illness onset between January 1, 2017, and April 30, 2017. Case patients were interviewed to identify common exposures. Traceback and facility investigations were conducted; food samples were tested for STEC.

RESULTS: We identified 32 cases from 12 states. Twenty-six (81%) cases occurred in children <18 years old; 8 children developed hemolytic uremic syndrome. Twenty-five (78%) case patients ate the same brand of soy nut butter or attended facilities that served it. We identified 3 illness subclusters, including a child care center where person-to-person transmission may have occurred. Testing isolated an outbreak strain from 11 soy nut butter samples. Investigations identified violations of good manufacturing practices at the soy nut butter manufacturing facility with opportunities for product contamination, although the specific route of contamination was undetermined.

CONCLUSIONS: This investigation identified soy nut butter as the source of a multistate outbreak of STEC infections affecting mainly children. The ensuing recall of all soy nut butter products the facility manufactured, totaling >1.2 million lb, likely prevented additional illnesses. Prompt diagnosis of STEC infections and appropriate specimen collection aids in outbreak detection. Child care providers should follow appropriate hygiene practices to prevent secondary spread of enteric illness in child care settings. Firms should manufacture ready-to-eat foods in a manner that minimizes the risk of contamination.

[a]*Centers for Disease Control and Prevention, Atlanta, Georgia;* [b]*Caitta, Inc, Herndon, Virginia;* [c]*US Food and Drug Administration, College Park, Maryland;* [d]*California Department of Public Health, Sacramento, California;* [e]*Oregon Health Authority, Portland, Oregon;* [f]*Arizona Department of Health Services, Phoenix, Arizona;* [g]*Washington State Department of Health, Shoreline, Washington;* [h]*Public Health–Seattle and King County, Seattle, Washington;* [i]*Eagle Medical Services, Huntsville, Alabama;* [j]*G[2]S Corporation, San Antonio, Texas; and* [k]*California Department of Public Health, Richmond, California*

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

Ms Hassan developed the data collection instruments, coordinated the data collection, conducted the analysis, and drafted and revised the manuscript; Dr Neil reviewed and revised data collection instruments, supervised the coordination of data collection and analysis, and critically reviewed and revised the manuscript; Dr Jhung supervised the coordination of data collection and analysis and critically reviewed and revised the manuscript; Ms Peralta, Ms Booth, Ms Tewell, Ms Melius, Ms Gonzales, and Dr Vugia reviewed and revised data collection instruments, collected and interpreted epidemiological data, coordinated product sampling, and critically (Continued)

WHAT'S KNOWN ON THIS SUBJECT: Shiga toxin-producing *Escherichia coli* (STEC) O157 causes ~63 000 illnesses annually in the United States. The highest incidence is among young children, who are at higher risk of severe infection. Foodborne STEC outbreaks are often associated with beef and leafy greens.

WHAT THIS STUDY ADDS: We identified soy nut butter as the source of a multistate outbreak of STEC infections affecting mainly children. This outbreak highlights the risk of STEC infection among young children and the critical role health care providers play in outbreak detection.

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Shiga toxin-producing *Escherichia coli* (STEC) O157 is an important cause of foodborne illness in the United States, causing an estimated 63 000 illnesses, 2000 hospitalizations, and 20 deaths annually.[1] The highest incidence of laboratory-confirmed STEC O157 infection occurs in children <5 years old (3.72 infections per 100 000 people in 2015).[2] Symptoms include abdominal cramps and diarrhea, which frequently becomes bloody by the second or third day of illness.[3] Symptoms typically begin 3 to 4 days after infection and last 6 to 8 days.[3,4] Approximately 5% to 10% of STEC infections are complicated by hemolytic uremic syndrome (HUS), which is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure.[3–6] HUS usually occurs 1 week after symptom onset, when diarrhea is improving.[7] Among children <5 years old infected with STEC O157, ~15% develop HUS.[6] Foodborne STEC O157 outbreaks have previously been associated with undercooked beef, raw produce (such as leafy vegetables and sprouts), unpasteurized dairy and cider products, deli meats, raw dough, and dough mix.[8–11]

Peanut allergies have increased among US children over the past decades, leading some child care centers and schools to implement peanut-free policies.[12,13] In a 2014 survey, 36% of school districts banned foods because of allergies, and 97% of these districts specifically banned peanuts.[13] Consequently, peanut butter alternatives have gained popularity in the United States because parents and caregivers seek safe alternatives for their children.[14,15] Peanut butter substitutes include spreads made from tree nuts (such as almonds, pistachios, walnuts, and pecans) and nut alternatives (such as sunflower seeds, sesame seeds, and soy beans).[14,15]

In this article, we report findings from a rapid and collaborative investigation that identified a novel food vehicle, soy nut butter, as the source of a multistate foodborne illness outbreak, which mainly affected young children.

State public health laboratories throughout the United States routinely perform molecular-based subtyping of clinical isolates using pulsed-field gel electrophoresis (PFGE).[16,17] Clinical isolates are obtained when clinicians order laboratory testing as part of a patient's diagnostic evaluation. PFGE patterns are uploaded by participating laboratories to PulseNet, the national molecular subtyping network for foodborne disease surveillance. The Centers for Disease Control and Prevention (CDC) PulseNet team detects potential multistate outbreaks of STEC and other enteric bacteria by identifying clusters of uploaded isolates with indistinguishable patterns, which are more likely to be from a common source. These clusters are referred to epidemiologists for investigation to determine if the illnesses are linked to a common vehicle.

On February 17, 2017, PulseNet detected 7 *E coli* O157:H7 infections in Arizona, California, Maryland, and New Jersey with an indistinguishable PFGE *Xbal-Blnl* restriction enzyme pattern combination that had not been previously seen in the PulseNet database. Local and state health departments, the CDC, and the US Food and Drug Administration (FDA) initiated an investigation to determine the source of the outbreak and prevent additional illnesses.

METHODS

Case Definition and Case Finding

During the investigation, 2 STEC O157 infections with similar PFGE *Xbal-Blnl* pattern combinations were identified and added to the outbreak on the basis of whole-genome sequencing (WGS) showing that isolates were closely related to those in the initial cluster and an epidemiological link to the suspected vehicle. We defined an outbreak-associated case as infection with 1 of 3 *E coli* O157:H7 PFGE *Xbal-Blnl* pattern combinations constituting the outbreak strains in a person with illness onset between January 1, 2017, and April 30, 2017. We used PulseNet throughout the investigation to identify additional cases.

Epidemiological Investigation

Local and state health departments interviewed case patients or their proxies (eg, parents, guardians, or caregivers) with state-specific enteric disease questionnaires or a modified version of the National Hypothesis Generating Questionnaire (NHGQ). The NHGQ includes questions on >300 food and animal exposures in the week before illness, including fresh produce, meats, dairy products, and processed foods.[18] After early interviews narrowed the list of potential exposures, investigators interviewed case patients with a focused questionnaire, which included detailed questions on suspected foods. Investigators attempted to identify illness subclusters, in which 2 or more unrelated case patients had exposure to the same location or venue before illness, such as a child care center or restaurant, to narrow the scope of suspected foods.

Product Traceback and Facility Investigations

Local, state, and FDA investigators conducted a traceback investigation of the suspected product and its ingredients through the distribution chain to determine if there was a common source. Local and state investigators collected food menus from child care centers and other institutions attended by case patients to identify foods in common. The FDA conducted inspections at firms of

interest, including the brand headquarters, contract manufacturing facilities, and ingredient suppliers. Product lot codes and best-by dates were used to identify common lots of interest.

Product Testing and Laboratory Investigations

State public health laboratories subtyped clinical STEC O157 isolates using standard PFGE methodology.[16,17] Local and state health departments collected opened, leftover products from case patient homes and child care centers and unopened products from retail locations. The FDA collected finished-product and ingredient samples during facility inspections. State public health and FDA laboratories tested food samples for STEC. STEC isolates were subtyped by PFGE.[16] Selected food and clinical isolates underwent WGS to further characterize genetic relatedness.[19–21]

RESULTS

Outbreak Description

We identified 32 cases from 12 states (Fig 1). Illness onset dates ranged from January 4, 2017, to April 18, 2017 (Fig 2). Case patients were 41% female, and ages ranged from 1 to 70 years (median: 9). Twenty-six (81%) case patients were children <18 years old, including 11 (34%) who were <5 years old. Twelve (38%) hospitalizations and no deaths were reported. Nine (28%) case patients developed HUS; of these, 8 (89%) were children <18 years old, including 3 (33%) children <5 years old.

Epidemiological Investigation

Among 9 case patients interviewed with state-specific questionnaires by February 23, 2017, 6 (67%) ate leafy greens, 5 (56%) ate ground beef, and 2 (22%) ate different prepackaged smoothies. Five (56%) case patients ate foods purchased from natural and/or health food stores. One case patient noted regularly eating soy-based, dairy-alternative products.

On February 28, 2017, California investigators noted 1 case patient, on reinterview with the modified NHGQ, reported eating Brand A soy nut butter. The next day, on reinterview, 2 additional case patients from California and Maryland reported eating Brand A soy nut butter, and investigators discovered through review of menus that all 4 Arizona case patients attended 2 child care centers that served Brand A soy nut butter and granola coated in soy nut butter.

In total, we identified 3 illness subclusters. One subcluster consisted of three 2-year-old children who attended the same Arizona child care center that served Brand A soy nut butter and soy nut butter–coated granola. Specific food consumption histories for these children were not available. Another subcluster consisted of 2 adults who attended the same residential institution in Oregon that served Brand A soy nut butter; 1 case patient reported eating soy nut butter while at the facility, and the other was unable to be reached for interview.

The third illness subcluster occurred at an Oregon child care center and included 6 children aged 1 to 2 years and 1 adult teacher; all attended or worked in the same classroom. Six illnesses began between March 2, 2017, and March 5, 2017, but 1 began >1 week later, on March 13, 2017. Although the child care center did not serve soy nut butter, 1 child ate Brand A soy nut butter at home and often brought it to the classroom for lunch; this child was the first in this subcluster to become ill. None of the remaining 6 case patients or their proxies reported exposure to soy nut butter at home. Although lunch seating was unassigned, 5 of the ill children, including the child who often brought soy nut butter for lunch, often ate at the same table with another child who did not become ill. The sixth ill child ate at a neighboring table. Each table had a compost bucket in which children put leftover foods, and 2 children who became ill had a history of reaching into the bucket to eat leftover foods.

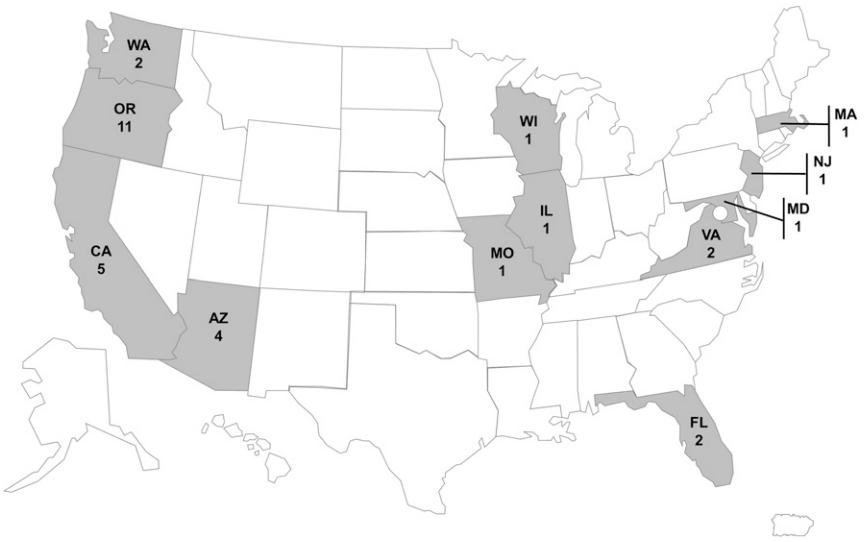

FIGURE 1
People infected with the outbreak strains of *E coli* 0157:H7 (n = 32) by state of residence (United States, 2017).

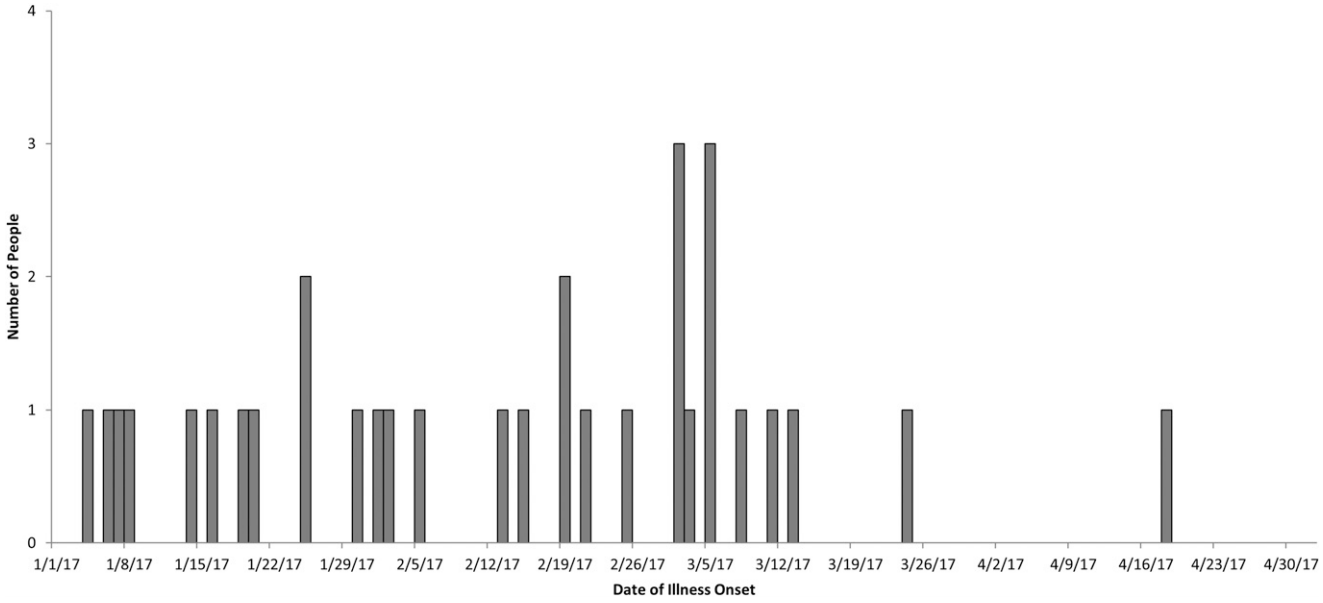

FIGURE 2
People infected with the outbreak strains of *E coli* 0157:H7 (n = 32) by date of illness onset (United States, 2017).

All 32 case patients or proxies were interviewed; 25 (78%) reported eating Brand A soy nut butter at home in the week before they became ill (19 case patients), attending a facility that served Brand A soy nut butter (2 case patients), or attending child care centers that served Brand A soy nut butter and granola (4 case patients). All 23 case patients with information reported the original creamy variety, and 13 of 14 available containers had best-by dates of August 30 to 31, 2018. Of the 7 case patients without reported exposure to soy nut butter, 6 were part of the Oregon child care center mentioned above, and 1 was not associated with any of the identified subclusters and denied eating soy nut butter.

During the outbreak, investigators identified 2 ill people who either developed HUS or had a culture-independent diagnostic test (CIDT) showing infection with STEC bacteria. In interviews, both patients reported eating Brand A soy nut butter in the week before the illness. However, the CDC did not include these people as case patients because no bacterial isolates were available for molecular subtyping, so we were unable to confirm if they were infected with 1 of the outbreak strains.

Product Traceback and Facility Investigations

The product traceback investigation found that Brand A soy nut butter and Brand A granola were made by 2 different contract manufacturers in separate facilities. Both contract manufacturing facilities obtained ingredients from multiple suppliers with multiple product lots; however, the sole supplier of soy nut butter used to manufacture the granola was the contract manufacturer of the Brand A soy nut butter.

The FDA conducted inspections at the soy nut butter contract manufacturer from March 3 to 15, 2017, and subsequently issued an FDA Form 483 to notify the firm of observed objectionable conditions that may be considered violations of the Federal Food, Drug, and Cosmetic Act and related acts.[22,23] These included a failure to follow good manufacturing practices, poor cleaning and sanitation, evidence of pest and animal activity around food production equipment, opportunities for contamination, failure to ensure adequate heat treatment, and inadequate microbial testing.[23] The FDA also conducted inspections at the granola manufacturing facility and at 1 ingredient supplier to the soy nut butter manufacturer, and no violations or issues were noted.

Product Testing and Laboratory Investigations

Local and state investigators collected 89 samples of Brand A soy nut butter and soy nut butter–coated granola from case patient homes, child care centers, and retail locations. An outbreak strain of STEC O157 was isolated from 11 Brand A creamy soy nut butter samples. Multiple STEC isolates were identified from some samples. Nine samples were from opened, leftover products from case patient homes in California, Oregon, and Washington, and 2 samples were from unopened containers from retail stores in California; all

had best-by dates of August 30, 2018 (10 products) or August 31, 2018 (1 product). The FDA collected 17 product samples from the soy nut butter manufacturer and a distribution center. Testing isolated STEC O134 and O180 from 3 Brand A creamy soy nut butter samples from the manufacturing facility, which were produced during the FDA inspection on March 6, 2017. A PulseNet query did not identify any clinical isolates with PFGE patterns indistinguishable from these non-O157 strains. No STEC was isolated from any granola samples tested. The FDA collected 5 ingredient samples from 1 ingredient supplier; none yielded STEC. Fifteen clinical isolates representing all 3 outbreak strains and 13 food isolates were closely related genetically by WGS (0–6 high-quality single nucleotide polymorphisms [hqSNPs]; Fig 3).

Control Measures

On March 3, 2017, the CDC and FDA warned the public that Brand A soy nut butter and granola products were a likely source of the outbreak, advising that consumers not eat these products.[24,25] States and the CDC also sent public health advisories to school and child care center Listservs to warn against serving implicated products.

On March 3, 2017, the company recalled Brand A original creamy soy nut butter with certain best-by dates.[25] This recall was subsequently expanded to encompass all Brand A soy nut butter products, including granola. In total, >1.2 million lb of products were recalled.[26–29] Additionally, 2 downstream product recalls were issued for products containing recalled soy nut butter.[30,31]

The soy nut butter contract manufacturer provided the FDA with a list of actions taken to correct the conditions reported in FDA Form 483. However, the FDA determined that these actions were insufficient to ensure that products were not contaminated with STEC; therefore, the FDA issued a Suspension of Food Facility Registration Order on March 27, 2017.[32] While a suspension order is in effect, no food product can leave the facility for sale or distribution, and the FDA will only reinstate the food facility registration when adequate grounds no longer exist to continue the suspension.[32] At the time this report was submitted for publication,

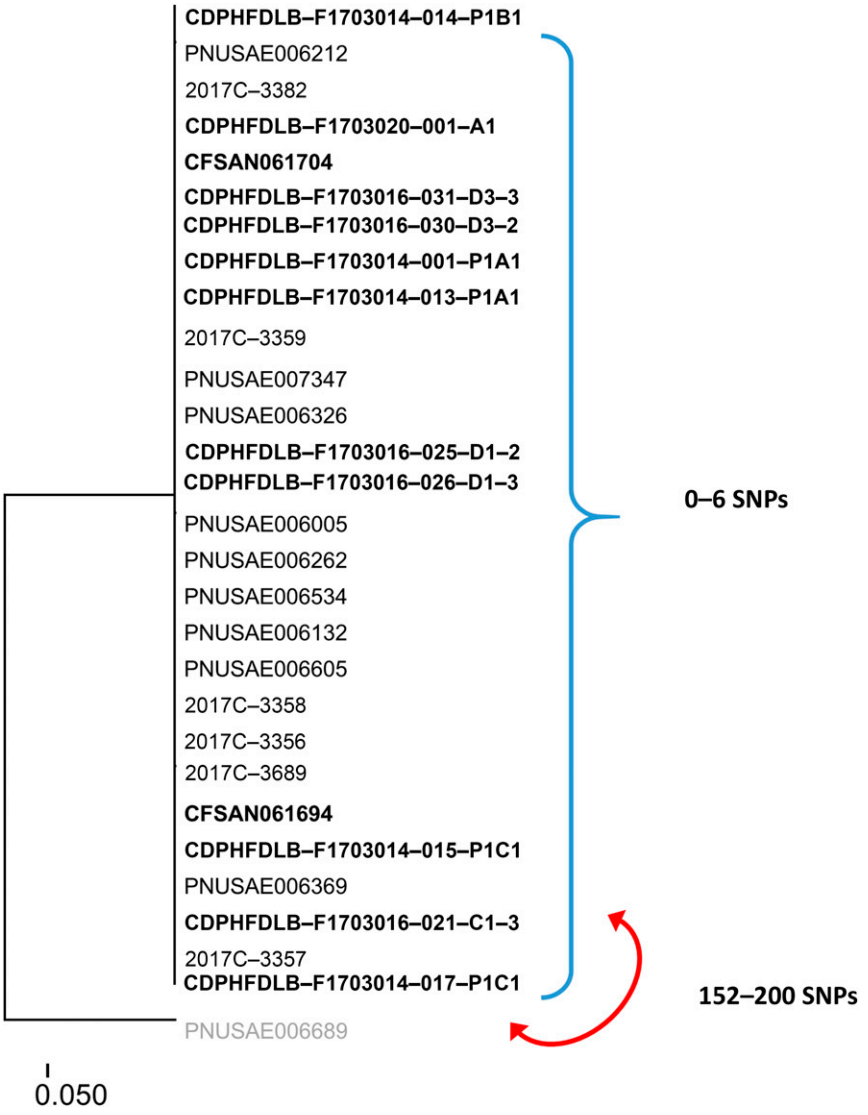

FIGURE 3

E coli O157:H7 WGS analysis: phylogenetic analysis of *E coli* O157:H7 genomes. The maximum-likelihood phylogenetic tree was constructed from 223 whole-genome hqSNPs by using Lyve-SET version 1.1.4f and the Sakai chromosome (BA000007) as a reference. hqSNP analysis was performed by using Lyve-SET version 1.1.4f with the O157:H7 Sakai strain as a reference for the single nucleotide polymorphism calling and the following options specified: –mask-phages, –min_coverage "20," –min_alt_frac "0.95," and –allowedFlanking "5" bp. The phylogenetic tree was visualized by using Molecular Evolutionary Genetics Analysis version 7. Genomes in bold are from soy nut butter isolates, genome PNUSAE006689 in gray is a nonoutbreak-associated outgroup, and the remaining are clinical genomes. The relevant single nucleotide polymorphism differences are noted on the right of the outbreak clade and between the outbreak clade and the outgroup genome. Fifteen clinical genomes representing the 3 outbreak PFGE pattern combinations and 13 soy nut butter genomes are closely related genetically (0–6 hqSNPs). More than 1 isolate was identified from some soy nut butter samples.

the suspension order was still in effect.

DISCUSSION

Epidemiological, traceback, and laboratory evidence identified soy nut butter as the source of a multistate outbreak of STEC O157 infections affecting mainly children. This is the first time a peanut butter alternative such as soy nut butter has been implicated as the source of an outbreak of STEC infections in the United States. Quick investigative work by local, state, and federal agencies led to initial product recalls and consumer advisories within 2 weeks of initiating the investigation, likely preventing additional illnesses.

This outbreak emphasizes the critical role health care providers play in detecting and investigating enteric illness outbreaks. Quick identification and subtyping of bacteria such as STEC is essential to detecting outbreaks. Prompt diagnosis by clinicians not only aids treatment but is important for timely reporting of illnesses to public health officials. The use of CIDTs, such as multiplex polymerase chain reaction assays, immunoassays, or nucleic acid amplified tests, in clinical settings is increasing because CIDTs allow clinicians to rapidly diagnose and treat the cause of a patient's diarrheal illness.[33,34] However, because PulseNet requires a bacterial isolate for molecular subtyping, increasing use of CIDTs without culturing specimens with positive results to isolate and characterize bacterial strains may hinder PulseNet's ability to detect foodborne outbreaks, particularly geographically dispersed outbreaks.[33–38] In this outbreak, we likely only recognized that the 2 additional ill people with STEC infection diagnosed by CIDT alone or HUS without an isolate were likely associated with the multistate outbreak because soy nut butter was an unusual food. To facilitate rapid and reliable outbreak detection, several public health experts recommend that patient specimens with positive results for STEC by CIDT be cultured and isolates be sent to a public health laboratory for further characterization.[35,38,39]

This outbreak also highlights the risk STEC infections pose to the pediatric population. More than one-quarter of the case patients developed HUS, and all but 1 were children <18 years old. The minimum infective dose for STEC can be low, which increases secondary transmission risk in settings of close person-to-person contact.[40,41] We identified a subcluster in an Oregon child care center where secondary transmission might have contributed to the spread of the outbreak given the wide range of onset dates and the fact that soy nut butter was not served there. Although we did not determine how all case patients became infected with STEC, the use of compost buckets that were accessible to toddlers and the large number of diapered children are risk factors for infection. We hypothesize that case patients might have become infected from eating leftover soy nut butter at the lunch table, cross-contamination due to exposure to the compost bucket, person-to-person transmission, or a combination of these. This outbreak serves as a reminder to child care providers of the importance of appropriate hand-washing and hygiene practices to prevent the spread of infections in these settings.[42] Additionally, children with STEC O157 infection should be excluded from attending child care centers until 2 stool cultures (obtained at least 48 hours after antimicrobial therapy, if given, has been discontinued) have negative results for STEC.[7]

This investigation is subject to several limitations. First, we were unable to determine if case patients in the Arizona and Oregon child care center subclusters had eaten soy nut butter through interviews because of their young ages. However, because they were infected with the novel outbreak strain and had several opportunities for primary or secondary exposure at the child care center, we believe it is exceeding unlikely that they would all have an unknown exposure outside the child care center. Additionally, although we identified Brand A soy nut butter as the cause of the outbreak, we were unable to determine how it became contaminated with STEC. Product contamination may have occurred through use of a contaminated ingredient or cross-contamination from contact with contaminated equipment or surfaces during manufacturing. However, because ingredient sample results were negative and multiple objectionable conditions were identified during the facility's inspection, it was not possible to determine which specific route led to product contamination. Given the complexities of outbreak investigations and the time delay from when the contaminated product was manufactured to facility inspection, it is generally uncommon to definitively identify routes of product contamination. Regardless, successfully identifying the contaminated product led to multiple product recalls and the suspension of the firm's ability to sell or distribute food, ultimately stopping the outbreak.

Finally, this outbreak serves as a reminder of the important role manufacturers play in preventing foodborne outbreaks and the role brand owners have in overseeing their product safety. Soy nut butter is a ready-to-eat food with a long shelf life, and multiple foodborne outbreaks have been identified over

the past few years linked to other ready-to-eat, long-shelf-life foods, such as a powdered meal replacement product, sprouted nut butters, and chia powder.[43–45] Ready-to-eat foods are those that consumers would not typically further treat or process in a way that would minimize bacterial risk before eating (eg, cooking to temperature).[46] In all these instances, consumers presume foods are safe to eat and do not require further processing or cooking, so they rely on manufacturers to produce foods in a way that eliminates bacterial contamination. Ready-to-eat foods, particularly those often fed to children, should be manufactured to minimize the risk of bacterial contamination. In addition, it is always important that consumers practice good hygiene to prevent the spread of infectious diseases, particularly in settings with vulnerable populations, such as child care centers.

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ABBREVIATIONS

CDC: Centers for Disease Control and Prevention
CIDT: culture-independent diagnostic test
FDA: US Food and Drug Administration
hqSNP: high-quality single nucleotide polymorphism
HUS: hemolytic uremic syndrome
NHGQ: National Hypothesis Generating Questionnaire
PFGE: pulsed-field gel electrophoresis
STEC: Shiga toxin-producing *Escherichia coli*
WGS: whole-genome sequencing

reviewed and revised the manuscript; Ms Olson and Ms Gladney conducted laboratory analyses, interpreted laboratory data, and critically reviewed and revised the manuscript; Ms Seelman and Dr Whitney interpreted traceback data, conducted traceback analyses, and critically reviewed and revised the manuscript; Ms Sexton and Ms Dwarka reviewed facility inspection data, reviewed inspectional evidence and data, and critically reviewed and revised the manuscript; Ms Dowell drafted, revised, and coordinated the dissemination of risk communication messages and critically reviewed and revised the manuscript; Mr Vidanes and Dr Kiang coordinated product sampling, interpreted product testing data, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Address correspondence to Rashida Hassan, MSPH, Outbreak Response and Prevention Branch, Division of Foodborne, Waterborne, and Environmental Diseases, US Centers for Disease Control and Prevention, 1600 Clifton Rd, MS-H24-10, Atlanta, GA 30333. E-mail: rhassan1@cdc.gov

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