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Review

Identification of Biological Hazards in Produce Consumed in Industrialized Countries: A Review

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ABSTRACT

Microbial contamination of fresh produce (fresh fruits and vegetables) poses serious public health concerns worldwide. This study was conducted as a comprehensive analysis of biological hazards in the global fresh produce chain. Data about produce-related outbreaks and illness were collected from the annual reports and databases of foodborne outbreak surveillance systems in different regions and countries from 2010 to 2015. The global patterns of and regional differences in documented outbreaks and cases were analyzed, and produce commodities and pathogens of greatest concern were identified. Data on sporadic illnesses were also collected through a comprehensive literature review of case-control studies. We found 988 produce-related outbreaks (with known agents) and 45,723 cases in all regions and countries. The numbers of produce-related outbreaks per million person-years were approximately 0.76, 0.26, 0.25, 0.13, 0.12, and 0.05 in New Zealand, Australia, the United States, the European Union, Canada, and Japan, respectively. The top three food categories and pathogens contributing to produce-related outbreaks were vegetables and nonfruits (i.e., food other than fruits; 27.0%), unspecified vegetables (12.2%), and vegetable row crops (11.7%) and norovirus (42.4%), *Salmonella enterica* (19.9%), and *Staphylococcus aureus* (7.9%), respectively. Produce consumption was identified as a protective factor, a risk factor, and either a protective or risk factor for sporadic illnesses in 11, 5, and 5 studies, respectively, among 21 case-control studies. Risks associated with produce consumption in the United States and the European Union have been linked to various factors such as irrigation water, cross-contamination, storage time and temperature abuse, infected food handlers, and unprocessed contaminated ingredients. The results of the current study indicate the complexity of produce products consumed across the globe and the difficulty in tracing illnesses back to specific food ingredients.

Key words: Illnesses; Industrialized countries; Outbreaks; Pathogens; Produce; Surveillance

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The growing international trade of food products has raised increasing concerns over food safety issues *(1, 21)*. Biological hazards account for most reported foodborne illness outbreaks and cases worldwide. Fresh produce (fresh fruits and vegetables) has been frequently implicated in foodborne outbreaks and illnesses *(6, 30, 32)*. In the United States, produce ranks fourth as the food category contributing most to the burdens of foodborne diseases, with 14 of 31 major pathogens causing an estimated 1.2 million illnesses, 7,300 hospitalizations, and 140 deaths at a cost of $1.4 billion and a loss of 1,400 quality-adjusted life-years *(3)*. Produce was also responsible for about one-third of the outbreaks and over 80% of outbreak cases associated with imported foods in the United States during 1996 to 2014 *(21)*. Several produce-pathogen pairs have been frequently involved in fresh produce outbreaks, such as *Salmonella* in sprouts, seeded vegetables, and melons, norovirus in leafy greens and berries, and Shiga toxin–producing *Escherichia coli* (STEC) in leafy greens. The specific produce-pathogen linkage also differs among regions and countries *(6)*.

Understanding the biological hazards of greatest concern associated with food commodities from a global perspective can inform risk management activities to protect public health and enhance international trade and food safety. Several studies have been conducted to review fresh produce outbreaks and illnesses in various regions and countries *(6, 21, 30, 45)*. However, these studies have focused on a limited number of geographical areas or some specific aspects of fresh produce outbreaks and illnesses or have included data from previous years that may not reflect current trends. No comprehensive study has been published to identify biological hazards in the global produce chain

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TABLE 1. *Categorization of microbiological hazards*

Bacteria	Virus	Parasites
Bacillus spp.[a]	Hepatitis A virus	*Ascaris* spp.
Brucella spp.	Hepatitis E virus	*Cyclospora* spp.
Campylobacter spp.	Norovirus	*Cryptosporidium* spp.
Clostridium botulinum[a]	Rotavirus	*Entamoeba* spp.
Clostridium perfringens[a]	Sapovirus	*Giardia* spp.
EAEC, ETEC, EPEC, EIEC[b]	Other viruses	*Toxoplasma gondii*
Shiga toxin–producing *E. coli*		Other parasites
Listeria monocytogenes		
Salmonella enterica (nontyphoidal)		
Shigella spp.		
Staphylococcus aureus[a]		
Vibrio parahaemolyticus		
Other *Vibrio* spp.		
Yersinia spp.		
Other bacteria		

[a] Outbreaks caused by these bacteria were all toxin related.
[b] EAEC, enteroaggregative *E. coli*; ETEC, enterotoxogenic *E. coli*; EPEC, enteropathogenic *E. coli*; EIEC, enteroinvasive *E. coli*.

based on recent data that reflects global and regional trends and patterns.

This study was conducted as a comprehensive review of recent data to identify biological hazards and associated food products in the global produce chains. This information can be used to inform future risk assessment studies and support risk management activities. The specific objectives of this review were (i) to review the currently available information from worldwide foodborne outbreak surveillance systems and studies on sporadic cases and relevant literature; (ii) to provide a detailed analysis of the global patterns and regional differences in documented foodborne diseases for various categories of foods and pathogens; (iii) to prioritize food commodities, pathogens, and food-pathogen pairs of greatest concern based on the frequency of foodborne diseases globally and regionally; and (iv) to summarize the sources and risk factors for produce-related outbreaks.

METHODS

This review was focused on three types of microbiological hazards (bacteria, parasites, and viruses) in fresh produce. Based on data availability, our analysis focused on estimating the food safety and public health impacts of produce-related outbreaks and cases and of sporadic cases of foodborne illness in the United States, the European Union (EU), Canada, Australia, New Zealand, and Japan. The study draws on data from 2010 to 2015.

Categorization of microbiological hazards. Because many types of biological hazards and produce are involved in produce-related outbreaks and illness cases worldwide and surveillance systems use different categories of produce types, a harmonized classification scheme across different systems was developed to characterize pathogen profiles and attribute food sources for outbreaks. Twenty-nine microbiological hazards in the major categories of bacteria, viruses, and parasites were included in this study (Table 1).

Categorization of produce. Table 2 lists the major and minor food categories and examples of food commodities in each minor category. The four major food categories, vegetables, fruits, fruits and vegetables, and mixed foods, were further divided into specific subcategories. The major categories of vegetables and fruits contain several subcategories: (i) single food commodities as defined by the U.S. Interagency Food Safety Analytics Collaboration (IFSAC), such as seeded vegetables, vegetable row crops, sprouts, melons, and small fruits *(42)*, (ii) multivegetable or multifruit foods containing several vegetables or fruits, and (iii) unspecified vegetables or fruits listed as either vegetables or fruits but without further elaboration. The major category "fruits and vegetables" refers to produce-related foods containing both fruits and vegetables, e.g., a food vehicle containing cranberry and coleslaw. The major category "mixed" refers to food vehicles comprising vegetables and/or fruits plus nonproduce foods such as meat, grains, and nuts. Most of the vehicles in this group were salads. Categorizing salads was challenging because each salad has a different recipe with complex ingredients. For each salad type, an Internet search was performed, and the three to five top recipes from the search results were reviewed. The salad type was then assigned to the appropriate food category based on the most common ingredients *(36, 39)*. For example, raw carrot salad and green salad were assigned to the multivegetable group, and fruit salad and grape salad were assigned to the multifruit group. Salads without specific ingredient information, i.e., foods labeled "salad" or "salad/unspecified" were categorized as mixed foods because these salads may have contained nonproduce ingredients.

Assignment of foods to food categories. Table 3 lists examples of how foods were assigned to categories using outbreak surveillance data based on the categorization method in Table 2. The examples show the type of food consumed and which ingredient within the food, if any, was implicated as contaminated. Single contaminated food commodities were simply assigned to their respective categories, e.g., sliced tomatoes to seeded vegetables. When the implicated food items contained multiple ingredients or food commodities, the following rules were employed: (i) when only one ingredient was contaminated, the contaminated ingredient was used to determine the food attribution; (ii) when multiple ingredients of the same category were implicated, the food was assigned to that category, e.g., foods with contaminated lettuce and spinach were categorized as vegetable row crops; (iii) when the implicated ingredients were not in the same category, the food was assigned to one of the mixed categories, e.g., foods with contaminated avocado and cream sauce were assigned to "fruits and nonvegetables"; and (iv) when the known cause of the outbreak was associated with a contaminated nonproduce ingredient, the outbreak was not included in the review regardless of whether the food vehicle also contained fresh produce items.

Outbreak data collection and analysis. Outbreak and outbreak case data were collected from databases and reports published by the outbreak surveillance systems of various regions or countries (Table 4). Not all countries have well-established outbreak surveillance systems or Internet-accessible outbreak information. We obtained outbreak data from 2010 to 2015 from the United States, EU, Canada, Australia, New Zealand, and Japan. All laboratory- and nonlaboratory-confirmed and suspected outbreaks and outbreak cases from these surveillance systems

TABLE 2. *Categorization and examples of produce-related foods*

Produce category	Examples[a]
Vegetables	
Vegetable row crops	Leaves: lettuce, spinach, cabbage; stems: asparagus, celery; flowers: broccoli, artichokes
Seeded vegetables	Vine grown: squashes, cucumbers; solanaceous: tomatoes, eggplants, peppers; legumes: green beans, snap beans, lima beans, snow beans, beans, lentils, peas
Roots, underground	Carrots, onions, potatoes, beets
Sprouts	Alfalfa, mung bean
Herbs	Basil, cilantro, mint, parsley
Fungi	Mushrooms
Multivegetable foods	Raw carrot salad, spinach salad, garden salad, green salad, coleslaw
Unspecified vegetables	
Fruits	
Melons	Cantaloupes, watermelons
Pome fruits	Apples, pears, quinces
Stone fruits	Apricots, cherries, plums, peaches
Small fruits	Blueberries, strawberries, raspberries, elderberries, blackberries, grapes
Tropical fruits	Bananas, mangoes, papayas, coconuts, pineapples
Subtropical fruits	Avocados, oranges, pomegranates
Multifruit foods	Fruit salad, grape salad
Unspecified fruits	
Fruits and vegetables	Cranberry and cabbage slaw
Mixed	
Mixed foods (vegetables, fruits, and nonproduce food)	Cobb salad, other complex salads
Vegetables and nonfruits	Antipasto salad, house salad, chef salad, Greek salad, Caesar salad
Fruits and nonvegetables	Fruit salad with cake

[a] Not all food examples listed have been linked to outbreaks, and many foods not listed have been linked to outbreaks.

were included in this study. From the EU data, outbreaks with both strong and weak evidence were used to identify food vehicles, and all microbiological and epidemiological evidence was used to identify causative agents.

The outbreak data were screened, and all produce-related outbreaks were extracted and analyzed based on the following criteria: (i) food source attribution for various pathogens, which included estimates of the contribution of outbreaks and illnesses associated with a particular biological hazard that could be attributed to a specific food category; (ii) pathogen profiles for various food categories, which included estimates of the contribution of outbreaks or illnesses associated with a particular food category caused by certain biological hazards; (iii) rank of the top food commodities, biological hazards, and food-pathogen pairs by outbreaks and illnesses; and (iv) description of the global patterns and comparison of the regional differences in outbreaks and illnesses for the various food categories and biological hazards.

TABLE 3. *Contaminated food items assigned to produce categories based on outbreak surveillance data*

Food vehicle	Contaminated ingredient(s)	Assigned produce category
Strawberry	Strawberry	Small fruits
Tomato	Sliced tomato	Seeded vegetables
Green salad	Lettuce, spinach	Vegetable row crops
Chicken salad	Celery, onion	Multivegetable foods
Egg roll	Cabbage, carrots, pork, mayonnaise	Vegetables with nonfruits
Cream sauce	Avocado, cream sauce	Fruits with nonvegetables
Mixed salad	Unspecified	Mixed foods

Numbers of outbreaks or illness cases for a country or region were standardized by dividing by the population size and years of data to convert these numbers to rates, which allow comparison of outbreaks and cases in different regions and countries. The distribution of outbreak sizes (number of cases per outbreak) was examined for combinations of pathogens and major food categories (fruits, vegetables, fruits and vegetables, and mixed) for the U.S. and EU data for each pathogen–food category pair associated with more than 10 outbreaks. The normality of both the original and log-transformed outbreak size distributions was tested using Q-Q plots and the Anderson-Darling test ($\alpha = 0.05$).

The Kruskal-Wallis test ($\alpha = 0.05$) was conducted to compare the median number of cases per outbreak between the United States and the EU, both overall and for specific pathogens or produce categories.

Literature review for sporadic illnesses. A comprehensive literature review of published case-control studies was conducted to identify risk factors for sporadic cases of produce-related diseases. We searched the Web of Science database to identify studies from January 2000 to December 2016 without setting language restrictions. We used the following search terms: (microbial OR microbiological OR bacteria* OR pathogen* OR *E. coli* OR "*Escherichia coli*" OR *Salmonella* OR *Listeria* OR *Campylobacter* OR *Bacillus* OR *Staphylococcus* OR *Yersinia* OR *Shigella* OR *Brucella* OR *Vibrio* OR *Clostridium* OR virus* OR norovirus OR rotavirus OR sapovirus OR "hepatitis E" OR "hepatitis A" OR *Shigella* OR parasit* OR parasite* OR protozoa OR cyclospor* OR *Cryptosporidium* OR *Giardia* OR *Toxoplasma*) AND (case-control OR sporadic) AND (food*). The search resulted in 994 articles, and we reviewed all titles and abstracts for relevance. Nonrelevant studies were excluded based on the following criteria: nonhuman infections (animal infections), outbreak-related illnesses, cases occurred before 2000, not a case-control study design, no food-related exposure (only environmental or occupational), and other source attribution studies (genetic typing or expert elicitation). We then uploaded the records of 118 remaining articles to Endnote Web, reviewed the full articles, and excluded studies using additional criteria: primary objective not for risk factor identification, produce not identified as a risk factor, and nonfood related infections or risk factors (environment, animal contact, hygienic practice, dietary habits, or lifestyle). When analyzing the remaining 21 case-control studies, risk factors that were significant in the initial univariate regression analysis but not significant in the multivariate analysis were not included. The following information was extracted for each included case-control study for further analysis: country, year of

TABLE 4. *Outbreak and case data from various outbreak surveillance systems, 2010 to 2015*

Country or region	Data source	Organization	Reference(s)
United States	FOOD Tool database	CDC	https://wwwn.cdc.gov/foodborneoutbreaks/
European Union	Outbreak database and EU annual summary reports	EFSA and European CDC	*(12–17)*
Australia	OzFoodNet national and quarterly reports, NSW quarterly reports[a]	Department of Health	http://health.gov.au/internet/main/publishing.nsf/Content/cdna-ozfoodnet-reports.htm; http://www.health.nsw.gov.au/Infectious/foodborne/Pages/ozfoodnet-rpt.aspx
New Zealand	Annual summary of outbreaks	Institute of Environmental Science and Research Limited	https://surv.esr.cri.nz/surveillance/annual_outbreak.php
Japan	Annual outbreak reports	Ministry of Health, Labour and Welfare	http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/shokuhin/syokuchu/04.html#j4-3; data collected and translated by Dr. Hajime Toyofuku (Yamaguchi University)
Canada	Outbreak Summaries Reporting System and federal monitoring systems[b]	Public Health Agency of Canada	Outbreak Management Division, Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada

[a] Australian outbreak data included the national annual reports from 2010 to 2011, national quarterly reports from 2012 to 2014, and New South Wales (NSW) quarterly reports in 2015.

[b] Outbreak Summaries is a voluntary reporting platform for enteric outbreaks in Canada. Although the platform is used for surveillance purposes, outbreaks are not systematically reported (e.g., not all provinces and territories use the platform to report outbreaks, and the type of outbreaks reported differs by province).

cases, age group of individuals affected, etiology, produce, odds ratio (OR), and population attributable fraction (PAF).

RESULTS

Global produce-related outbreaks. Table 5 provides an overview of the total and standardized foodborne outbreaks and produce-related outbreaks and cases in each country or region. Although New Zealand had the smallest population, it had the highest reported rate of foodborne and produce-related outbreaks and cases. Japan had the lowest reported rate of produce-related outbreaks and cases per million person-years. The reported rates of foodborne outbreaks and cases in Canada were the lowest. Although the EU and the United States had high numbers of produce-related outbreaks and cases, the reported rates were much lower after standardization. Australia had moderate reported rates of foodborne and produce-related outbreaks and cases. It is uncertain whether differences in reported rates between regions and countries represent true differences in disease burden or differences in the surveillance systems.

Food sources and etiology of outbreaks globally. Figures 1 and 2 present produce-related outbreaks and cases, respectively, by food categories globally and by region. The three food categories making the greatest contributions to produce-related outbreaks were vegetables and nonfruits (27.0%, 267 outbreaks), unspecified vegetables (12.2%, 121 outbreaks), and vegetable row crops (11.7%, 116 outbreaks) (Fig. 1). The categories of vegetables only, fruits only, and fruits and vegetables accounted for 42.5, 13.5, and 1.6% of the total outbreaks, respectively. Therefore, globally 57.6% of outbreaks were attributed to categories containing only produce (fruits and vegetables) and the remaining 42.4% were attributed to the mixed categories (produce and nonproduce food commodities). The three food categories making the greatest contribution to produce-related outbreak cases were small fruits (27.8%, 12,703 cases), vegetables and nonfruits (17.3%, 7,889 cases), and sprouts (11.2%, 5,121 cases) (Fig. 2). The categories of vegetables only, fruits only, and fruits and vegetables accounted for 37.0, 33.4, and 2.2% of the total outbreak cases, respectively. Therefore, 72.6% of cases were attributed to the produce-only categories (fruits and vegetables) and the remaining 27.4% were attributed to the mixed categories (produce and nonproduce food commodities). The highest number of outbreaks and cases across all food categories occurred in the EU and United States, but the produce vehicles were not always the same. For example, outbreaks and cases involving herbs, small fruits, and unspecified vegetables were mainly reported from the EU, whereas outbreaks and cases associated with many other produce such as seeded vegetables, roots (underground), multivegetable foods, melons, tropical fruits, unspecified fruits, and multifruit foods were mainly reported from the United States. Outbreaks and cases associated with fungi, pome fruits, stone fruits, and subtropical fruits were reported from only the United States.

Figures 3 and 4 present produce-related outbreaks and cases, respectively, by pathogen globally and by region. The top three pathogens contributing to produce-related outbreaks were norovirus (42.4%, 419 outbreaks), *Salmonella enterica* (19.9%, 197 outbreaks), and *Staphylococcus aureus*

TABLE 5. *Reported foodborne and produce-related outbreak data in various regions and countries, 2010 to 2015*

Country or region	Population[a]	Foodborne outbreaks[b] No. of outbreaks	No. of outbreaks/million persons/yr[d]	No. of cases	No. of cases/million persons/yr	Produce-related outbreaks[c] No. of outbreaks	No. of outbreaks/million persons/yr	No. of cases	No. of cases/million persons/yr
European Union	506.6	31,082	10.22	303,201	99.75	401	0.13	27,544	9.06
United States	316.2	5,075	2.67	86,910	45.81	472	0.25	14,430	7.61
Canada	35.2	145	0.69	4,424	20.95	25	0.12	727	3.44
Japan	127.4	6,525	8.54	137,162	179.44	38	0.05	1,279	1.67
Australia	23.1	808	6.57	11,670	94.88	32	0.26	1,260	10.24
New Zealand	4.4	680	25.76	4,896	185.45	20	0.76	483	18.30
Total		44,352		549,943		988		45,723	

[a] Population in million persons in 2013; http://data.worldbank.org/indicator/SP.POP.TOTL.
[b] Including outbreaks with known and unknown food vehicles and known and unknown pathogens and both laboratory-confirmed and suspected outbreaks and cases.
[c] Including produce-related outbreaks with known produce and known agents and both laboratory-confirmed and suspected outbreaks and cases.
[d] Values for million persons per year for countries other than Australia were calculated based on their respective national population size multiplied by 6 years. Available data for Australian outbreaks were national data for 2010 through 2014 and New South Wales (NSW) data for 2015. Thus, the values for Australia were calculated as follows: (23.1 million population in Australia × 5 years) + (7.5 million NSW population × 1 year).

(7.9%, 78 outbreaks) (Fig. 3). The top three pathogens in outbreak cases were norovirus (49.8%, 22,765 cases), *S. enterica* (18.9%, 8,636 cases), and STEC (12.6%, 5,747 cases) (Fig. 4). The United States and the EU together reported most outbreaks and cases for all pathogens except *Yersinia* spp. and *Cyclospora* spp. Most outbreaks and cases caused by *S. enterica,* enteroaggregative *Escherichia coli,* enterotoxogenic *E. coli, Listeria monocytogenes,* and saprovirus were reported in the United States, whereas most outbreaks and cases caused by *Campylobacter* spp., *Clostridium perfringens, Bacillus* spp., *S. aureus,* other bacteria, hepatitis A virus (HAV), rotavirus, *Cryptosporidium* spp., and *Giardia* spp. were reported in the EU. The greatest number of outbreaks of STEC and norovirus were reported in the United States, whereas the greatest number of outbreak cases of STEC and norovirus were reported in the

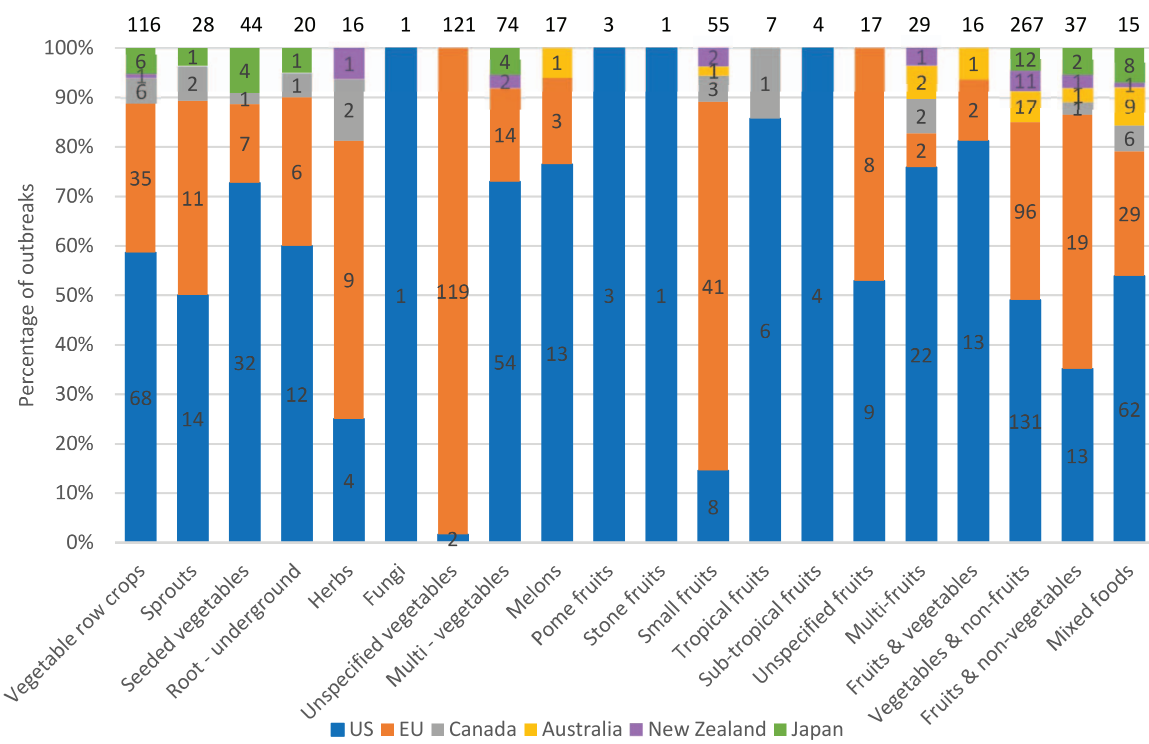

FIGURE 1. *Global and regional foodborne outbreaks, 2010 to 2015, by food categories. Numbers above each column are the total numbers of outbreaks associated with each food category. Numbers within each bar are the numbers of outbreaks associated with that food category in each region or country.*

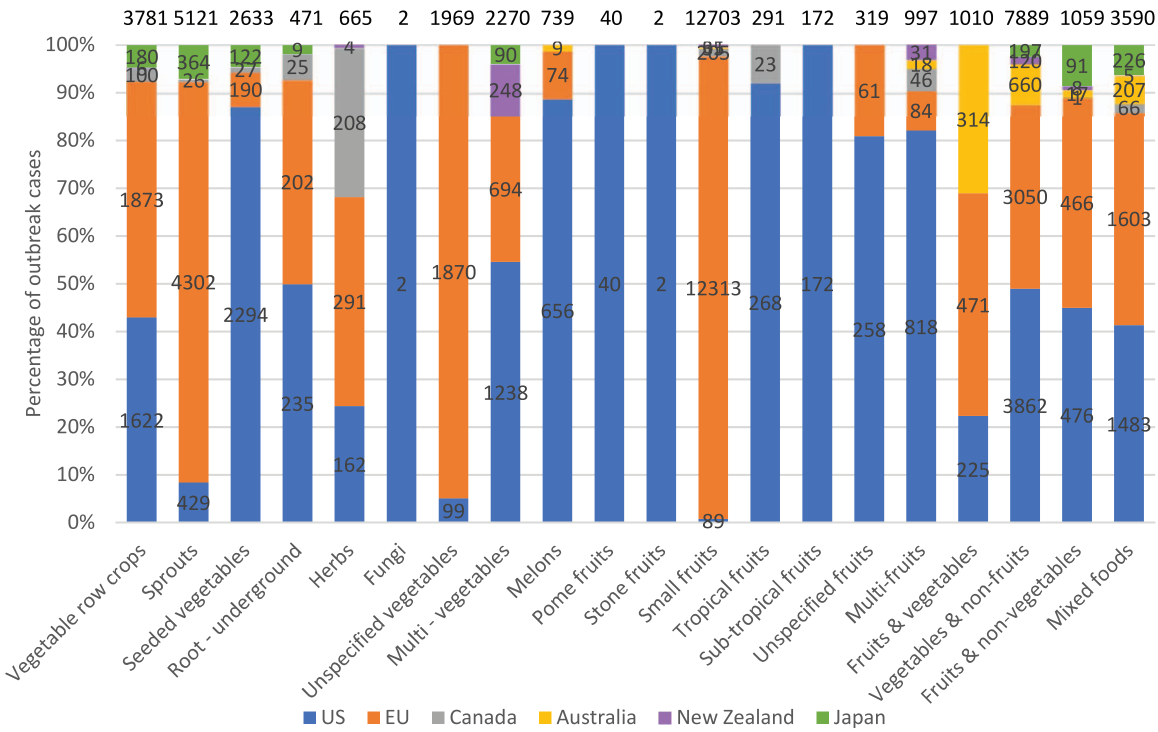

FIGURE 2. *Global and regional foodborne outbreak cases, 2010 to 2015, by food categories. Numbers above each column are the total numbers of outbreak cases associated with each food category. Numbers within each bar are the numbers of outbreak cases associated with that food category in each region or country.*

EU, indicating that the outbreaks of these two pathogens involved more persons in the EU. Conversely, the number of outbreaks of *C. botulinum* and *Shigella* spp. were higher in the EU, whereas case numbers for these pathogens were higher in the United States.

Comparison of global produce-related outbreak cases on FERG data. Our estimates of the number of outbreak cases were compared with the number of produce-related illnesses estimated by the Foodborne Disease Burden Epidemiology Reference Group (FERG) of the World

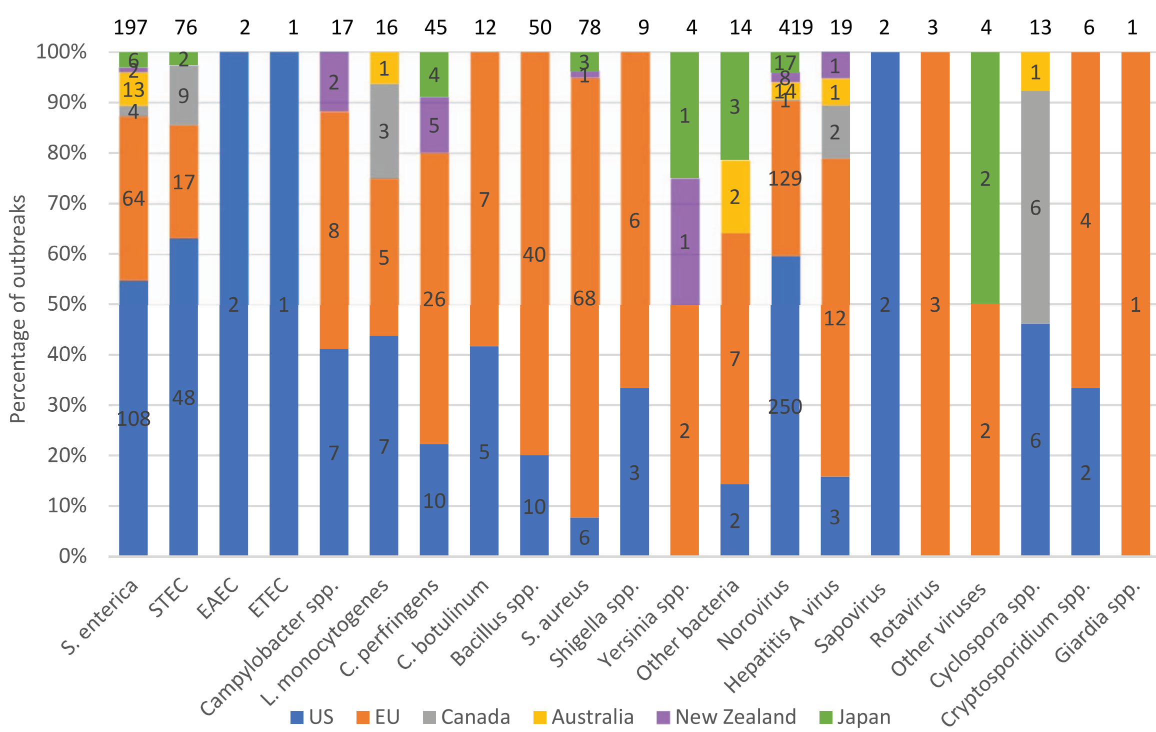

FIGURE 3. *Global and regional foodborne outbreaks, 2010 to 2015, by pathogens. Numbers above each column are the total numbers of outbreaks associated with each pathogen. Numbers within each bar are the numbers of outbreaks associated with that pathogen in each region or country.*

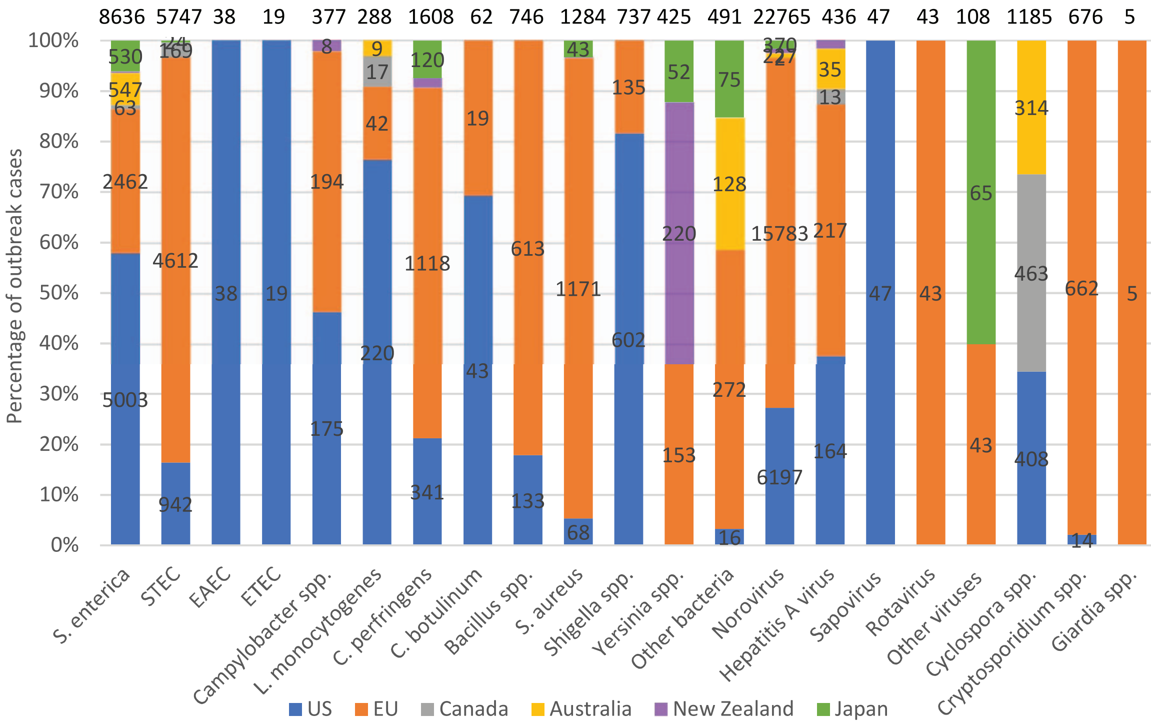

FIGURE 4. *Global and regional foodborne outbreak cases, 2010 to 2015, by pathogens. Numbers above each column are the total numbers of outbreak cases associated with each pathogen. Numbers within each bar are the numbers of outbreak cases associated with that pathogen in each region or country.*

Health Organization *(24),* which attributed diseases to food sources for 11 major foodborne diseases in each of 14 world subregions in 2010 and specified the percentage of illnesses attributed to produce for *Campylobacter* spp., *S. enterica,* and *Cryptosporidium* spp. *(26)*. Mean and median numbers of outbreak cases per year in the United States and Canada together (representing North America) and in the EU from the current study were compared with the produce-related illnesses data in the AMR A and EUR A regions in the FERG study, respectively (Table 6). The FERG estimates of the number of produce-related illnesses caused by *Campylobacter* spp., *S. enterica,* and *Cryptosporidium* spp. in 2010 were several orders of magnitude higher than the corresponding annual number of outbreak cases in the present study. This indicates that most of the foodborne illnesses might be sporadic rather than outbreak related but also that only a very small portion of the produce-related illnesses can be detected with the outbreak surveillance systems, probably due to considerable underreporting of produce-related cases in outbreaks. The United States and Canada together detected more *S. enterica* outbreak cases than did the EU. However, more *Campylobacter* spp. and *Cryptosporidium* spp. outbreak cases were detected in the EU than in the United States and Canada (no produce-related *Campylobacter* spp. or *Cryptosporidium* spp. outbreaks or cases were reported in Canada).

Food sources and pathogen profiles for outbreaks in various regions and countries. In the United States, norovirus was the number one cause of produce-related outbreaks (53.0%, 250 outbreaks) and cases (43.0%, 6,197 cases) followed by *S. enterica* (22.9%, 108 outbreaks; 34.7%, 5,003 cases) and STEC (10.2%, 48 outbreaks; 6.5%, 942 cases) (Supplemental Figs. S1 and S2). Vegetables and nonfruits were associated with the highest number of outbreaks (27.8%, 131 outbreaks) followed by vegetable row crops (14.4%, 68 outbreaks) and mixed foods (13.1%, 62 outbreaks) (Figs. S3 and S4).

In the EU, norovirus was also the leading cause of produce-related outbreaks (32.2%, 129 outbreaks) and cases (57.3%, 15,783 cases) followed by *S. aureus* (17.0%, 68 outbreaks; 4.3%, 1,171 cases) and *S. enterica* (16.0%, 64 outbreaks; 8.9%, 2,462 cases). Although STEC outbreaks accounted for only 4.2% (17 outbreaks) of the total outbreaks, 16.7% (4,612 cases) of the total number of outbreak cases were caused by STEC (Figs. S5 and S6). The highest number of outbreaks (29.7%, 119 outbreaks) was attributed to unspecified vegetables (Fig. S7) because the vegetable products could not be identified during the outbreak investigations. Other commonly implicated food categories were vegetables and nonfruits (23.9%, 96 outbreaks), small fruits (10.2%, 41 outbreaks), and vegetable row crops (8.7%, 35 outbreaks). The highest number of outbreak cases (44.7%, 12,313 cases) was attributed to small fruits followed by sprouts (15.6%, 4,302 cases) and vegetables and nonfruits (11.1%, 3,050 cases) (Fig. S8).

The food source attribution and pathogen profiles for the outbreaks and cases in Japan, New Zealand, Australia, and Canada are presented in Figures S9 to S24.

Top pathogen-produce pairs ranked globally by number of outbreaks. The top five pathogen-food pairs for

TABLE 6. *Comparison of produce-related outbreak cases reviewed in this study with produce-related illnesses estimated by FERG for* Campylobacter *spp.,* Cryptosporidium *spp., and* S. enterica

Study parameter	*Campylobacter* spp.				*S. enterica*				*Cryptosporidium* spp.			
	AMR A[a]	EUR A[a]	United States + Canada	EU	AMR A	EUR A	United States + Canada	EU	AMR A	EUR A	United States + Canada	EU
FERG study												
Median no. of foodborne illnesses in 2010	1,254,852	2,326,017			1,072,185	797,668			137,047	73,777		
% illnesses attributed to produce	0.088	0.04			0.141	0.06			0.909	0.87		
No. of produce-related illnesses in 2010	110,427	93,041			151,178	47,860			124,576	64,186		
This study												
No. of produce-related outbreak cases 2010–2015			175	194			5,066	2,462			14	662
Avg (median) no. of produce-related outbreak cases/yr			29 (23.5)	32 (21.5)			844 (687)	410 (396)			2 (0)	110 (5)

[a] Countries included in AMR A and EUR A regions were described by Havelaar et al. *(24)*.

all regions and countries ranked by the number of outbreaks are summarized in Table 7. Norovirus in vegetables and nonfruits and in mixed foods were ranked first and second, with 99 and 76 outbreaks, respectively, followed by *S. enterica* in vegetables and nonfruits with 64 outbreaks and norovirus in vegetable row crops with 55 outbreaks. Norovirus in multivegetable foods and *S. aureus* in unspecified vegetables both were associated with 48 outbreaks (ranked fifth).

Top pathogen-produce pairs ranked globally by number of cases. Table 8 lists the top five pathogen-food pairs ranked globally by number of outbreak cases. Norovirus in small fruits was ranked first with 12,165 cases, many more cases than second-ranked STEC in sprouts, with 3,902 cases. Norovirus in vegetables and nonfruits and in mixed foods and *S. enterica* in seeded vegetables were ranked third, fourth, and fifth, respectively.

Top pathogen-produce pairs ranked by number of outbreaks in various regions and countries. Supplemental Table S1 lists top pathogen-food pairs ranked by number of outbreaks in the United States and the EU. When evaluating all produce categories, *S. aureus* in unspecified vegetables and norovirus in vegetables and nonfruits were the most common pairs associated with outbreaks in the EU and United States, respectively. For vegetables only, *S. aureus* in unspecified vegetables and norovirus in multivegetable foods ranked highest in the EU and United States, respectively. For fruits only, norovirus in small fruits and norovirus in multifruit foods ranked highest in the EU and United States, respectively.

The top food-pathogen pairs ranked by number of outbreaks for Japan, Australia, New Zealand, and Canada are presented in Table S2.

Top pathogen-produce pairs ranked by number of outbreak cases in various regions and countries. The top pathogen-food pairs ranked by number of outbreak cases in the United States and the EU are listed in Table S3. For all produce, norovirus in small fruits ranked first in the EU. *S. enterica* in seeded vegetables ranked highest in the United States, followed by norovirus in vegetables and nonfruits, in mixed foods, and in multivegetable foods, indicating that norovirus is one of the major pathogens of concern in produce in the United States. For vegetables only, STEC in sprouts and *S. enterica* in seeded vegetables ranked first in the EU and United States, respectively. For fruits only, norovirus in small fruits and norovirus in multifruit foods ranked highest in the EU and United States, respectively.

The top food-pathogen pairs ranked by outbreak cases for Japan, Australia and New Zealand, and Canada are presented in Table S4.

Comparison of median number of cases per outbreak between the United States and the EU. The median number of cases per outbreak for some major pathogens and produce categories in the United States and the EU are shown in Figure 5 because significantly more

TABLE 7. *Top five pathogen-produce pairs ranked by global number of outbreaks*

Rank	Pathogen–produce pair	No. of outbreaks
1	Norovirus–vegetables and nonfruits	99
2	Norovirus–mixed foods (vegetables, fruits, and nonproduce)	76
3	*S. enterica*–vegetables and nonfruits	64
4	Norovirus–vegetable row crops	55
5[a]	Norovirus–multivegetable foods	48
5	*S. aureus*–unspecified vegetables	48

[a] Two categories tied for rank 5.

TABLE 8. *Top five food-pathogen pairs ranked by global number of outbreak cases*

Rank	Pathogen–produce pair	No. of outbreak cases
1	Norovirus–small fruits	12,165
2	STEC–sprouts	3,902
3	Norovirus–vegetables and nonfruits	2,767
4	Norovirus–mixed foods (vegetables, fruits, and nonproduce)	2,276
5	*S. enterica*–seeded vegetables	2,188

data are available for these regions and countries. The overall median number of cases per outbreak for all produce-related outbreaks in the United States and the EU were 16 and 14, respectively, and were not significantly different ($P = 0.11$). For pathogens, the median numbers of cases per outbreak for *S. enterica,* norovirus, STEC, and HAV were higher in the EU than in the United States. Conversely, the median numbers of cases per outbreak of *Campylobacter*

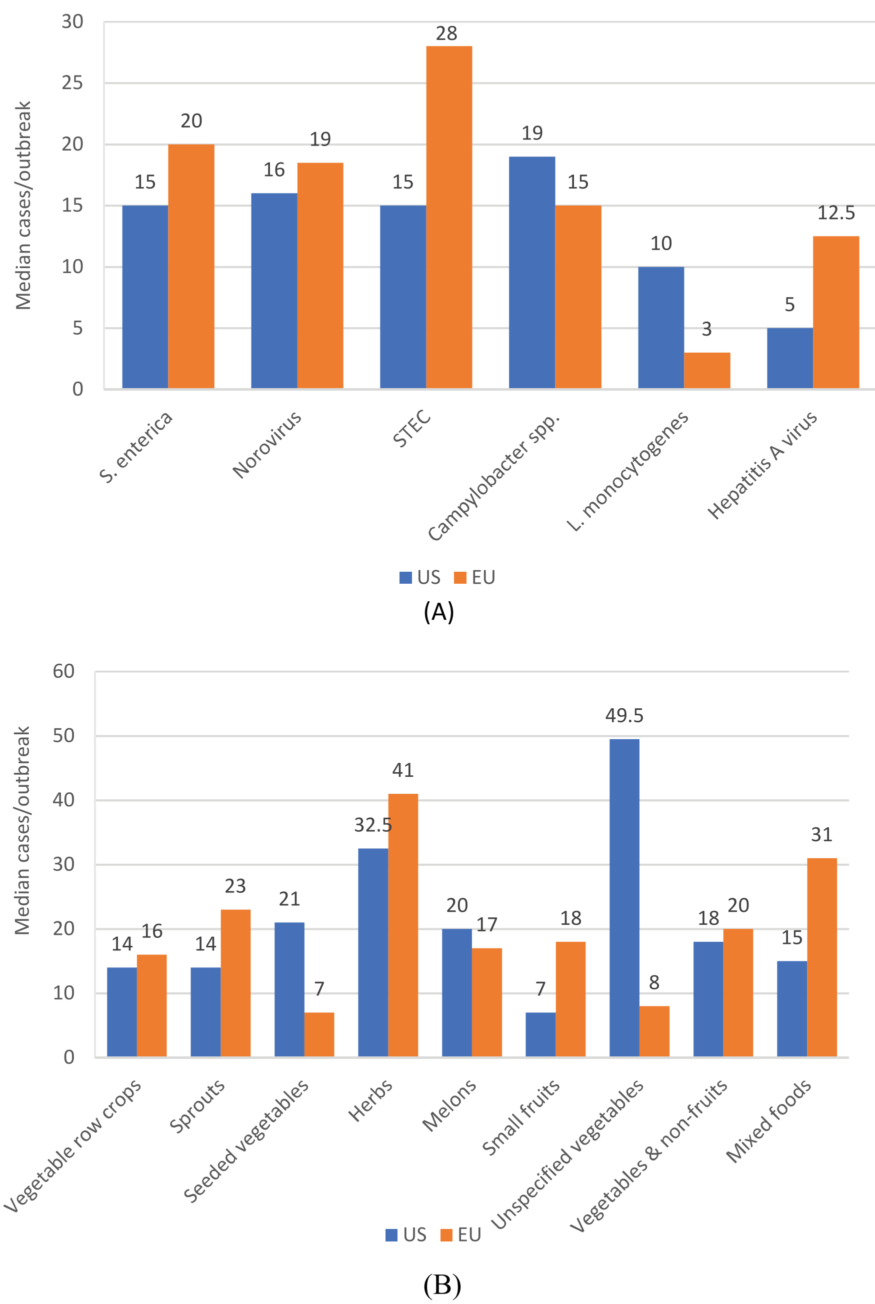

FIGURE 5. *Comparison of median number of cases per outbreak between the United States and the EU for common pathogens (A) and food categories (B).*

spp. and *L. monocytogenes* were higher in the United States than in the EU. However, only the differences in STEC cases were significant ($P = 0.018$). For produce categories, the median number of cases per outbreak associated with unspecified vegetables was marginally higher in the United States than in the EU ($P = 0.055$), whereas the median number of cases per outbreak associated with mixed foods was marginally higher in the EU than in the United States ($P = 0.057$). No significant differences in other produce categories were found between the United States and the EU ($P > 0.05$).

Sources and risk factors for outbreaks in the United States and the EU. The sources and risk factors for produce-related outbreaks were explored for all the studied regions and countries, and most information was available for the EU and the United States. Table S5 lists all produce-related outbreak investigations conducted by the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) from 2010 through 2015. Most of the outbreaks involved *S. enterica, L. monocytogenes, E. coli* O157:H7, and *Cyclospora* spp. in cucumbers, sprouts, melons, leafy greens, herbs, and fruits. In many investigations, contamination was traced back to specific growers or producers, but the root causes were not identified. Several outbreaks involved imported produce from Mexico, and the sources were not identified or reported in any of these outbreaks. The FDA typically investigated potential routes for contamination in the areas of agricultural production and packing operations, such as agricultural water, soil, wild animal excreta, adjacent land use, employee health and hygiene practices, storage, and transportation, which are common risk factors for pathogen contamination or cross-contamination. However, produce types and pathogens may have various routes of contamination. The source investigations listed in Table S5 indicated the likely sources and routes of contamination for various types of fresh produce. For example, outbreaks associated with sprouts were frequently attributed to seed lots, irrigation water, and sanitary practices. The initial contamination of cantaloupes likely occurred in the production fields and was spread by operations and practices within the packinghouse. The contamination then probably proliferated during storage and transport to market. Low-level sporadic *L. monocytogenes* contamination from the agricultural environment and incoming cantaloupes may have allowed for establishment of a harborage or niche for *L. monocytogenes* in the packing facility and cold storage. Root causes for outbreaks associated with other produce types, such as cucumbers, vegetable row crops, herbs, salads, papayas, and mangoes, were not identified even though thorough outbreak investigations were conducted. One *E. coli* O157:H7 outbreak associated with lettuce in 2013 had a high risk from the areas surrounding the harvest field and the close proximity to cattle operations. One *L. monocytogenes* outbreak associated with caramel apples in 2014 was traced back to environmental contamination in the field.

In the EU data, the places of origin of the problem are defined as the places where the mishandling of the food took place and/or where the contamination occurred. Tables S6 and S7 list the number of outbreaks that were attributed to various places of origin by produce categories and pathogens, respectively, for 222 outbreaks for which that information was available. Most produce-related outbreaks occurred at restaurants, cafés, pubs, bars, hotels, or catering services (41.4%), followed by canteen and workplace catering (12.2%), households (11.7%), and farms (9.0%) (Table S6). The places of origin for specific produce types are also indicated, e.g., vegetable row crops can be contaminated across various stages from farm to food consumption and sprouts can be contaminated at the farm or at processing plants. Noroviruses, *S. enterica,* and STEC contamination can occur at various stages from farm to consumption (Table S7). Noroviruses were found most often in restaurant and catering settings, and *S. enterica* was found most often in restaurant, household, and farm environments. Toxin-producing bacteria (*Bacillus cereus, Clostridium botulinum, C. perfringens,* and *S. aureus*) most frequently occurred in restaurants, households, and other food preparation places.

Tables S8 and S9 list the countries from which the food vehicles and pathogens originated. This information was available for 148 EU outbreaks, of which 126 outbreaks originated from the EU member countries, 2 were from the European economic area, and 20 were associated with foods imported from non-EU countries. Most produce-associated pathogen outbreaks originated from the EU countries, and only a few were from the European economic area and non-EU countries (Tables S8 and S9).

Tables S10 and S11 list various risk factors for the EU outbreaks by produce category and pathogen, respectively. Risk factors were identified in 210 outbreaks, among which 154 were attributed to a single risk factor and others were attributed to more than one risk factor. Among the single risk factors, unprocessed contaminated ingredients and infected food handlers were most common. Cross-contamination, storage time and temperature abuse, and inadequate heat treatment were also important risk factors.

Case-control studies for sporadic cases. Table 9 summarizes case-control studies for various pathogens that cause produce-related sporadic illnesses. These case-control studies include the OR, which indicates how much higher the odds of exposure to risk factors are among case-patients than among controls, and if available the PAF, which represents the proportion of cases that would be prevented by controlling the exposure. The OR indicates the strength of the effect, and the PAF takes into account the proportion of the population that is exposed.

Most of the eligible case-control studies were conducted in developed countries; only two studies were from developing countries. These studies focused on common pathogenic bacteria such as C*ampylobacter* spp., *S. enterica,* STEC, *L. monocytogenes, Vibrio parahaemolyticus,* HAV, and *Giardia lamblia*. Produce was identified as a protective factor for sporadic illnesses in most of the studies but as a risk factor in several other studies *(5, 8, 40)*. Generally, eating fruits and berries had a protective effect against

TABLE 9. *Summary of case-control studies of various pathogens implicated in produce-related sporadic illnesses*

Country	Year	Age group	Pathogen	Produce	OR, PAF (95% CI)[a]	Reference
United States	2010	General population	*Campylobacter* spp.	Cantaloupe	OR = 2.6 (1.2–5.7)	*40*
				Blueberries	OR = 0.4 (0.2–0.94)	
				Other raw fruit	OR = 0.4 (0.2–0.9)	
				Tomatoes	OR = 0.3 (0.1–0.7)	
	2004	General population	*S. enterica* Javiana	Uncooked tomatoes	aOR = 0.5 (0.3–0.9)	*7*
	2002	General population	*S. enterica* Enteritidis	Carrots	OR = 0.5 (0.2–0.8)	*23*
				Cantaloupe	OR = 0.3 (0.1–0.8)	
				Watermelon	OR = 2.1 (1.1–4.1)	
				Produce	PAF = 9.4% (2.6–15.3%)	
	2000–2003	General population	*L. monocytogenes*	Melons at a commercial establishment	OR = 2.63 (1.39–4.96); PAF = 10.6%	*44*
Netherlands	2012–2013	General population	HAV	Iceberg lettuce	OR = 24.0 (1.1–519)	*5*
	2002–2003	5–59 yr	*C. jejuni*	Salad	OR = 0.7 (0.6–0.9)	*9*
				Fruit with skin	OR = 0.6 (0.5–0.8)	
		>60 yr		Fruit	OR = 0.5 (0.3–0.8)	
	2008–2012	>10 yr	STEC	Raw vegetables	OR = 0.5 (0.3–0.9)	*19*
	2002–2003	General population	*Campylobacter*	Salad	OR = 0.7 (0.6–0.9)	*35*
				Vegetarian diet	OR = 0.4 (0.2–0.9)	
	2002–202003	General population	*S. enterica*	Raw vegetables	aOR = 0.7 (0.6–0.9)	*34*
				Cooked vegetables	aOR = 0.6 (0.5–0.8)	
				Fruit	aOR = 0.7 (0.5–0.9)	
Germany	2007–2008	General population	*Giardia lamblia*	Green salad, daily	aOR = 2.9 (1.2–7.2)	*11*
	2012–2013	Immunocompromised patients	*L. monocytogenes* (not pregnancy associated)	Carved and packaged raw fruit, fruit salads, etc.	OR = 0.27 (0.11–0.72)	*41*
	2008–2010	General population	*S. enterica*	At least one of raw tomatoes, uncooked peppers, uncooked herbs (fresh or dried)	OR = 0.55 (0.37–0.83)	*46*
United Kingdom	2005–2008	>60 yr	*L. monocytogenes*	Fresh vegetables	OR = 0.03 (0.02–0.05)	*20*
				Mixed salad	OR = 1.72 (1.20–2.47)	
	2001	General population	*Campylobacter*	Salad vegetables	aOR = 1.73 (1.09–2.73); PAF = 21% (2–36%)	*18*
Ireland	2003–2004	General population	*Campylobacter*	Lettuce	aOR = 2.6 (1.3–5.2); PAF = 58.5%	*8*
				Salad (other than lettuce)	cOR = 0.6 (0.4–09); mOR = 0.4(0.2–0.8)	
Norway	1999–2000	General population	*Campylobacter*	Fruits or berries	mOR = 0.9 (0.9–1.0)	*29*
Canada	1999–2000	General population	*S. enterica* Typhimurium non-DT104 and DT104	Green salad	OR = 0.4 (0.2–0.7) for non-DT104; OR = 0.5 (0.3–1.0) for DT104	*10*
Australia[b]	2003–2007	General population	STEC O157	Homegrown fruit, vegetables, or herbs	OR = 0.4 (0.2–0.95)	*33*
			STEC non-O157	Homegrown fruit, vegetables, or herbs	OR = 0.4 (0.2–0.8)	
				Raw vegetables	OR = 0.3 (0.2–0.6)	
New Zealand	2011–2012	General population	STEC	Raw vegetables	OR = 0.52 (0.27–0.99)	*27*
Kenya	Unspecified	3–25 yr	Gastrointestinal illnesses	Spinach	OR = 0.5 (0.3–0.9)	*28*
				Carrots	OR = 2.8 (1.0–7.5)	
China	2012	General population	*Vibrio parahaemolyticus*	Vegetable salad	OR = 12.1 (5.2–28.2)	*31*
			V. parahaemolyticus O3:K6	Vegetable salad	OR = 10.5 (4.3–25.5)	

[a] Odds ratio (OR) and population attributable fraction (PAF) were preferably obtained from the multivariate logistic regression. Otherwise, these values were obtained from the univariate analysis. aOR, adjusted OR; cOR, crude OR; mOR, Mantel-Haenszel OR. OR > 1 is a risk factor; OR < 1 is a protective factor.

[b] Information for Australia, 2003 to 2007, covered food consumed in the 10 days and environmental exposure in the 4 weeks before illness for case patients and before interview for control participants.

pathogenic infections *(9, 40, 41),* whereas eating melons such as watermelons and cantaloupes tended to be a risk factor *(40, 44)* in all except one study, in which cantaloupe consumption was identified as a protective factor *(23)*. Eating fresh and raw vegetables, spinach, tomatoes, herbs, and peppers was found to be protective *(7, 20, 27, 33–35, 46),* but eating lettuce was identified as a risk factor *(5, 8)*. Consumption of other products such as carrots and vegetable-based salads could be a protective factor *(9, 10, 23)* or a risk factor *(8, 11, 18, 28, 31)*.

DISCUSSION

The attribution of food contamination to the correct source relies on the appropriate categorization of suspected food vehicles and hazards. The produce-related outbreaks could be attributed to either single or complex produce commodities with multiple ingredients. Attribution of outbreaks to single commodities was relatively straightforward, but attribution to complex foods is difficult because information needed for tracing contamination back to a specific food ingredient is lacking for many outbreaks and no formal agreement on food attribution can be made in such cases *(3, 22)*. Many of the foodborne illness source attribution methods, such as those used by the IFSAC and the European Food Safety Authority (EFSA) are focused on single food commodities to improve the accuracy of food attribution. However, these methods may not include all produce-related outbreaks because more implicated produce items are in the complex food categories rather than in single fruit and vegetable categories, as found in the present study. The CDC has taken a further step by partitioning illnesses due to complex food into each commodity in the implicated food *(37)*. For each of these commodities, a minimum estimate can be made by attributing illness to a simple food associated with that commodity, and a maximum estimate can be made by adding the minimum estimate to the proportion of the complex food that contains that commodity. This method is based on the assumption that when an outbreak is associated with a complex food, the likelihood that any commodity is the source is proportional to the frequency of illnesses due to contamination with simple foods associated with that commodity. In the present study, we took a conservative approach by including the complex foods as separate categories in addition to single produce commodities to provide a broader picture of global produce-related outbreaks and illnesses. This approach is similar to those of Batz et al. *(3)* and Greig and Ravel *(22),* who developed similar hierarchical classification systems to group food into main categories and included a complex foods category to capture multi-ingredient foods from which the precise source of infection cannot be identified.

The source attribution for produce-related outbreaks differs among countries and regions. The produce-only categories accounted for most produce-related outbreaks and cases in most regions and countries except Australia and New Zealand, where 15.6 and 35.0% of outbreaks and 29.8 and 65.0% of cases, respectively, were attributed to the produce-only categories. For single vegetable commodities, vegetable row crops were the leading category associated with outbreaks in the EU, United States, Canada, Japan, and New Zealand. No outbreaks were associated with single vegetable commodities in Australia. Seeded vegetables in the United States, sprouts in the EU and Japan, herbs in Canada, and multivegetable foods in New Zealand were the leading categories associated with outbreak cases related to vegetables in these countries. Among the single fruit commodities, the leading categories associated with outbreaks were small fruits in the EU, Canada, Australia, and New Zealand and melons in the United States. No outbreaks associated with single fruits were reported from Japan.

Very large foodborne outbreaks can affect the interpretation of the data. The Q-Q plots and Anderson-Darling tests indicated that the original outbreak size for all pathogen-food pairs was not normally distributed but was adequately described by a lognormal distribution, except for norovirus-fruits and *S. aureus*–vegetables in the EU (data not shown). Therefore, we compared the median number of cases per outbreak (Fig. 5) and the median and mean number of outbreak cases per year (Table 6). An extremely large number of outbreak cases (12,313) associated with small fruits in the EU (Fig. 2) accounted for about 97% of the total 12,703 outbreak cases worldwide. The large number of cases were mainly due to a 2012 norovirus outbreak in Germany associated with frozen strawberries imported from China that resulted in 10,950 illness cases and 38 hospitalizations *(4)*. Another large outbreak was the STEC–verotoxigenic *E. coli* O104:H4 outbreak in Germany in 2011 associated with sprouted seeds imported from Egypt, which affected more than 3,800 persons, was linked to cases in 15 other countries, and accounted for about 74% of the total 5,121 sprout-associated outbreak cases (Fig. 2) *(13)*.

The pathogen profiles revealed that norovirus was the leading causative agent of produce-related outbreaks in all regions and countries except Canada, where only one norovirus outbreak was reported, from mixed foods. However, norovirus outbreaks are not systematically reported through the federal outbreak surveillance system by all provinces and territories in Canada. Norovirus outbreaks were associated with a wide range of produce-related vehicles, including produce only and mixed categories. Norovirus was also the main pathogen implicated or confirmed in outbreaks attributed to vegetable row crops and roots (underground) in the United States and the EU. In the EU, a substantial proportion of the norovirus outbreaks were associated with frozen berries and could be attributed to several concomitant factors, such as increased berry importation and consumption in the EU over the last decades, technical developments in the detection of pathogens in food, and increased notifications from the Rapid Alert System for Food Products (https://ec.europa.eu/food/safety/rasff_en) for contaminated frozen berries, indicating extensive environmental and traceback investigations performed by the affected countries when experiencing a large foodborne outbreak *(43)*. Several HAV outbreaks associated with frozen berries also occurred but were less numerous than norovirus outbreaks. The difference may be partially explained by the prevalence of individuals with long-lasting HAV immunity after infection or vaccination, a high proportion of asymptomatic HAV infections, and the challenge associated with identifying outbreaks and the implicated food item(s) because of the long HAV incubation period and recall bias *(25, 43)*.

S. enterica was the second-most frequent cause of produce-related outbreaks in the United States, Japan, and Australia and the pathogen most frequently associated with sprout- and melon-associated outbreaks in both the United States and the EU. STEC was the leading cause of outbreak cases associated with sprouts in the EU and with produce-related outbreaks in Canada. Overall, a greater number of pathogens were involved in outbreaks containing complex foods than in outbreaks associated with a single produce commodity, most likely because of the complexity of contaminated ingredients in the mixed food categories. Although there were more similarities between the United States and the EU compared with other regions, differences still exist in food attribution for some pathogens and pathogen profiles for some food categories. For example, outbreaks associated with small fruits were caused by norovirus, *S. aureus,* and HAV in the EU (Fig. S7), whereas in the United States these outbreaks were also caused by *S. enterica,* STEC, *Cyclospora* spp., and *Cryptosporidium* spp. (Fig. S3). Another difference is the sources of contamination in the EU and the United States. In the EU, most reported produce-related outbreaks were due to mishandling or cross-contamination at the food preparation stage, with only a small proportion attributed to contamination on the farm (Table S6), whereas in the United States more problems were found at the food production stages such as in the fields and packinghouses (Table S5). Nevertheless, the U.S. outbreak investigations reviewed in this study were all multistate outbreaks in which the majority (if not all) involved contamination prior to food handling. The proportion of outbreaks involving contamination during food preparation for single state outbreaks (for which data are not available) would probably be much higher.

Differences in the outbreak data available were inherent to each of the surveillance systems because reporting agencies have different types of resources and methods for conducting and/or reporting outbreak investigations. For example, outbreak data in the United States, Canada, and New Zealand were collected from public health units at the state, provincial, or local levels, and data from the EU, Australia, and Japan were collected in a centralized database populated by mandatory data submissions from EU member states, Australian states and territories, and Japanese local public health centers, respectively. Surveillance systems also may capture the number of outbreaks and cases differently, with differences in the guidelines for what is considered a cluster of illnesses, how strong the evidence must be to include illnesses in the outbreak, and which illnesses can be included in the data. More data were available from the United States and the EU than from other countries, which might be related with the larger populations in these regions. Therefore, in this study the outbreak data were standardized per million persons per year to compare outbreaks in different regions and countries on an equal basis. The environmental conditions and percentage of people living in rural areas may also play important roles in the number of outbreaks. For example, the higher rates in Australia may be partially explained by the fact that 39% of Australia is in the tropical zone *(2),* providing optimal growth conditions for foodborne pathogens (Table 5). Overall, more uncertainty was associated with produce-related outbreaks in Canada, Japan, Australia, and New Zealand because of relative data sparsity, and caution should be exercised when interpreting data from these countries. Other reasons for the variations among countries and regions might be differences in epidemiological aspects of foodborne diseases (such as detection bias and information bias), differences in produce growing and processing, differences in microbial ecology and low levels or inhomogeneous distributions of pathogens in produce, and the short shelf life of produce, leading to difficulty in tracing implicated products.

Outbreak investigations focus on diseases occurring from a single source, whereas case-control studies of sporadic cases include multiple disease cases with multiple sources. Although it may be difficult to identify sources of contamination in case-control studies because of biases inherent in such studies, these studies are valuable tools for identifying potential risk factors for human infections from various sources of exposures (e.g., foodborne, environmental, and occupational). For example, in one study *(8),* the population-attributable fraction for lettuce explained about 60% of sporadic *Campylobacter* illnesses, identifying a less well-known risk factor compared with other commonly recognized factors such as eating chicken. However, lettuce consumption as a risk factor is plausible because lettuce may become contaminated from soil in the field or irrigation water during harvesting *(8)*. Fresh produce may also be cross-contaminated during food preparation from kitchen utensils or food contact surfaces due to poor handling, hygiene, or storage practices *(8, 18)*. Risk assessment studies have indicated that when a potentially large amount of product is consumed, even very low pathogen prevalence can lead to substantial risk of illnesses. For example, a low *Campylobacter* prevalence of 0.0054 in packaged salad was estimated to result in an average of 1.7×10^4 illness cases annually in The Netherlands *(38)*.

In most case-control studies, consumption of fruits and vegetables was protective with respect to human diseases (OR $<$ 1) compared with consumption of other food products such as meat, cheese, milk, and eggs. Despite these protective effects, produce consumption has been considered a risk factor for human microbial infections *(5, 8, 40)*. These conflicting results may be attributed to numerous factors affecting study outcomes, such as gender, age, season, degree of urbanization, and the inherent safety of the produce. The protective effect of produce also may be more likely related to differences in diet, in which high-risk foods such as meats are consumed less often by individuals who tend to eat more produce.

The present study has some limitations. First, the data on produce-related outbreaks were collected from developed countries. Foodborne outbreak data could not be obtained from some countries and regions possibly because of less complete foodborne disease surveillance systems or the lack of access to the data from these systems. This scenario is similar to that for case-control studies of sporadic illnesses, where more data were available from developed than from developing countries. Second, in most outbreak investigations a specific contaminated food vehicle that caused the outbreak could not be identified, i.e., a causative food or ingredient was identified in only a small proportion of all outbreaks. For example, the percentages of foodborne outbreaks from 2010 to 2015 for which the vehicle was unknown were 69.8, 63.2, 62.8, 58.1, 44.3, and 29.0% in the EU, New Zealand, Japan, the United States, Australia, and Canada, respectively (Table S12). These outbreaks with unknown food vehicles might include produce-related outbreaks. Third, among outbreaks with known produce vehicles, many outbreaks were caused by biological hazards that could not be identified by the surveillance systems, and these outbreaks could not be included in our analysis. We included outbreaks and cases with both laboratory-confirmed and suspected causes from all countries and regions and outbreaks with weak evidence linking the consumption of a particular food to an outbreak case. We also included outbreaks associated with mixed food vehicles where the actual source may have been a nonproduce component. Inclusion of these outbreaks might have resulted in overestimation of the actual number of produce-related outbreaks. Because outbreak investigations may last for several months or years, the reporting agencies can update, alter, add, and remove outbreak data and information during the process. Therefore, new findings in outbreak investigations by these agencies may alter the previous number of outbreaks and cases and the food-pathogen pair rankings.

CONCLUSIONS AND FUTURE RECOMMENDATIONS

In summary, 988 produce-related outbreaks and 45,723 outbreak cases from 2010 to 2015 were reviewed in all studied regions and countries. The United States and the EU jointly contributed approximately 90% of the total outbreaks and cases used in the current analysis. After standardization for population sizes and years, 0.76, 0.26, 0.25, 0.13, 0.12, and 0.05 produce-related outbreaks per million people per year were found in New Zealand, Australia, the United States, the EU, Canada, and Japan, respectively. The overall food safety of these regions is difficult to assess because of the variability, complexity, and differences in available resources among surveillance systems in various regions and countries. The median number of cases per outbreak was 16 in the United States and 14 in the EU. No significant differences between the United States and the EU were found in the median number of cases per outbreak for most pathogens and produce categories.

Among produce-related outbreaks, approximately 57.6% of outbreaks and 72.6% of outbreak cases could be attributed to the produce-only categories, with the remaining 42.4% of outbreaks and 27.4% of cases attributed to the mixed food categories. Approximately 30% of produce-related outbreaks with known vehicles were attributed to single produce commodities, and the majority of outbreaks were attributed to complex produce categories, which indicates the complexity of produce consumed across the globe and the difficulty in tracing illnesses back to specific food ingredients. For example, most salad-related outbreaks were simply attributed to food vehicles such as "fresh fruit salad," "house salad," and "chicken Caesar salad with raw egg dressing" without explicitly mentioning which food items in the salads or dressings (which have been directly involved in several produce outbreaks) that were responsible for the outbreaks. Improvements in epidemiological study design, outbreak investigations, diagnostic methods, and other relevant factors may enhance the accuracy of specific food source identification. Numerous salad-associated outbreaks were placed in the mixed categories, which emphasizes the need to provide more effective intervention strategies to control foodborne pathogens in produce-based salads.

The food categories making the greatest contributions to produce-related outbreaks were vegetables and nonfruits (27.0%), unspecified vegetables (12.2%), and vegetable row crops (11.7%). The pathogens making the greatest contributions to produce-related outbreaks were norovirus (42.4%), *S. enterica* (19.9%), and *S. aureus* (7.9%). Outbreaks of most pathogens were associated with multiple food categories. Norovirus, *S. enterica,* and STEC outbreaks were generally associated with more produce categories than were other pathogens. More microbiological studies in the field, processing plants, retail outlets, and consumption areas are needed to understand the contamination routes along produce supply chains as a basis for developing appropriate preventive measures.

Some food-pathogen pairs were more frequently associated with produce-related outbreaks, e.g., *S. enterica* in seeded vegetables and sprouts, norovirus in mixed food categories and small fruits, and STEC in vegetable row crops. More efforts should be focused on these food-pathogen pairs to prevent produce-related outbreaks and illnesses. Risk assessment studies can be conducted to estimate the exposure to important pathogens in relevant supply chains, the risk of particular food-pathogen pairs to public health, and relative effectiveness of interventions to reduce the health risks.

A limited number of case-control studies were available, mainly in developed countries for common pathogens such as *Campylobacter* spp., *S. enterica,* STEC, and *L. monocytogenes*. Produce consumption was identified as a protective factor in most of the case-control studies but as a risk factor in some studies.

The sources and risk factors for outbreaks were available for only a small proportion of outbreaks in the regions and countries included in this study. In the United States, multistate outbreaks have been linked to various factors including irrigation water, environmental contamination, and livestock operations in the production stage. In the EU, the most common risk factors are cross-contamination, infected food handlers, storage time and temperature abuse, inadequate chilling and heating, and unprocessed contaminated ingredients. These findings highlight the importance of implementing food safety management systems, such as good agricultural and manufacturing practices, and effective intervention strategies, such as irradiation, natural antimicrobial agents, and appropriate processing, transportation and storage temperatures, to minimize the outbreak risk factors along the produce chain.

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SUPPLEMENTAL MATERIAL

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