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Research Paper Foodborne Illnesses from Leafy Greens in the United States: Attribution, Burden, and Cost



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ARTICLE INFO ABSTRACT Keywords: Leafy green vegetables are a major source of foodborne illnesses. Nevertheless, few studies have attempted to Burden of illness estimate attribution and burden of illness estimates for leafy greens. This study combines results from three Cost of illness outbreak-based attribution models with illness incidence and economic cost models to develop comprehensive Food attribution pathogen-specific burden estimates for leafy greens and their subcategories in the United States. We find that Leafy greens up to 9.18% (90% CI: 5.81%-15.18%) of foodborne illnesses linked to identified pathogens are attributed to Norovirus leafy greens. Including 'Unknown' illnesses not linked to specific pathogens, leafy greens account for as many Shiga toxin-producing Escherichia coli as 2,307,558 (90% CI: 1,077,815-4,075,642) illnesses annually in the United States. The economic cost of these illnesses is estimated to be up to \$5.278 billion (90% CI: \$3.230-\$8.221 billion) annually. Excluding the pathogens with small outbreak sizes, Norovirus, Shiga toxin-producing Escherichia coli (both non-O157 and O157:H7), Campylobacter spp., and nontyphoidal Salmonella, are associated with the highest number of illnesses and greatest costs from leafy greens. While lettuce (romaine, iceberg, "other lettuce") takes 60.8% of leafy green outbreaks, it accounts for up to 75.7% of leafy green foodborne illnesses and 70% of costs. Finally, we highlighted that 19.8% of Shiga toxin-producing Escherichia coli O157:H7 illnesses are associated with romaine among all food commodities, resulting in 12,496 estimated illnesses and \$324.64 million annually in the United States.

Foodborne illnesses pose a substantial public health concern in the United States, with 48 million cases reported leading to economic costs of up to \$90 billion (Scallan et al., 2011; Scharff, 2020). Although research has been conducted to estimate the incidence and economic burden of foodborne illnesses, for policy purposes, it is also crucial to understand the attribution of foodborne illnesses to specific food ingredients. This paper aims to develop unique burden of illness estimates based on outbreak-based attribution models for leafy greens, a food category of importance due to both the risks and consumption levels of these products. Although prior studies have explored the attribution of foodborne illness outbreaks across food categories, there is limited research specifically focusing on leafy green products.

Leafy green commodities require particular attention due to their increasing consumption and their potential to cause foodborne illnesses. The 2018–2019 FoodNet Population Survey estimated that 80.5% of families consumed leafy greens in the past 7 days, an

increase from 50.6% during the 2006-2007 survey. Ansai and Wambogo (2021) found that 26.3% of Americans consume leafy greens. Furthermore, leafy greens have been repeatedly implicated in foodborne illness outbreaks or contaminations associated with dangerous pathogens, such as Shiga toxin-producing Escherichia coli (STEC) (Bottichio et al., 2020; Irvin et al., 2021; Kintz et al., 2019; Marshall et al., 2020), nontyphoidal Salmonella (Mishra et al., 2017; Sant'Ana et al., 2014), and L. monocytogenes (Buchanan et al., 2017; Farber et al., 2021; Mishra et al., 2017; Sant'Ana et al., 2014). These case reports and risk models, while useful as epidemiological or biological tools, do not shed light on the aggregate burden of disease or how this burden is distributed across food categories. Although some have reported the number of outbreaks associated with leafy greens (Bean et al., 1996; Gould et al., 2013; Olsen et al., 2000), formal attribution estimates are lacking for leafy green subcategories. Anderson et al. (2011) did include leafy green subcategories in a risk-ranking

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Abbreviations: IFSAC, Interagency Food Safety Analytics Collaboration; STEC, Shiga toxin-producing *Escherichia coli*; NORS, National Outbreak Reporting System; CDC, Centers for Disease Control and Prevention; M1, A weighted average of simple food outbreaks attribution model adapted from Interagency Food Safety Analytics Collaboration, 2021; M2, Triangular distribution-based attribution model adapted from Painter et al., 2013; M3, Dirichlet-Multinomial based attribution model adapted from Pires et al., 2019.

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study that identified outbreaks by food-pathogen pairs, but they did not generate attribution estimates.

Material and Methods

In this study, we systematically estimate the attribution of foodborne illnesses to leafy greens, the incidence of these illnesses, and resulting economic costs. The need to attribute illnesses to specific foods has been addressed by researchers employing a variety of attribution methods, including the analysis of outbreak data and expert elicitations (Batz et al., 2005; Hoffmann et al., 2017; Painter et al., 2013; Pires et al., 2009; Mangen et al., 2015). Consistent with most studies, we use approaches based on outbreak data (Greig & Ravel, 2009; Painter et al., 2013; Pires et al., 2012, 2019; Scharff, 2020). Distinctively, our study covers a broad range of etiologies, a perspective notably absent in most other research (Gould et al., 2013; Pires et al., 2012, 2019; Batz et al., 2012, 2021; IFSAC, 2021). We combine attribution estimates with Scallan et al. (2011) pathogen-based incidence estimates and updated economic cost of illness estimates based on Scharff (2012, 2015, 2020) as illustrated in Figure 1.

Attribution Modeling Choices. Outbreak-based attribution models vary based on specifications and inherent biases. Choices include single vs. complex food outbreaks, weighting by the number of illnesses, discounting older outbreaks, and including suspected etiologies. These choices affect outcomes and may introduce biases, highlighting the complexity of attribution modeling.

To illustrate the impact of modeling choices on attribution values, we estimate three attribution models (denoted M1, M2, and M3). The first model (M1), based on the approach taken by the Interagency Food Safety Analytics Collaboration (IFSAC) in the United States, only includes simple food outbreaks, but weights outbreaks by the log of illnesses and discounts past outbreaks (IFSAC, 2021). The default estimates for M1 use IFSAC parameter estimates for the discount factor and bootstrapping to address uncertainty. The second model (M2), based on Painter et al. (2013) includes complex foods and weight outbreaks by illnesses but does not apply a discount factor to past outbreaks. Complex food attribution is estimated using a triangular distribution with weights from simple food outbreak counts used to calculate food attribution in complex outbreaks. The final model (M3), based on Pires et al. (2019), includes complex foods, does not weigh for illness numbers, and does not discount past outbreaks. For complex foods, M3 calculates weights using simple food outbreaks that follow Dirichlet distributions. Then, the weights are used as preliminary attribution values to calculate the final attribution estimates for each complex food using Multinomial distributions. Each of the three models we estimated used outbreak data from 1998 to 2020 and included outbreaks with suspected etiologies, though alternate assumptions are tested in a sensitivity analysis. Modeling choices for M1, M2 and M3 are described and reported in greater detail in Appendix A and Table A1. We provide multiple estimates based on alternative modeling assumptions in a sensitivity analysis.

For several pathogen categories, the total number of outbreaks is too small to generate statistically significant leafy green attribution estimates. This study uses the Agresti-Coull interval to estimate the necessary sample size within a defined margin of error. This approach is described in Appendix B. Estimates for pathogens not meeting these criteria should be interpreted as "suggestive".

Outbreak Data. The study utilizes data from National Outbreak Reporting System (NORS) released by the U.S. Centers for Disease Control and Prevention over the years 1998 to 2020. The initial data set included 23,059 outbreaks, which were reduced to 21,763 after eliminating outbreaks with flawed food vehicle data. Consistent with previous studies, 519 outbreaks with more than one pathogen were omitted (Painter et al., 2013; IFSAC, 2021). We also removed outbreaks with unknown food ingredients and those linked to chemical contamination. Outbreaks associated with known food ingredients, but unknown etiologies are included in a separate category titled "Unknown". The resulting dataset consisted of 8,809 outbreaks. To ensure successful integration with the illness and economic models, pathogen categories were chosen based on the presence in the Scallan et al. (2011) illness study and the Scharff (2020) economic cost study. Our analysis includes outbreaks due to 28 etiologic agents plus those with "Unknown" origin.

Attribution to Leafy Greens. The NORS dataset identifies outbreaks as one of 17 Interagency Food Safety Analytics Collaboration (IFSAC) food categories (IFSAC, 2021), including a category for multiple foods (complex foods), greens are part of a larger category titled "Vegetable Row Crops." To assess attribution for leafy greens, we established subcategories based on foods identified in NORS. Then, we implemented a decision rule relying on the IFSAC category, ingredients, and food vehicles. First, foods not categorized as either "Vegetable Row Crops" or "Multiple" (e.g., IFSAC category is "Chicken") were coded as not being leafy greens. For the remaining outbreaks, we used "ingredients" identified as being implicated in the outbreak to assess the foods involved in the outbreak. If no ingredients were listed, we assessed foods based on foods identified in the broader "food vehicle" category. The top-down algorithm is shown in Figure 2. Through this process, we identified ten subcategories of leafy greens: iceberg, romaine, other lettuce, spinach, cabbage, kale, parsley, arugula, "other leafy," and "mixed leafy". "other leafy" refers to specific leafy green ingredients that do not fit into the earlier subcategories. "mixed leafy" covers complex food sources, comprising vegetablebased salads, spring mixes, mesclun, and other analogous salads.

Burden of illness model. To assess the number of illnesses associated with leafy greens, we combined the derived food attribution

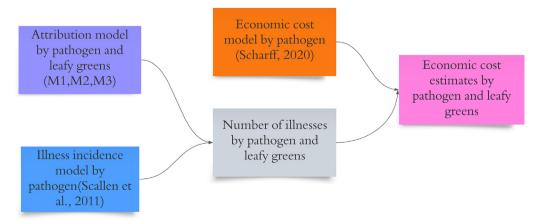


Figure 1. Modeling Approach

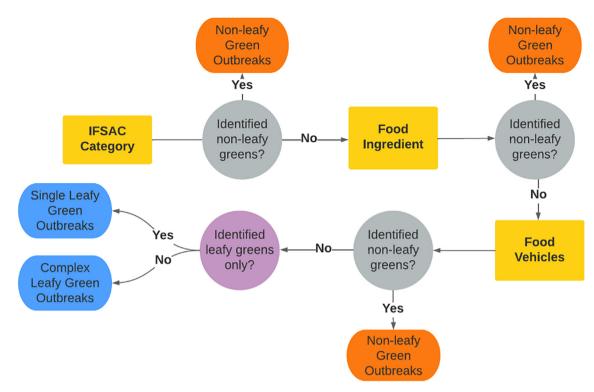


Figure 2. Leafy Green Attribution Process

estimates for each pathogen with Scallan et al.'s (2011) pathogenspecific illness estimates. Though somewhat dated, Scallan et al.'s (2011) estimates for the number of foodborne illnesses caused by the major known and unknown pathogens in the United States continue to be used as official estimates in the United States (Centers for Disease Control and Prevention, 2018). We also calculated illness estimates for illness due to unknown pathogens.

Economic cost model. The economic cost of foodborne illnesses associated with leafy greens is assessed by combining pathogen-based cost-per-case estimates from Scharff's (2012, 2020) cost model with the food/pathogen-based number of illnesses from the burden of illness model. Cost estimates in the Scharff model have been updated to account for commodity-specific increases in prices, workforce compensation and participation, and income. Cost is calculated as $Cost_p =$ -Hospital_p + Physician_p + Pharma_p + CProd_p + VSL_p + QALY_p, where Hospital_p, Physician_p, and Pharma_p represent the medical costs for each pathogen p; CProd_p denotes the productivity losses due to childcare for each pathogen p; VSL_p and QALY_p are the values assigned to statistical life loss and quality-adjusted life year loss (QALY) respectively (for each pathogen p). All estimates are updated to March 2023 dollars.

Results

Attribution Estimates. The attribution results in this study are derived from simple and complex food outbreak samples from the NORS dataset. Table 1 displays the breakdown of leafy green outbreaks within these samples and across leafy green subcategories. The inclusion of leafy greens in complex foods increased the overall contribution to outbreaks, suggesting a deficiency of only relying on simple food outbreaks. Moreover, outbreaks associated with "other lettuce" and "romaine lettuce" are prevalent. Aggregating "romaine", "iceberg", and "other lettuce" into a "lettuce family" reveals that 60.8% of simple and complex leafy green outbreaks are related to this category.

The outbreak samples (Table 1) are used in models M1 (IFSAC, 2021), M2 (Painter et al., 2013), and M3 (Pires et al., 2019). We pro-

vide leafy green attribution estimates for 28 pathogens in Tables 2 and 3. Pathogens with sufficient sample size (as determined in Appendix B) are represented in bold font. Results for other pathogens should be viewed as suggestive.

Among bacterial pathogens, Shiga toxin-producing *Escherichia coli* (STEC) is prominently attributed to leafy greens, with varying proportions for O157:H7 (11.86% to 32.56%) and non-O157 (22.38% to 46.94%) serotypes. *Cyclospora cayetanensis* is the primary parasite associated with leafy greens, along with *Giardia* spp. and Norovirus among viruses. However, caution is advised with *Giardia* spp. due to its low sample size. Additionally, 1.09% to 4.05% of illnesses from unknown etiologies are attributed to leafy greens, indicating their potential role in outbreaks across different pathogens.

M3 generally underestimates leafy greens' attribution compared to M2 (Table 3). Overall, M2 attributes 5.20% and M3 attributes 1.67% of total outbreaks to leafy greens. This trend is consistent with M3's tendency to underestimate specific food categories. To better understand the effect of food categorization on attribution estimates, we used the broader IFSAC "Vegetable Row Crop" category to generate simple food outbreak weights for M2 and M3 (the two models that used simple food as weights in the estimation of complex food attribution). As Figure 3 illustrates, both M2 and M3 are affected by how foods are categorized, though the effect on M3 is much larger. Figure 4 further shows the effect on the estimates of M3 for each leafy subcategory. For this and other reasons (see the discussion), we do not believe M3 is a reliable estimator for foods with relatively small sample sizes, such as leafy greens. Consequently, we do not present burden and cost estimates that build on results from M3.

Many modeling decisions are not uniformly superior to others. For this reason, we examined alternate modeling assumptions in a sensitivity analysis for models M1 and M2. Specifically, we examined how attribution estimates varied when the sample was restricted to (1) outbreaks excluding suspected etiologies, (2) recent years (2015–2020), (3) outbreaks weighted by log illnesses, (4) outbreaks weighted by illnesses and year discounting, and (5) outbreaks using log illnesses and year discounting. Results from models with different combinations of

Table 1

Simple and Complex Food Outbreaks: Leafy Greens from 1998 to 2020 in the United States^a

Food Categories	Simple Food	Outbreaks			Simple and Complex Food Outbreaks				
	Bacterial	Parasitic	Viral	Unknown	Bacterial	Parasitic	Viral	Unknown	
Lettuce	32	2	38	17	82	4	235	108	
Romaine	22	3	9	1	36	3	42	27	
Iceberg	8	0	6	0	14	0	13	1	
Spinach	8	0	2	1	11	1	14	7	
Cabbage	3	0	2	1	29	1	40	40	
Kale	1	1	0	0	2	1	0	1	
Parsley	2	0	1	1	6	0	2	1	
Arugula	1	1	0	0	2	1	0	0	
Other Leafy	17	0	31	6	25	0	42	12	
Mixed Leafy	0	0	0	0	28	1	71	27	
Leafy Outbreaks	94	7	89	27	235	12	459	224	
Lettuce family Outbreaks	62	5	53	18	132	7	290	136	
All Outbreaks	2,626	109	711	1,042	4,053	135	2,031	2,590	
Proportion ^b	3.6%	6.4%	12.5%	2.6%	5.8%	8.9%	22.6%	8.6%	

^a The number of outbreaks is summarized from 1998 to 2020 in the United States.

^b Proportion of leafy outbreaks in all food outbreaks.

Table 2

Attribution results by pathogens: Bacteria between 1998 and 2020 in the United States

	M1 ^b			M2			M3	
Pathogen ^a	no.	Mean	90% CI	no.	Mean	90% CI	Mean	90% CI
Bacillus cereus	125	0.39	0.01-1.18	270	3.14	0.58-6.83	0.30	0.24-0.36
Brucella spp.	6	0.00	0.00-0.00	6	0.00	0.00-0.00	0.00	0.00-0.00
Campylobacter spp.	268	4.43	3.94-5.13	331	6.66	5.78-7.92	2.07	1.90 - 2.23
Clostridium botulinum	50	0.00	0.00-0.00	62	0.00	0.00-0.00	0.00	0.00-0.00
Clostridium perfringens	377	0.16	0.01-0.47	636	0.35	0.17-0.62	0.29	0.22-0.35
STEC 0157:H7	271	32.56	20.30-48.60	341	24.14	21.69-27.66	11.86	11.48-12.23
STEC Non-O157	38	46.94	21.15-65.58	45	21.68	20.33-23.83	22.38	21.90-22.86
Enterotoxigenic E. coli (ETEC)	3	13.92	1.30-32.14	20	5.25	3.40-7.89	12.14	11.76-12.52
Listeria monocytogenes	48	5.13	0.25-16.10	61	2.29	2.22-2.40	1.82	1.66-1.97
Salmonella, nontyphoidal								
(Salmonella spp.)	979	2.47	0.99-4.87	1,478	2.13	1.40-3.18	1.43	1.29-1.56
Shigella, spp.	26	0.07	0.03-0.33	73	14.04	12.31-16.54	3.13	2.92-3.33
Staphylococcus aureus	187	0.00	0.00-0.00	434	0.65	0.05-1.52	0.00	0.00-0.00
Streptococcus spp.	1	0.00	0.00-0.00	3	0.00	0.00-0.00	0.00	0.00-0.00
Vibrio cholerae	11	0.00	0.00-0.00	11	0.00	0.00-0.00	0.00	0.00-0.00
Vibrio parahaemolyticus	173	0.00	0.00-0.00	184	0.05	0.00-0.12	0.00	0.00-0.00
Vibrio vulnificus	2	0.00	0.00-0.00	2	0.00	0.00-0.00	0.00	0.00-0.00
Vibrio spp., other	14	0.00	0.00-0.00	15	0.00	0.00-0.00	0.00	0.00-0.00
Yersinia enterocolitica	10	0.00	0.00-0.00	11	0.00	0.00-0.00	0.00	0.00-0.00
Other bacteria	29	0.00	0.00-0.00	57	0.00	0.00-0.00	0.00	0.00-0.00
All bacterial causes	2,626	5.47	3.44-8.02	4,053	3.92	3.10-5.10	2.33	2.15 - 2.51

^a Pathogens that meet sample size criteria for both simple food and complex food outbreaks in bold. Other pathogens meet simple size criteria for complex food outbreaks only.

^b These models are represented as follows: Interagency Food Safety Analytics Collaboration, 2021 (M1), Triangular distribution-based attribution model adapted from Painter et al., 2013 (M2), and Dirichlet-Multinomial based attribution model adapted from Pires et al., 2019 (M3).

these assumptions are available in Appendix Table D.1. Attribution to bacteria is generally less affected by assumptions compared to parasites. The divergence from base model estimates is greater for parasites, possibly due to the small sample size effects of parasitic outbreaks. In any event, across models and etiologies, differences are generally swamped by the confidence intervals associated with individual model estimates.

Illness Burden. We integrated the illness incidence model with attribution results to investigate the number of illnesses for pairs of pathogens and leafy products using models M1, M2, and M3. Aggregating across all pathogen categories, Table 4 presents the number of illnesses attributed to leafy green subcategories using the estimated attribution percentages. Table D.2 highlights the number of illnesses by the pathogens that meet the sample size criteria in bold.

Table 4 reveals that the lettuce family, including romaine, iceberg, and "other lettuce", are associated with the majority of leafy green-

related foodborne illnesses, ranging from 58.8% to 75.7% across models M1 and M2. Tainted spinach and cabbage are also major sources of illness. Overall, leafy greens contribute to 1.70 million to 2.31 million annual illnesses. Nearly half of these illnesses are attributed to outbreaks with unknown etiologies.

Norovirus is the primarily identified pathogen, followed by STEC, *Salmonella*, and *Campylobacter*, as Appendix Table D.2 demonstrates.

We also examined how leafy green illnesses are distributed across pathogen categories in M1 and M2. Bacterial pathogens account for the largest portion, followed by parasites and viruses. A full set of these estimates are available in Appendix Tables D.3 and D.4.

Economic Burden. We derived estimates for the economic burden of illness by combining estimates from the illness burden model (see Table 4) with the cost model, as described in "Cost Modeling" in Discussion and Appendix C. As shown in Table 5, annual cost estimates of leafy green – associated illnesses are primarily related to the lettuce

Table 3

Attribution results by pathogens: Parasites and Viruses between 1998 and 2020 in the United States

Pathogen ^a	M1 ^b			M2	M2			M3	
	no.	Mean	90% CI	no.	Mean	90% CI	Mean	90% CI	
Cryptosporidium spp.	13	10.44	0.58-29.96	18	4.37	3.36-5.82	5.24	5.24-5.50	
Cyclospora cayetanensis	63	9.20	2.17-20.16	79	8.87	7.66-10.62	6.30	6.02-6.58	
Giardia spp.	7	23.87	1.35-66.05	9	21.72	18.57-26.14	12.73	12.34-13.11	
Trichinella spiralis	21	0.00	0.00-0.00	23	0.00	0.00-0.00	0.00	0.00 - 0.00	
Toxoplasma gondii	3	0.00	0.00-0.00	3	0.00	0.00-0.00	0.00	0.00 - 0.00	
Other Parasites	2	0.00	0.00-0.00	3	0.00	0.00-0.00	0.00	0.00 - 0.00	
All parasitic causes	109	9.05	2.78-18.61	135	8.62	7.41–10.37	5.15	4.89–5.40	
Astrovirus	0	0.00	0.00-0.00	0	0.00	0.00-0.00	0.00	0.00-0.00	
Hepatitis A	24	0.86	0.04-2.55	32	1.67	1.17-2.40	3.30	3.09-3.51	
Norovirus	664	14.08	8.85-21.04	1,958	10.72	4.66-19.44	5.26	5.00 - 5.51	
Rotavirus	5	0.00	0.00-0.00	7	0.00	0.00-0.00	0.00	0.00 - 0.00	
Sapovirus	3	0.00	0.00-0.00	7	12.36	0.94-28.78	0.00	0.00 - 0.00	
Other viruses	15	11.12	2.02-25.79	27	16.51	13.40-20.98	7.45	7.14-7.75	
All viral causes	711	13.07	8.23-19.81	2,031	10.41	4.58-18.79	4.73	4.48-4.98	
Known	3,489	9.18	5.81-15.18	6,334	8.21	6.40-15.21	4.02	3.59-4.43	
Unknown	999	2.14	1.15-4.45	2,475	4.05	1.79-7.30	1.09	0.96 - 1.21	
Total	4,488	3.49	2.05-6.52	8,809	5.20	3.08-7.91	1.66	1.48 - 1.84	

^a Pathogens meeting sample size criteria in bold.

^b These models are represented as follows: Interagency Food Safety Analytics Collaboration, 2021 (M1), Triangular distribution-based attribution model adapted from Painter et al., 2013 (M2), and Dirichlet-Multinomial based attribution model adapted from Pires et al., 2019 (M3).

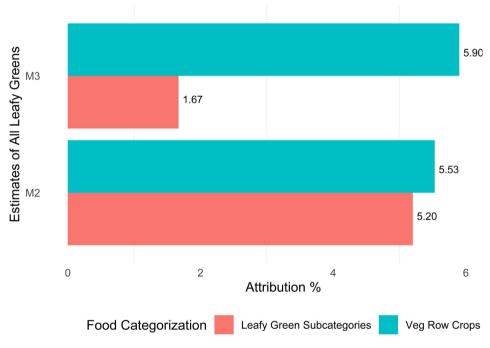


Figure 3. Sensitivity of Leafy Green Attributions to Food Categorization

family. Illnesses associated with "other lettuce" make up the largest category of costs, followed by romaine lettuce or unspecified leafy greens, depending on the attribution model.

Detailed cost estimates by etiology are presented in Appendix Table D.5 for pathogens with sufficiently large sample sizes, finding that illnesses involving unknown etiologies, Norovirus, *Campylobacter* spp., STEC O157:H7, and *Salmonella* (nontyphoidal) represent the largest economic costs from contaminated leafy greens. Across etiology types (see Appendix Tables D.6 and D.7), leafy greens account for costs of \$1,937 million for bacterial, \$204 (90% CI: 13–565) million for parasitic, \$800 million for viral, and \$1,236 million for unknown illnesses annually (based on M1). M2 produces similar results. **Comparison of Burden Estimates.** Attribution, illness, and economic cost estimates represent different measures used to associate illness with foods. Attribution measures the likelihood that a particular illness is associated with a given food and pathogen. Illness measures convert attribution estimates to the aggregate number of persons affected by each pathogen. Finally, measures of economic burden weigh illnesses with a proxy for the severity of illness (cost). As a result, the pathogen with the highest attribution estimate may not have the highest illness or economic burden.

Table 6 summarizes attribution, illness, and cost estimates for major pathogens, along with rankings in each burden category and model. Across all models, STEC O157:H7/Non-O157 and Norovirus illnesses are largely attributed to leafy greens. Attribution of *Shigella*,

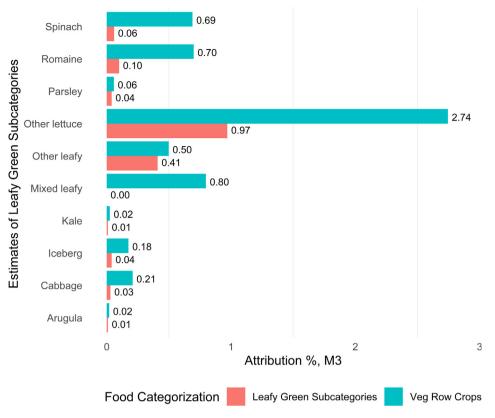


Figure 4. Sensitivity of Leafy Green Subcategory Attributions to Food Categorization, M3

Table 4 The number of illnesses caused by all pathogens attributed to leafy greens per year^a

	# of illnesses	90% CI ^b	% in all leafy	# of illnesses	90% CI	% in all leafy	
Models	M1 ^d			M2			
Lettuce family	1,284,967	(444,998–2,675,127)	75.7	1,357,179	(632,961-2,398,639)	58.8	
Other Lettuce c	1,022,804	(383,758-2,072,926)	60.3	1,195,884	(582,398-2,078,236)	51.8	
Romaine ^c	228,645	(56,712-516,416)	13.5	132,959	(32,076–278,025)	5.8	
Iceberg ^c	33,518	(4,529-85,786)	2.0	28,336	(18,538-42,426)	1.2	
Cabbage	136,591	(1,579-436,759)	8.1	221,661	(50,709-467,442)	9.6	
Spinach	90,721	(12,128-220,415)	5.3	46,053	(12,374–94,478)	2.0	
Kale	6,157	(333–17,987)	0.4	3,002	(2,028–4,402)	0.1	
Parsley	126,434	(7-400,015)	7.5	68,674	(65,729–70,496)	2.9	
Arugula	7,862	(373–23,722)	0.5	1,978	/	0.1	
Other Leafy	44,011	(33,704–64,648)	2.6	309,907	(289,429-339,352)	13.4	
Mixed Leafy	0	/	0	300,093	(6,628–203,282)	13.0	
All Leafy	1,696,756	(1,007,926-3,139,791)	100	2,307,558	(1,077,815-4,075,642)	100	

^a All pathogens include known and unknown pathogens from Scallan et al. (2011).

^b 90% CI is the 90% confidence interval.

^c The estimates of three lettuce subcategories sum up to the estimate of lettuce family.

^d These models are represented as follows: Interagency Food Safety Analytics Collaboration, 2021 (M1), and Triangular distribution-based attribution model adapted from Painter et al., 2013 (M2).

spp. to leafy greens ranks 3rd in M2 but much behind in M1. Despite STEC not being associated with the largest number of illnesses, Norovirus leads in leafy green-associated illnesses, followed by STEC Non-O157, and *Campylobacter* spp. using M1. M2 maintains the same pathogens but alters the order between the two STECs. Additionally, M1 ranks Norovirus, *Campylobacter* spp., STEC O157:H7, and *Salmonella* spp. as the pathogens with the highest economic costs. M2 also lists these pathogens as the top four but in a different sequence. Outbreaks with unknown etiologies are excluded from this table, but "Unknown" would constitute the largest number of illnesses and highest cost category if included.

Discussion

Results in Context. In this study, we employed three attribution models to explore the relationship between leafy greens and foodborne illnesses. We found that leafy greens are responsible for up to 9.18% (90% CI: 5.81–15.18%, M1) of all known pathogen-caused foodborne illnesses, or 2,307,558 (90% CI: 1,077,815–4,075,642) illnesses annually. This leads to health-related costs of up to \$5.278 billion (90% CI: \$3.230–\$8.221 billion), emphasizing the significant burden on health-care and productivity due to the consumption of contaminated leafy greens.

Table 5

Economic Cost of Leafy Green Illnesses (\$million) per year a

	Economic Cost	90% CI ^b	% in all leafy	Economic Cost	90% CI	% in all leafy
	M1 ^d			M2		
Lettuce family	2,925.07	(844.21-6,553.32)	70.0	3,207.24	(2,060.50-4,855.65)	60.8
Other Lettuce ^c	1931.71	(575.07-4300.72)	46.2	2664.07	(1717.83-4024.09)	50.5
Romaine ^c	728.52	(239.20-1529.26)	17.5	377.53	(220.81-602.87)	7.2
Iceberg ^c	264.84	(29.95–723.34)	6.3	165.64	(121.83-228.64)	3.1
Cabbage	310.63	(5.23-980.59)	7.4	401.44	(96.48-839.97)	7.6
Spinach	181.58	(27.88-442.54)	4.3	126.31	(79.12–194.17)	2.4
Kale	30.55	(1.49-89.85)	0.7	11.77	(10.13–14.14)	0.2
Parsley	144.36	(0.08-456.42)	3.5	327.09	(322.15-334.21)	6.2
Arugula	26.01	(1.23–78.49)	0.6	10.92	(6.32–17.55)	0.2
Other Leafy	558.86	(492.06-688.19)	13.4	648.56	(614.50-697.55)	12.3
Mixed Leafy	0	1	0.0	544.60	(41.34–1268.32)	10.3
All Leafy	4177.99	(2324.85-7688.04)	100	5277.95	(3230.48-8221.11)	100

^a The major cost components change in CPI was updated to the March 2023 level and cost estimates from Scharff (2012).

 $^{\rm b}$ 90% CI is the 90% confidence interval.

^c The estimates of three lettuce subcategories sum up to the estimate of lettuce family.

^d These models are represented as follows: Interagency Food Safety Analytics Collaboration, 2021 (M1), and Triangular distribution-based attribution model adapted from Painter et al., 2013 (M2).

Table 6 Leafy Green Attribution, Annual Illnesses, and Annual Economic Costs in the United States

Models	Attribution percentage (Ranking)		# of illnesses (Ra	nking)	Economic Cost (million \$) (Ranking	
	M1 ^e	M2	M1	M2	M1	M2
Pathogen ^a						
Bacillus cereus ^c	0.39 (9)	3.14 (7)	249 (7)	1,993 (7)	0.11 (10)	0.86 (11)
Campylobacter spp.	4.43 (6)	6.66 (6)	37,425 (3)	56,259 (2)	550.64 (2)	827.75 (1)
STEC 0157:H7	32.56 (2)	24.14 (1)	20,561 (5)	15,244 (6)	534.15 (3)	396.02 (4)
STEC Non-O157	46.94 (1)	21.68 (2)	52,931 (2)	24,449 (3)	175.13 (6)	80.89 (7)
Listeria monocytogenes	5.13 (5)	2.29 (8)	82 (9)	36 (10)	188.91 (5)	84.41 (6)
Salmonella, nontyphoidal	2.47 (7)	2.13 (9)	25,356 (4)	21,926 (4)	468.96 (4)	405.52 (3)
Shigella,spp ^b	0.07 (10)	14.04 (3)	91 (8)	18,434 (5)	1.44 (8)	291.83 (5)
Staphylococcus aureus	0.00 (11)	0.65 (11)	0 (11)	1,577 (8)	0.00 (11)	1.75(10)
Vibrio parahaemolyticus	0.00 (11)	0.05 (12)	0 (11)	0 (12)	0.00 (11)	0.00 (12)
Cyclospora cayetanensis	9.20 (4)	8.87 (5)	1,049 (6)	1,012 (9)	6.20 (7)	5.98 (8)
Hepatitis A ^b	0.86 (8)	1.67 (10)	14 (10)	26 (11)	0.92 (9)	1.78 (9)
Norovirus	13.00 (3)	10.72 (4)	710,121 (1)	585,688 (1)	799.42 (1)	659.34 (2)
Giardia spp. ^d	23.87	21.72	18,339	16,690	171.36	155.95

^a Pathogens meet all sample size criteria for both simple food and complex food outbreaks in bold.

^b Pathogens meet simple size criteria for only complex food outbreaks not in bold.

^c the most significant etiologies with respect to attribution percentage, burden of illnesses, and economic costs are in bold.

^d Giardia spp. does not meet the sample size criteria, but we still present the estimates without rankings.

^e These models are represented as follows: Interagency Food Safety Analytics Collaboration, 2021 (M1), and Triangular distribution-based attribution model adapted from Painter et al., 2013 (M2).

The paucity of comprehensive estimates for leafy green attribution limits our ability to make direct comparisons with other studies in the United States. Our estimates are lower than Painter et al.'s (2013) estimates for "leafy", partly because their definition of "leafy" covers a broader group of foods. Additionally, our lower values may be a result of improved surveillance and regulatory successes on leafy greens. In any case, similar to Painter, and other outbreak characterization studies (Kintz et al., 2019; Marshall et al., 2020), we find that leafy greens make up a large portion of *Escherichia coli* outbreaks and illnesses (though low sample size ETEC illnesses are less likely to be attributed to leafy greens in our study). IFSAC (2021), which only covers the broader "vegetable row crop" category, predictably has higher attribution estimates than ours.

Attribution Modeling. Numerous models have been developed to attribute illnesses to foodborne pathogens. In countries with welldeveloped surveillance systems, outbreak-based attribution studies are a feasible method for using routinely collected data to link foods with specific pathogens. Outbreak-based food attribution studies have been published covering many global regions including the United States (IFSAC, 2021; Scharff, 2020; Painter et al., 2013; Hoffmann et al., 2012), Canada (Ravel et al., 2009), Europe (Chanamé Pinedo et al., 2022; Pires et al., 2009; Van Cauteren et al., 2017), Japan (Kumagai et al., 2020), and China (Li et al., 2020), among others. Pires et al. (2019) used outbreak data to examine the larger category "produce" for major global regions, finding lower STEC attribution estimates in the Americas than our study has and even lower estimates for European and Western Pacific regions. Though foodborne illness is a problem everywhere, results from outbreak-based studies differ regionally due to variations in environmental conditions, industry practices, and data quality.

Other modeling approaches have also been used to estimate food attribution for select pathogens. Expert elicitation approaches are widely used where outbreak data is sparse or unreliable. For example, a World Health Organization Study (Hoffmann et al., 2017) used expert elicitation to examine food attribution for 11 pathogens across 14 global regions, including those with only rudimentary surveillance systems. Sapp et al. (2022) used a similar approach to attribute 9 food groups to 7 pathogens in 3 African countries. Expert elicitation has also been used in developed countries to supplement outbreak estimates (e.g. Batz et al., 2012). More recently, improved microbial subtyping of pathogens (e.g. through whole genome sequencing) has allowed for the estimation of attribution estimates for sporadic cases (e.g. Franz et al., 2016; Mughini-Gras et al., 2018, 2022). This approach is promising where widespread testing of all foods and ill humans (in the absence of an outbreak) is conducted and available to researchers.

Consistent with most foodborne illness attribution studies in the United States, we use outbreak data as the basis for our analysis. Within this literature, multiple models have been developed to convert outbreak data to attribution estimates. Each involves making multiple decisions that balance biases inherent in the data. For this reason, we derived attribution estimates based on multiple models including one (M1) that is currently being used by a consortium of experts from the U.S. FDA, USDA, and CDC (IFSAC, 2021), one (M2) that has been the basis for published CDC estimates (Painter et al., 2013), and a highly cited newer model (M3) (Pires et al., 2019) that seeks to improve upon M1 and M2.

The modeling decision of whether to include outbreaks tied to single foods or complex foods is crucial. Limiting to single food/ingredient outbreaks reduces false attributions but underestimates risks from foods typically found as ingredients in complex foods. Three approaches highlighted in this paper represent different approaches to this problem: M1 bases estimates on simple food outbreaks, M2 includes complex foods and their ingredients, and M3 includes complex foods but uses compound probability distributions. While M3 aims to reduce bias, it generates less accurate estimates, especially sensitive to how food categories are defined. Moving from broad categories to specific ones like romaine lettuce reduces matches for specific foods, affecting attribution estimates. This exclusion may technically improve accuracy, but biases result due to overestimations in other categories.

Additionally, leafy green representation in simple food outbreaks is much smaller than in complex food outbreaks. This may mean that leafy greens are safer in simple foods than their presence in complex outbreaks, or it may mean that leafy greens, as one of many ingredients in complex foods, are not as likely to be correctly identified as the single cause of a given outbreak.

Other modeling choices that varied across the models were whether to weigh outbreaks by number of illnesses and whether to discount or omit older outbreaks. Results from alternative specifications of models M1 and M2 can be found in Appendix Table D1.

In conclusion, no attribution model is "perfect" or universally accurate in generating point estimates. M1 that omits the complex food may also bias the attributions. M2's estimates assume a triangular distribution and can be imperfect. However, M1 and M2 are not sensitive to different food categorizations. On the other hand, M3 is extremely sensitive to the size of food ingredients in food categories and hence results in a downward bias in leafy subcategories. Since our main goal is to estimate the leafy greens and leafy subcategories, M1 and M2 are more appropriate for leafy green attributions.

Cost Modeling. Our cost model is based on the enhanced cost of illness model pioneered by Scharff et al., (2009), as updated in Scharff (2020). Costs consist of direct medical costs, lost productivity for caregivers, and indirect nonmedical costs, including estimates for the value of statistical life and QALY losses. This approach is similar to the approach used by the U.S. FDA (Minor et al., 2015) and represents an effort to include all economic costs. Direct costs in our model are similar to those in Hoffmann et al. (2012) which uses a more conservative cost of illness approach but replaces QALY losses with wage-based productivity losses. Recognizing lost quality of life as an important component of economic burden, Hoffmann does report nonmone-tized QALY losses separately. European studies generally use a more conservative cost-of-illness approach (e.g. Tariq et al., 2011; Mangen et al., 2015), generally avoiding the calculation of nonmonetary losses.

We adjusted our cost model to account for the high inflation rate in the United States since April 2021. This has affected all components in the cost model, including medical costs and valuation of mortality risk and QALYs. In response, the cost model has been updated from September 2019 (Scharff, 2020) to March 2023 dollars to reflect changing prices and income. In particular, the U.S. Bureau of Labor Statistics (2023) estimated 12.9%, 7.2%, and 5.0% increases in hospital services, physician services, and pharmaceutical prices to consumers during this period. Productivity and wages also increased by 4.2% and 18.2% over the same period, resulting in higher cost estimates for the value of statistical life, QALY losses, and productivity losses. The inflation trend in the United States differs from the economic circumstances in European countries so the update of our cost estimates only reflects certain macroeconomic circumstances in the U.S.

Limitations and Future Research. Though we believe that the attribution estimates are the best possible given available data and models, we do recognize that there are several limitations associated with our approach. We have already discussed some of the modeling limitations in the section. Most importantly, our dataset is limited to outbreaks that were identified and reported to NORS. Given that only a fraction of foodborne illnesses is linked to identified and reported outbreaks, the NORS data may not accurately represent the entirety of foodborne illnesses. Specifically, the use of outbreaks to estimate attribution across all foodborne illnesses is built on the assumption that outbreaks are roughly representative of sporadic cases. This assumption may be mistaken if outbreaks associated with some foods or pathogens are easier to detect than others. For example, if sporadic outbreaks are more likely to occur on leafy greens than the other food, then we may underestimate the attribution percentage of outbreaks to leafy greens, and vice versa. Moreover, our attribution could underestimate the percentage of leafy greens in viruses among all pathogen categories. There are two reasons: first, bacterial causes of illnesses are generally easier to identify compared to viral causes of illnesses. Second, it is more likely to identify the source of outbreaks for less consumed food or recognized high-risk food. Thus, our attribution estimates, illnesses, and cost of leafy greens to viruses could be lower than the actual numbers because leafy greens are frequently consumed by U.S. consumers and are not "high risk" in bacteria. In the sensitivity analysis, we presented different weights using outbreaks, illnesses, or log illnesses to reflect the impact of a large-size outbreak on the weighted attribution estimates. However, if NORS data do not capture sporadic outbreaks, neither weights shall provide an unbiased attribution estimate though the model is perfectly accurate (Painter et al., 2013). Researchers should be aware of this problem when using attribution estimates.

Another limitation lies in the identification of specific food ingredients in complex foods. The use of recipes to derive the ingredients for these foods likely leads to the incorrect inclusion or omission of foods when the recipe used varies from the standardized recipe. To some extent, future efforts that build on sophisticated techniques such as machine learning may mitigate this problem, though it is likely to remain a problem for the foreseeable future.

The sample size is also a limitation for many of the food pathogen pairs that we examined. Though we have given some guidance on which estimates are more likely to be based on data with sufficient sample size, the actual sample size required depends on the precision of estimates that are needed. As illustrated above, many of the food/pathogen pairs investigated do not have sufficient sample sizes and should be used with caution.

In the future, both new data and attribution models are desired. To some extent, better detection of outbreaks will lead to NORS outbreak surveillance data that is more representative. As for modeling, there may be an opportunity to improve the general approach Pires et al. (2019) used by accounting for the scaling effects that currently introduce bias into the model. In this study, we derive new attribution, burden, and cost estimates for foodborne illnesses associated with leafy greens in the United States. Our primary focus is on the generation of new food attribution estimates for foods across 28 identified pathogens. These are combined with the existing burden of illness estimates (Scallan et al., 2011) and updated economic cost estimates (Scharff, 2020) to more fully capture burdens associated with illnesses from leafy green foods. Though others have examined attribution for the broader category of "produce" or examined the attribution for a single pathogen (e.g., Anderson et al., 2011; Marshall et al., 2020), this is the first study to examine the attribution of illness to leafy greens across a wide range of pathogens and for specific leafy green subcategories.

We believe our estimates are an advance over previous research in two ways. First, we provide attribution estimates for subcategories of leafy greens across a wide range of pathogens. Second, we build upon our attribution estimates to provide illness burden and economic cost estimates. These contributions give industry and government food safety experts a multifaceted tool to evaluate and prioritize risks associated with leafy greens. Attribution estimates, by themselves, can be used to prioritize efforts by those focused on examining a single pathogen. The addition of illness estimates allows for inter-pathogen comparisons of risk. Cost estimates play two roles. First, cost is highly correlated with illness severity and, thus, represents an alternative method of ranking risks by combining illness burden with illness severity. Unlike other risk rankings, cost is an objective measure that does not rely on subjectively assigning weights to various factors. Second, understanding cost is an important input in evaluating the effectiveness of targeted interventions. This is useful for both industry food safety specialists and government regulators.

CRediT authorship contribution statement

Xuerui Yang: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Robert Scharff:** Conceptualization, Data curation, Funding acquisition, Methodology, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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