Original Article

Food Allergy Characteristics Associated With Coexisting Eosinophilic Esophagitis in FARE Registry Participants

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What is already known about this topic? Eosinophilic esophagitis (EoE) and food allergy are important comorbidities, with current literature reporting coexisting food allergy in up to 70% of those with EoE.

What does this article add to our knowledge? Through novel comparison of self-reported food allergy characteristics in registry participants with and without EoE, this study suggests that coexisting EoE is associated with increased food allergies, food-related allergic reactions, and measures of reaction severity.

How does this study impact current management guidelines? The presence of coexisting EoE should be considered in food-allergic patients, especially those with a severe food allergy phenotype; and for those with known coexisting EoE, clinicians should anticipate potential increased health care needs.

BACKGROUND: Eosinophilic esophagitis (EoE) can coexist in individuals with food allergy.
OBJECTIVE: To evaluate the characteristics of food-allergic patients with and without coexisting EoE using a large food allergy patient registry.
METHODS: Data were derived from 2 Food Allergy Research & Education, Inc, Patient Registry surveys. A series of multivariable regression models were used to evaluate associations between demographic, comorbidity, and food allergy characteristics and the likelihood of reporting EoE.
RESULTS: Five percent (n = 309) of registry participants (n = 6074; ages <1 year->80 years, mean, 20.20 ± 15.37 years) reported having EoE. The odds of having EoE were significantly greater in male participants (adjusted odds ratio [aOR], 1.3; 95% CI, 1.04-1.72) and those with comorbid asthma (aOR, 2.0; 95% CI, 1.55-2.49), allergic rhinitis (aOR, 1.8; 95% CI, 1.37-2.22), oral allergy syndrome (aOR, 2.8; 95% CI, 2.09-3.70), food protein−induced enterocolitis syndrome (aOR, 2.5; 95% CI, 1.34-4.84), and hyper-IgE syndrome (aOR, 7.6; 95% CI, 2.93-19.92), though not atopic dermatitis (aOR, 1.3; 95% CI, 0.99-1.59), when adjusting for demographics (sex, age, race, ethnicity, and geographic location). Those with a greater number of food allergies (aOR, 1.3; 95% CI, 1.23-1.32), more frequent food-related allergic reactions (aOR, 1.2; 95% CI, 1.11-1.24), previous anaphylaxis (aOR, 1.5; 95% CI, 1.15-1.83), and health care utilization for food-related allergic reactions (aOR, 1.3; 95% CI, 1.01-1.67)—specifically intensive care unit admission (aOR, 1.2; 95% CI, 1.07-1.33)—were more likely to have EoE after controlling for demographics. However, no significant difference in ever using epinephrine for food-related allergic reactions was detected.
CONCLUSIONS: These self-reported data showed that coexisting EoE is associated with an increased number of food

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Abbreviations used
*Adj.*P- *false-discovery rate−adjusted* P *value*
aOR- adjusted odds ratio
EoE- eosinophilic esophagitis
FARE- Food Allergy Research & Education, Inc

allergies, food-related allergic reactions per year, and measures of reaction severity, calling attention to the likely increased health care needs of food-allergic patients with EoE. **(J Allergy Clin Immunol Pract 2023;11:1509-21)**

Key words: *Eosinophilic esophagitis; Food allergy; Comorbidities; Food allergy patient registry; Food-related allergic reactions*

INTRODUCTION

The coexistence of eosinophilic esophagitis (EoE) and IgE-mediated food allergy is commonly encountered in the clinical setting, though the interplay between these diseases is still incompletely understood. Studies of EoE cohorts indicate that food allergy occurs more frequently in those with EoE,[1-8] and up to approximately 25% experience anaphylaxis.[2,8] In addition, EoE appears to occur significantly more often in those with food allergy, with Hill et al[3] reporting 4.7% of food-allergic patients in their large database having coexisting EoE versus approximately 0.05% to 0.1% in the general population.[7,9,10]

As the field of allergy and immunology has evolved, it has come to recognize "food allergy" as encompassing a wide range of immunologic mechanisms—from the classic IgE-mediated reactions to non−IgE-mediated conditions. As such, EoE could be considered a unique form of food allergy, because it is felt to be food allergen−driven given the frequent success of food elimination diets in achieving disease control.[1,11-17] However, the predominant immune mechanism seems to involve a non−IgE-mediated process—supported by the often inability to identify food triggers with IgE-focused testing and the lack of efficacy of omalizumab (an anti-IgE mAb) in disease management.[13,18-22]

Previous studies have evaluated patients with EoE with and without IgE-mediated food allergy with a primary focus on comparison of EoE characteristics.[23,24] Pelz et al[24] found that those with EoE and food allergy presented at a younger age and had increased EoE-related symptoms—specifically dysphagia, gagging, cough, and poor appetite—compared with those with EoE without food allergy. However, characterization of food allergy in those with EoE is lacking.

Herein, we sought to use the Food Allergy Research & Education, Inc (FARE) Patient Registry[25,26] to evaluate the likelihood of food-allergic participants having EoE given specific personal or food allergy characteristics to determine whether there are associations that may impact the future consideration, evaluation, and management of food allergy in those with EoE. We hypothesized that those with a greater number of food allergies, more severe and frequent food-related allergic reactions, and increased health care utilization for these reactions—potentially representing a more severe food allergy phenotype—would have greater odds of having EoE.

METHODS

Study methods

Food allergy survey data from 6139 participants enrolled in the FARE Patient Registry (for registry details, see this article's Methods section in the Online Repository at www.jaci-inpractice.org) between its launch in May 2017 and data extraction in December 2020 were reviewed. Data were obtained primarily from the FARE Food Allergy History Survey—a 44-item electronic questionnaire eliciting information on demographics; comorbidities; food allergy diagnosis history; specific food allergies (14 major food allergen categories with subcategories when applicable); food-related allergic reaction symptoms, frequency, and treatment; health care utilization; and food allergy resolution. Additional reaction severity data were obtained from the FARE Food Allergy Reactions Survey—a 61-item electronic questionnaire focusing on the participant's most recent food-related allergic reaction (for surveys, see this article's Online Repository at www.jaci-inpractice.org). All registry participants/enrollees were prompted to complete the FARE Food Allergy History Survey. However, additional surveys, such as the FARE Food Allergy Reactions Survey, were completed at the volition of the participant/enrollee. Consequently, the total number of participants who had completed the FARE Food Allergy Reactions Survey was lower ($n = 4676$ participants).

Participants with insufficient data or no apparent food allergy ($n = 65$) were excluded (see this article's Methods section in the Online Repository). All participant responses were taken at face value without additional manual curation. Participants were divided into 2 subsets on the basis of self-report of coexisting EoE—those who selected EoE (+EoE) and those who did not select EoE (−EoE) when asked whether they had been diagnosed with any of a list of conditions.

Statistical analyses

Analyses based on data derived from the FARE Food Allergy History Survey included 6074 participants (+EoE = 309; −EoE = 5765). Only those participants who also had completed the FARE Food Allergy Reactions Survey were included in the reaction severity analyses ($n = 4075$; +EoE = 182; −EoE = 3893). Nominal age range values for ages less than 1 year and more than 80 years were converted to a representative numeric value (see this article's Methods section in the Online Repository). The geographic locations of the participants are presented in detail in the demographics table (Table I), but only the 2 main categories of "United States" and "International" were used during model fitting. Similarly, for race and ethnicity, detailed information is provided in the demographics table, but, because of limited sample sizes, the following categories were used during model fitting: "Asian," "Black or African American," "Multiracial" (representing participants with more than 1 race category selected, not including "Unknown"), "White," and "Other or Unknown." The "Other or Unknown" category included "American Indian or Alaska Native," "Native Hawaiian or Other Pacific Islander," "Unknown," and no entry. Overall, the responses "Unknown," "Prefer not to answer," and no entry were treated as 1 category in all statistical analyses. Responses for reaction severity and number of reactions per year were coded as integers for model fitting. Comorbidities or food allergens that were reported by less than 1% of participants in both study groups were excluded from the analyses and noted in footnotes of the respective tables.

Demographic variables were compared between the −EoE and +EoE subsets using Fisher exact test or Student t test. Furthermore, a series of multivariable logistic regression models in

TABLE I. Demographics of food allergic registry participants with and without coexisting EoE

Demographics	−EoE (n = 5765; 95%)	+EoE (n = 309; 5%)	*P* value*
Sex			
Female	3279 (57)	160 (52)	.087
Male	2486 (43)	149 (48)	
Current age at survey (y)			
Mean ± SD	19.42 ± 18.64	20.20 ± 15.37	.39
Range	0.01-80.00	0.5-78.00	
Age at food allergy diagnosis (y)			
Mean ± SD†	8.82 ± 14.77	8.13 ± 13.37	.38
Range	0.01-76.00	0.01-66.00	
Race			
American Indian/Alaska Native	27 (<1)	0	.045
Asian	221 (4)	3 (1)	
Black/African American	161 (3)	8 (3)	
Multiracial	426 (7)	20 (6)	
Native Hawaiian/Other Pacific Islander	8 (<1)	0	
Unknown/no entry	150 (2)	7 (<1)	
White	4772 (83)	271 (88)	
Ethnicity			
Hispanic/Latino	433 (8)	21 (7)	.77
Not Hispanic/Latino	3861 (67)	204 (66)	
Unknown/prefer not to answer	1471 (26)	84 (1)	
Geographic location			
United States‡	5500 (95)	300 (97)	.20§
Northeast	1423 (25)	69 (23)	
Midwest	1329 (23)	78 (26)	
South	1662 (29)	82 (27)	
West	1050 (18)	69 (23)	
Guam	1 (<1)	0 (<1)	
Puerto Rico	3 (<1)	0 (<1)	
Armed Forces abroad	1 (<1)	1 (<1)	
No state specified	31 (1)	1 (<1)	
Africa	7 (<1)	0	
Asia	22 (1)	1 (<1)	
Australia	10 (<1)	0	
Canada	96 (2)	4 (1)	
Caribbean Islands	6 (<1)	0	
Central America	3 (<1)	0	
Europe	85 (2)	1 (<1)	
Mexico	7 (<1)	3 (1)	
Middle East	13 (<1)	0	
New Zealand	2 (<1)	0	
South America	14 (<1)	0	

Values are n (%) unless otherwise indicated.
**P* values obtained by *t* test for continuous variables and Fisher exact test for categorical variables.
†−EoE n = 5557 and +EoE n = 304 for this variable due to missing data.
‡Regions of the United States as defined by the US Census Bureau.
§*P* value represents comparison of US vs international participants.

several stages were used. In the first stage, all demographic variables in Table I, except age at food allergy diagnosis, were evaluated in a multivariable logistic regression model with EoE as response variable (glm function from R package stats, version 4.1.0) to estimate independent associations with the probability of EoE. The category with the largest n was used as respective reference during model fitting. Age at food allergy diagnosis was excluded from all regression models because it was missing for 213 participants. In the second stage, 1 multivariable model was fitted for each variable of interest. For this, each variable of interest was added individually as main predictor variable to the demographics base model. That way, the associations between EoE and the individual variables were estimated while controlling for sex, age, race, ethnicity, and geographic location. In the last stage, sets of variables of interest were added as main predictors to the demographics base model. The first set included all comorbidities. The second included all 14 major food allergen categories and "Other" food allergen. A free text field was available for "Other" food allergen, but these data were not manually curated for

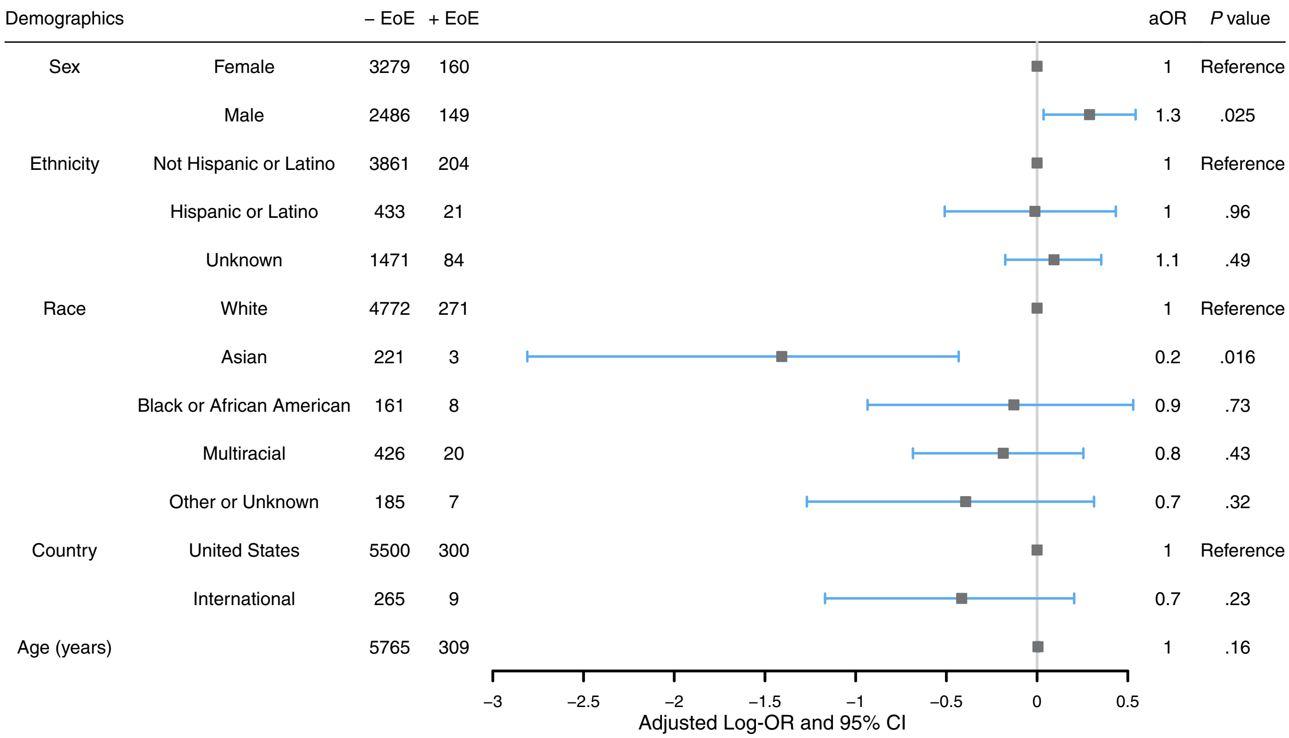

FIGURE 1. Independent associations of demographic characteristics with the odds of reporting coexisting EoE. Evaluation was conducted through a multivariable logistic regression including all shown demographic characteristics. aORs are shown. Log-aOR more than 0 (equivalent to aOR > 1) denotes a higher likelihood of reporting EoE.

the analyses. The results of the last stage as well as the demographics base model were represented as forest plots (R package forestplot, version 2.0.1). Adjusted odds ratios (aORs) with 95% CIs were reported for the independent variables modeled.

All statistical tests were performed 2-sided, and *P* less than .05 was considered significant. The *P* values for the variables of interest from the models in the second stage were adjusted for multiple comparisons within each set of variables represented as 1 table (ie, within all comorbidities) using the Benjamini and Hochberg approach to control the false discovery rate. False discovery rate−adjusted *P* (Adj.*P*) values less than .05 were considered significant. In these cases, 95% CIs were not adjusted for multiplicity, and the conclusions were based on the adjusted *P* values and not the CIs.[27] All statistical analyses were performed using R software[28] (version 4.1.0), and plotting of the data was done using the ggplot2 R package (version 3.3.5) unless otherwise stated. Mosaic plots were created using the R package ggmosaic (version 0.3.3).

RESULTS

Study population

A total of 6074 FARE Patient Registry participants were included in the analyses, ranging in age from less than 1 year to more than 80 years, with a mean age of 19.46 ± 18.49 years (median, 13 years). There was an overall slight female predominance (57%, n = 3439). Geographically, most participants reported residing in the United States (95%, n = 5800), with the remaining 5% (n = 274) composed of individuals from international locations (Table I). Race composition was largely White (83%, n = 5043), followed by Multiracial (7%, n = 446), Asian (4%, n = 224), and Black or African American (3%, n = 169). Seven percent (n = 454) identified as Hispanic or Latino; 67% (n = 4065) were not Hispanic or Latino, and the remaining 26% (n = 1555) selected "Unknown" or "Prefer not to answer."

Demographics and comorbidities of food-allergic participants with and without coexisting EoE

Five percent (n = 309) of food-allergic participants reported having coexisting EoE (+EoE); the remaining 95% (n = 5765) did not select EoE as a comorbidity (−EoE) (Table I). Current age at time of survey was not significantly different between subsets (+EoE: mean, 20.20 ± 15.37 years, median, 15 years; −EoE: mean, 19.42 ± 18.64 years, median, 13 years; see Figure E1 in this article's Online Repository at www.jaci-inpractice.org) (*P* = .39), nor was age at food allergy diagnosis (mean +EoE, 8.13 ± 13.37 years, −EoE, 8.82 ± 14.77 years) (*P* = .38). The subsets also did not differ in sex (*P* = .087), with both having a slight female predominance (+EoE female 52% [n = 160], −EoE female 57% [n = 3279]). However, when stratified by whether the enrollee was responding for self or on behalf of another individual, there was a female predominance in the self-responding participants, but a male predominance in the non−self-responding participants (see Figure E2 in this article's Online Repository at www.jaci-inpractice.org). As expected, the reported age was lower for the non−self-respondents (median age, 6 years; interquartile range, 9 years) compared with the self-respondents (median age, 36 years; interquartile range, 25 years). Furthermore, in the non−self-respondents, a significantly (*P* = .026) larger proportion of those with EoE were male (n = 124 [70%]) compared with those without EoE (n = 2163 [62%]). Similarly, in the self-respondents, the proportion of male

TABLE II. Adjusted* odds of EoE for food-allergic registry participants with specific comorbidities

Comorbidities†	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Allergic/immune-mediated conditions				
Allergic rhinitis	2235 (39)	161 (52)	1.8 (1.37-2.22)	3.9×10^{-05}
Asthma	2603 (45)	192 (62)	2.0 (1.55-2.49)	3.0×10^{-07}
Atopic dermatitis	2751 (48)	163 (53)	1.3 (0.99-1.59)	.099
Bee sting allergy	271 (5)	17 (6)	1.2 (0.68-1.96)	.73
Contact dermatitis	785 (14)	55 (18)	1.4 (1.00-1.84)	.092
Drug allergy	1163 (20)	78 (25)	1.4 (1.01-1.81)	.09
Food protein−induced enterocolitis syndrome	85 (1)	11 (4)	2.5 (1.34-4.84)	.014
Hyper-IgE syndrome	16 (<1)	6 (2)	7.6 (2.93-19.92)	1.7×10^{-04}
Latex allergy	375 (7)	28 (9)	1.5 (0.95-2.21)	.12
Mast cell disorder	61 (1)	3 (1)	0.91 (0.28-2.93)	.93
Oral allergy syndrome	582 (10)	72 (23)	2.8 (2.09-3.70)	3.8×10^{-11}
Cardiovascular conditions				
Arrhythmia	135 (2)	17 (6)	2.4 (1.41-4.14)	.0052
Heart defects	96 (2)	6 (2)	1.2 (0.51-2.72)	.79
High blood pressure	305 (5)	18 (6)	0.99 (0.58-1.71)	.98
Hypertension	152 (3)	10 (3)	1.1 (0.57-2.25)	.79
Endocrinologic conditions				
Thyroid disease	291 (5)	16 (5)	0.98 (0.56-1.70)	.96
Type 2 diabetes mellitus	90 (2)	1 (<1)	0.17 (0.02-1.25)	.12
Gastrointestinal conditions				
Celiac disease	139 (2)	12 (4)	1.6 (0.88-2.98)	.17
Gluten sensitivity	369 (6)	40 (13)	2.3 (1.62-3.36)	3.9×10^{-05}
Heartburn	1024 (18)	129 (42)	3.8 (2.92-4.88)	9.3×10^{-23}
Inflammatory bowel disease	62 (1)	10 (3)	3.0 (1.49-5.88)	.0071
Irritable bowel syndrome	436 (8)	29 (9)	1.3 (0.83-1.94)	.37
Lactose intolerance	531 (9)	40 (13)	1.5 (1.06-2.17)	.053
Neuropsychiatric conditions				
Attention deficit/hyperactivity disorder	427 (7)	34 (11)	1.5 (1.01-2.12)	.090
Autism	94 (2)	10 (3)	1.9 (0.98-3.71)	.099
Migraines	686 (12)	51 (17)	1.6 (1.10-2.19)	.030
Oncologic/rheumatologic/musculoskeletal conditions				
Cancer	114 (2)	3 (1)	0.41 (0.13-1.34)	.19
Connective tissue disorder	72 (1)	10 (3)	2.6 (1.32-5.15)	.017
Rheumatoid arthritis	81 (1)	6 (2)	1.4 (0.58-3.21)	.61
Osteoarthritis	215 (4)	11 (4)	0.85 (0.44-1.64)	.75
Other comorbidity	525 (9)	42 (14)	1.6 (1.10-2.17)	.030
No comorbidities	478 (8)	1 (<1)	0.037 (0.0052-0.26)	.0046

FDR, False-discovery rate; *OR*, odds ratio.
*Adjusted for sex, age, race, ethnicity, and geographic location in multivariable logistic regression models.
†"Histamine toxicity," "Stroke," "Heart disease," and "Type 1 diabetes mellitus" excluded because of <1% of participants reporting these comorbidities in both subsets.

participants was greater in the +EoE subset (n = 25 [19%]) than in the −EoE subset (n = 318 [14%]), though the difference did not reach statistical significance ($P = .13$).

To study the odds of reporting EoE when taking all demographic variables into account, a multivariable logistic regression including sex, age, race, ethnicity, and geographic location was used (Figure 1). In this model, male participants were more likely than female participants to have EoE ($P = .025$; aOR, 1.3; 95% CI, 1.04-1.72), and those who identified as Asian were less likely to report EoE than those who identified as White ($P = .016$; aOR, 0.24; 95% CI, 0.078-0.77)—both consistent with previous literature.[3,7,8,29−35] All further reported aORs were adjusted for these demographic factors (sex, age, race, ethnicity, and geographic location).

In analysis of participant personal characteristics, having a close relative (parent or sibling) with history of food allergy was associated with coexisting EoE ($P = 3.5 \times 10^{-09}$; aOR, 2.1; 95% CI, 1.63-2.66). The odds of having EoE were also higher for participants reporting several allergic/immune-mediated comorbidities, including asthma ($Adj.P = 3.0 \times 10^{-07}$; aOR, 2.0; 95% CI, 1.55-2.49), allergic rhinitis ($Adj.P = 3.9 \times 10^{-05}$; aOR, 1.8; 95% CI, 1.37-2.22), oral allergy syndrome ($Adj.P = 3.8 \times 10^{-11}$; aOR, 2.8; 95% CI, 2.09-3.70), food protein−induced enterocolitis syndrome ($Adj.P = .014$; aOR, 2.5; 95% CI, 1.34-4.84), and hyper-IgE syndrome ($Adj.P = 1.7 \times 10^{-04}$; aOR, 7.6; 95% CI, 2.93-19.92) after controlling for sex, age, race, ethnicity, and geographic location (Table II). However, notably, there was no significant difference in

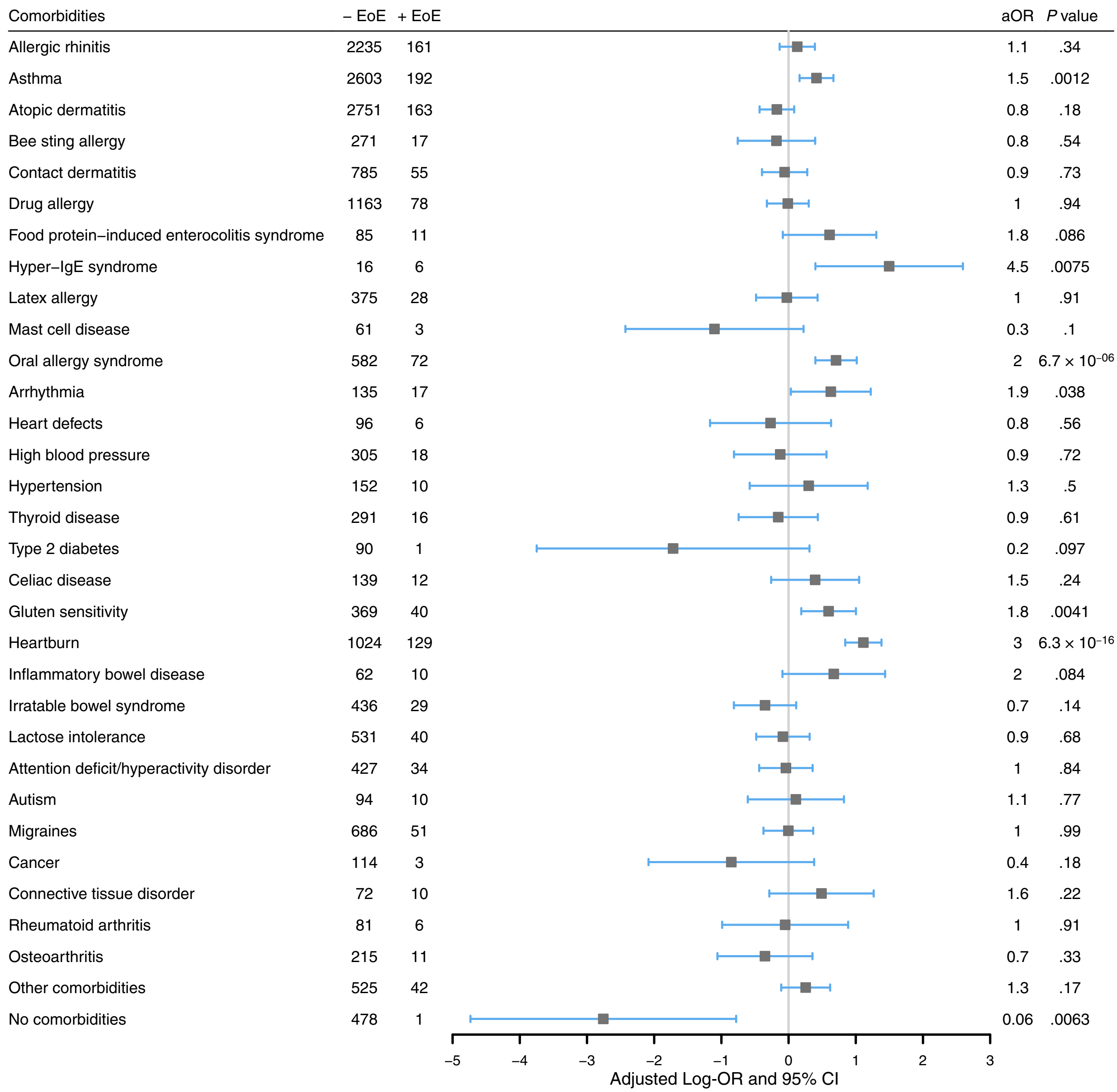

FIGURE 2. Independent associations between comorbidities and reported EoE. An aOR above 1 (equivalent to an adjusted log-OR above 0; gray line) denotes higher odds of reporting EoE. One multivariable logistic regression model with all 32 shown comorbidity categories was fit while also controlling for sex, age, race, ethnicity, and geographic location. *OR*, Odds ratio.

comorbid atopic dermatitis (Adj.P = .099; aOR, 1.3; 95% CI, 0.99-1.59). Although total numbers were low, it was additionally noted that several nonatopic conditions were associated with having EoE as well, such as arrhythmias and migraines (Table II). Only 1 of the participants with EoE reported having no comorbidities besides food allergy, whereas 478 participants without EoE reported no additional comorbidities (Adj.P = .0046; aOR, 0.037; 95% CI, 0.0052-0.26).

To identify comorbidities that were independently associated with reporting EoE, a multivariable logistic regression analysis including demographic variables and all comorbidities was performed (Figure 2). Several of the comorbidities that were found to be associated with having EoE while not controlling for the other comorbidities also resulted in higher odds of EoE in this assessment. Specifically, participants who reported asthma (P = .0012; aOR, 1.5; 95% CI, 1.18-1.95), hyper-IgE syndrome (P = .0075; aOR, 4.5; 95% CI, 1.49-13.40), oral allergy syndrome ($P = 6.7 \times 10^{-06}$; aOR, 2.0; 95% CI, 1.49-2.76), arrhythmia (P = .038; aOR, 1.9; 95% CI, 1.03-3.40), gluten sensitivity (P = .0041; aOR, 1.8; 95% CI, 1.21-2.73), or heartburn ($P = 6.3 \times 10^{-16}$; aOR, 3.0; 95% CI, 2.32-3.99) were more likely to report EoE after adjustment for the other comorbidities and demographic variables.

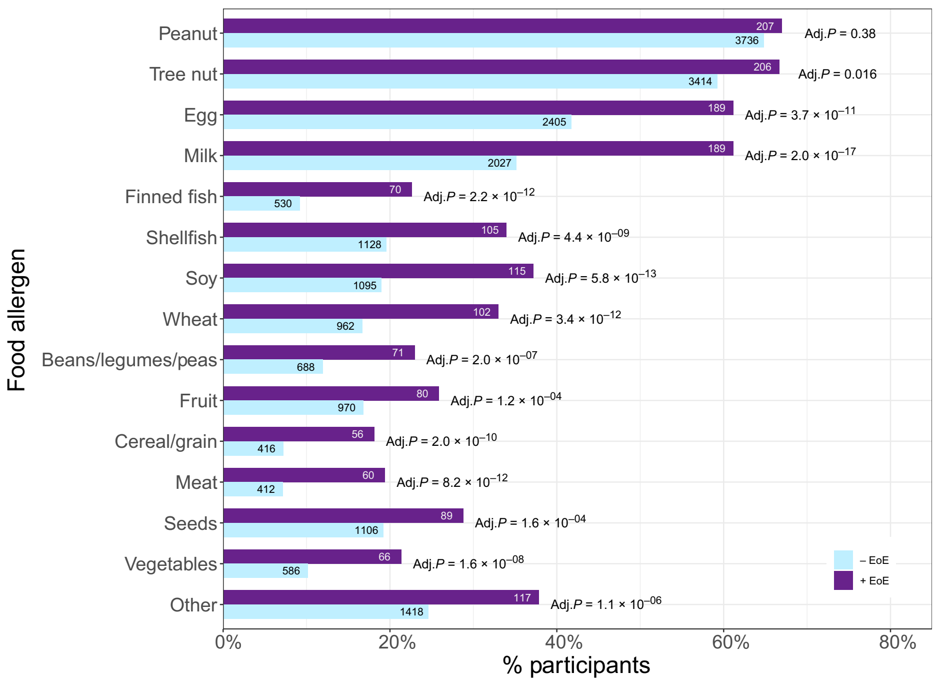

FIGURE 3. Percentage reporting allergies to the major food allergen categories. Percentage of participants in the −EoE (n = 5765) and +EoE (n = 309) subsets that reported allergy to the major food allergen categories or "Other" food allergen. For each food allergen category, a multivariable logistic regression model was fitted adjusting for demographic data (sex, age, race, ethnicity, and geographic location). *FDR*, False discovery rate. FDR-adjusted *P* values are shown.

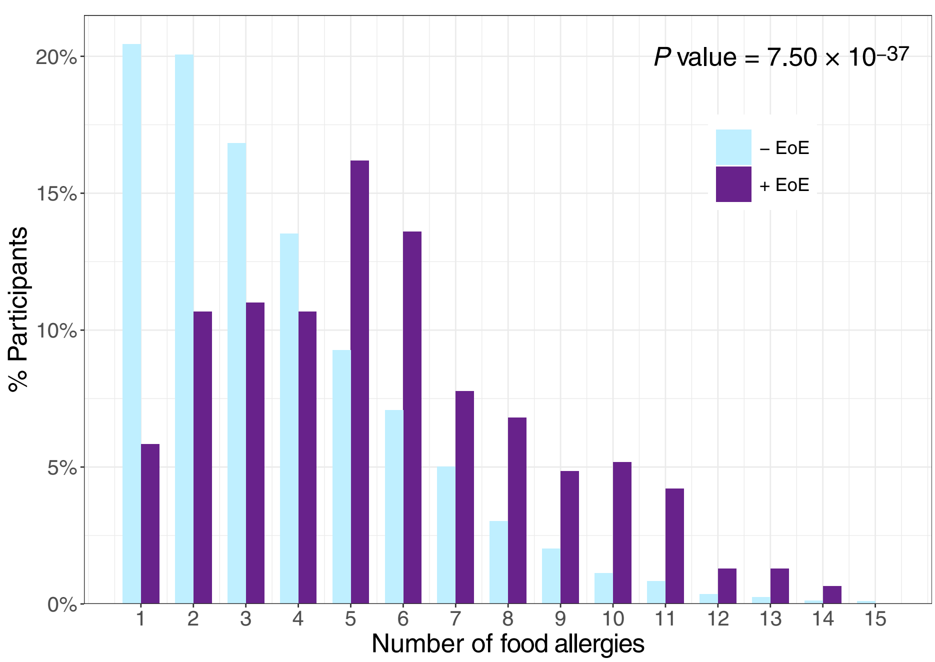

FIGURE 4. Number of major food allergies. The percentage of each study population reporting n number of allergies to the major food allergen categories or "Other." The mean number of food allergies for the −EoE and +EoE subsets is 3.62 and 5.57, respectively (aOR, 1.3; 95% CI, 1.23-1.32). Significance and odds ratio determined by multivariable logistic regression with adjustment for demographics.

Specific food allergies

The 4 most frequently reported major food allergen categories were the same for both +EoE and −EoE subsets—peanut, tree nuts, egg, and milk (Figure 3; see Table E1 in this article's Online Repository at www.jaci-inpractice.org). In individual multivariable logistic regression models for each of the major

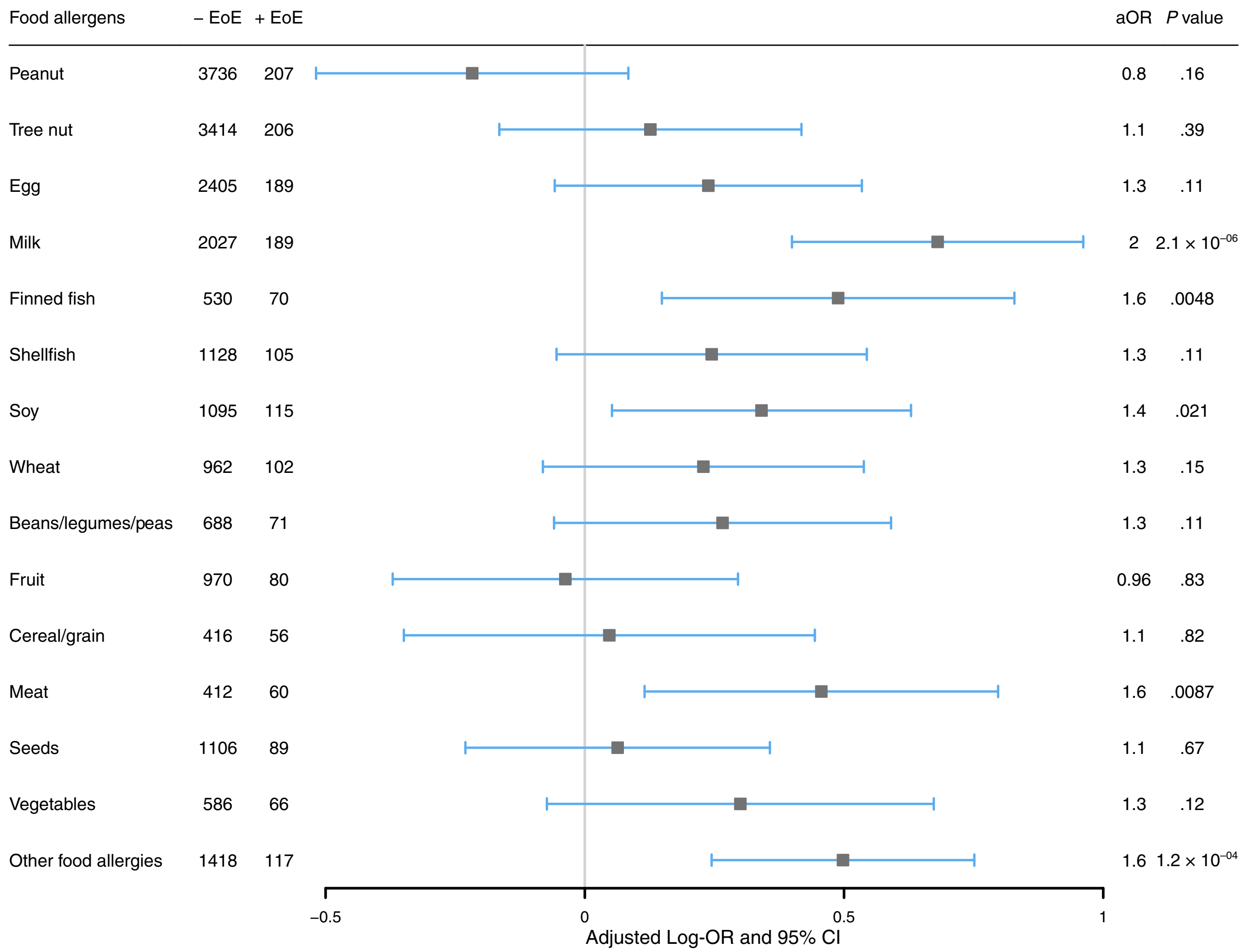

FIGURE 5. Independent associations between food allergen categories and reported EoE. An aOR above 1 (equivalent to an adjusted log-OR above 0; gray line) denotes a higher likelihood of reporting EoE. One multivariable logistic regression model with all 14 major food allergen categories and "Other" was fit while also controlling for demographic variables. *OR*, Odds ratio.

food allergen categories with adjustment for demographic variables, participants who reported the respective food allergy for 13 of the 14 major food allergens had higher odds of having EoE (*Adj.P* $<$ .05; Figure 3; Table E1). Peanut was the only major food allergen that showed no significant association with EoE (*Adj.P* $=$ .38; aOR, 1.1; 95% CI, 0.87-1.47). See Table E1 for reported allergies by food allergen subcategories with aORs and 95% CIs. When comparing the number of reported allergies to the 14 major food allergen categories or "Other" food allergen, participants with a greater number of food allergies were more likely to report EoE ($P = 7.5 \times 10^{-37}$; aOR, 1.3; 95% CI, 1.23-1.32) (Figure 4).

Similar to the comorbidity analysis, a multivariable logistic regression evaluation of coexisting EoE was conducted including these food allergen categories and demographic variables as predictors to estimate independent associations of the specific food allergies with reported EoE (Figure 5). The odds of EoE were significantly higher in those who reported an allergy to milk ($P = 2.1 \times 10^{-06}$; aOR, 2.0; 95% CI, 1.49-2.62), finned fish (P = .0048; aOR, 1.6; 95% CI, 1.16-2.29), soy (P = .021; aOR, 1.4; 95% CI, 1.05-1.88), meat (P = .0087; aOR, 1.6; 95% CI, 1.12-2.22), and "Other" foods ($P = 1.2 \times 10^{-04}$; aOR, 1.6; 95% CI, 1.28-2.12) compared with those who did not report these respective food allergies.

Food allergy reaction history and health care utilization

Participants with more frequent food-related allergic reactions per year were more likely to report having EoE than those with less frequent reactions after controlling for demographic variables (Figure 6, *A*; $P = 3.4 \times 10^{-08}$; aOR, 1.2; 95% CI, 1.11-1.24). Conversely, those without EoE were more likely to report never having had a previous food-related allergic reaction. There was no significant difference in the likelihood of having EoE based on self-reported subjective severity of most recent food-related allergic reaction (Figure 6, *B*; P = .15; aOR, 0.78; 95% CI, 0.55-1.10). However, those who reported ever having experienced anaphylaxis (Figure 6, *C*; P = .0015; aOR, 1.5; 95% CI, 1.15-1.83) or using acute health care services (urgent care, emergency department, hospital, or intensive care unit) for food-related allergic reactions (Figure 6, *D*; P = .043; aOR, 1.3; 95% CI, 1.01-1.67)—and specifically the intensive care unit

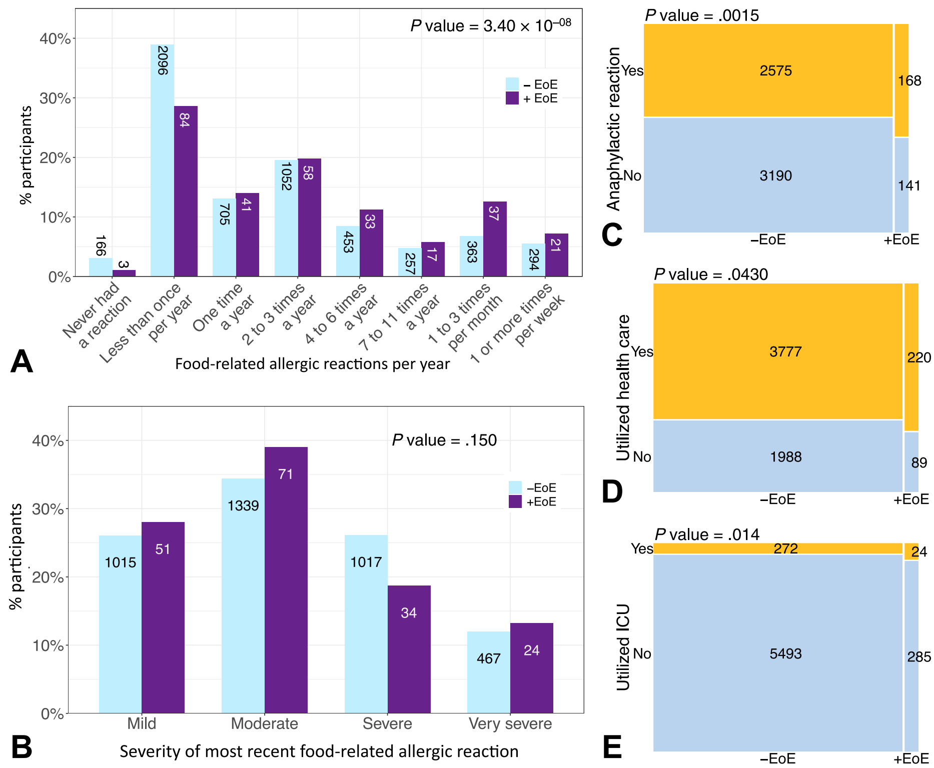

FIGURE 6. Food-related allergic reaction severity by subset. **(A)** Reaction frequency. **(B)** Severity of most recent reaction. Mosaic plots of **(C)** those with/without anaphylaxis, **(D)** those who have/have not used health care (urgent care, emergency department, hospitalization, or intensive care unit [ICU]) for food-related allergic reactions, and **(E)** those who have/have not required ICU admission for food-related allergic reactions. *P* values adjusted for demographics.

(Figure 6, *E*; $P = .014$; aOR, 1.7; 95% CI, 1.09-2.64)—had significantly higher likelihood of having EoE.

When considering food-related allergic reactions, those participants who reported systemic symptoms within 2 hours of eating the food(s), including gastrointestinal, autonomic, and motor involvement, were significantly more likely to have coexisting EoE, whereas those without EoE were more likely to report cutaneous symptoms (Table III). Those with EoE were also more likely to report respiratory symptoms, though this did not reach statistical significance. There was no significant difference between the 2 subsets in ever using intramuscular epinephrine (*Adj.P* = .73; aOR, 0.95; 95% CI, 0.70-1.28) or intravenous epinephrine (*Adj.P* = .10; aOR, 1.4; 95% CI, 0.95-1.99) for food-related allergic reaction management, though participants with EoE were more likely to report use of H1-antagonists (*Adj.P* = .027; aOR, 1.5; 95% CI, 1.07-2.04), H2-antagonists (*Adj.P* = 5.0×10^{-07}; aOR, 2.1; 95% CI, 1.61-2.78), oral corticosteroids (*Adj.P* = 4.2×10^{-04}; aOR, 1.6; 95% CI, 1.25-2.05), bronchodilators (*Adj.P* = 1.9×10^{-06}; aOR, 1.8; 95% CI, 1.45-2.33), and oxygen therapy (*Adj.P* = .0084; aOR, 1.8; 95% CI, 1.20-2.77) for reaction management when controlling for demographic variables.

Food allergy resolution

Thirty-four percent (n = 104) of participants with EoE reported outgrowing any food allergy compared with 29% (n = 1682) of those without EoE, though this difference was not statistically significant (see Table E2 in this article's Online Repository at www.jaci-inpractice.org).

DISCUSSION

Herein, we evaluated the impact of coexisting EoE in a large cohort of individuals with self-reported food allergy. The proportion of participants with reported coexisting EoE (5%) in this registry sample is consistent with previously published food allergy literature.[3] Notably, this study suggests that those with a greater number of food allergies, increased food-related allergic reaction frequency, and increased measures reflective of reaction severity, including history of systemic symptoms and health care utilization for food-related allergic reactions, have greater odds of EoE. Increased use of medications such as bronchodilators and oxygen therapy for reaction management in those with EoE further supports this. In addition, the observed increase in reported intensive care unit admission for food-related allergic reactions in those with EoE may signify more severe systemic disease in this population. However, there was no significant increase in ever using epinephrine for food-related allergic reactions in those with EoE, which may reflect the potential limitation of patient recall in such self-reported survey data. These findings, in combination with the limitations of the data, warrant further research attention.

The increased likelihood of EoE in participants with a greater number of food allergies could be influenced by the potentially

TABLE III. Adjusted* odds of EoE for food-allergic registry participants based on reported reaction symptoms for food-related allergic reactions

Reaction symptoms	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Skin	5060 (88)	230 (74)	0.41 (0.31- 0.54)	3.8×10^{-09}
Hives	3768 (65)	148 (48)	0.47 (0.37-0.59)	6.9×10^{-09}
Itching	3420 (59)	160 (52)	0.75 (0.60- 0.95)	.041
Flushing	2103 (36)	95 (31)	0.76 (0.59- 0.97)	.062
Swelling	2143 (37)	106 (34)	0.89 (0.70- 1.13)	.42
Rash	2797 (49)	122 (39)	0.70 (0.56- 0.89)	.012
Red, itchy, or watery eyes	1938 (34)	105 (34)	1.0 (0.79-1.29)	.93
Other skin manifestations	282 (5)	17 (6)	1.1 (0.69-1.90)	.64
Respiratory	3789 (66)	222 (72)	1.3 (1.04-1.74)	.056
Chest tightening	1318 (23)	94 (30)	1.5 (1.16-1.96)	.0065
Chest pain	407 (7)	53 (17)	2.8 (2.05-3.89)	3.8×10^{-09}
Coughing	1966 (34)	124 (40)	1.3 (1.03-1.65)	.057
Hoarse voice	1117 (19)	81 (26)	1.5 (1.13-1.94)	.012
Nasal congestion/runny nose	1948 (34)	119 (39)	1.2 (0.96-1.54)	.18
Sneezing	923 (16)	66 (21)	1.4 (1.09-1.91)	.027
Trouble breathing	1858 (32)	112 (36)	1.2 (0.94-1.53)	.21
Wheezing	1565 (27)	92 (30)	1.1 (0.88-1.45)	.44
Other respiratory manifestations	*1*96 (3)	8 (3)	0.73 (0.36- 1.50)	.47
Gastrointestinal	4359 (76)	274 (89)	2.6 (1.81-3.73)	1.9×10^{-06}
Bloating	776 (13)	65 (21)	1.9 (1.37-2.53)	4.4×10^{-04}
Bloody stools	92 (2)	6 (2)	1.2 (0.52-2.77)	.71
Constipation	290 (5)	34 (11)	2.4 (1.66-3.56)	3.8×10^{-05}
Diarrhea	1381 (24)	85 (28)	1.2 (0.93-1.58)	.22
Difficulty swallowing	1016 (18)	117 (38)	3.0 (2.36-3.89)	1.7×10^{-16}
Itchy throat/ears	1910 (33)	134 (43)	1.6 (1.25-2.01)	8.2×10^{-04}
Nausea	1710 (30)	129 (42)	1.7 (1.36-2.18)	4.1×10^{-05}
Odd taste	489 (8)	30 (10)	1.2 (0.79-1.74)	.50
Reflux	511 (9)	84 (27)	4.1 (3.13-5.45)	1.3×10^{-21}
Stomach pain/cramps	1770 (31)	140 (45)	2.0 (1.54-2.47)	3.7×10^{-07}
Tingling mouth	1557 (27)	106 (34)	1.4 (1.12-1.84)	.012
Tongue swelling/throat tightness	1511 (26)	108 (35)	1.6 (1.22-2.02)	.0019
Vomiting	2054 (36)	122 (39)	1.2 (0.95-1.52)	.21
Other gastrointestinal manifestations	182 (3)	21 (7)	2.2 (1.37-3.51)	.0042
Cardiovascular	1723 (30)	101 (33)	1.2 (0.90-1.49)	.37
Cardiac arrest	17 (<1)	4 (1)	4.9 (1.61- 14.86)	.014
Chest pain	245 (4)	33 (11)	2.8 (1.91-4.18)	1.9×10^{-06}
Irregular heart rate	285 (5)	22 (7)	1.5 (0.94-2.37)	.15
Lightheadedness/dizziness	967 (17)	61 (20)	1.2 (0.92-1.68)	.22
Low blood pressure	471 (8)	31 (10)	1.2 (0.85-1.83)	.37
Rapid heartbeat	813 (14)	46 (15)	1.1 (0.77-1.49)	.71
Slow heartbeat	83 (1)	9 (3)	2.1 (1.04-4.23)	.072
Turning blue	193 (3)	12 (4)	1.2 (0.66-2.17)	.61
Weak pulse	205 (4)	11 (4)	0.99 (0.53- 1.85)	.98
Other cardiovascular manifestations	100 (2)	3 (1)	0.53 (0.17- 1.69)	.39
Emotional	**4085 (71)**	**244 (79)**	**1.6 (1.19-2.10)**	.0061
Anxiety	2705 (47)	185 (60)	1.7 (1.36-2.2)	4.7×10^{-05}
Confusion	754 (13)	49 (16)	1.3 (0.92-1.73)	.22
Depression	421 (7)	26 (8)	1.2 (0.78-1.81)	.50
Fatigue	1256 (22)	83 (27)	1.3 (1.03-1.74)	.064
Headache	815 (14)	67 (22)	1.8 (1.30-2.36)	9.5×10^{-04}
Irritability	1386 (24)	86 (28)	1.3 (0.97-1.62)	.15
Impending doom	1012 (18)	72 (23)	1.5 (1.09-1.92)	.025
Panic	1527 (26)	94 (30)	1.2 (0.96-1.59)	.16
Sleep disturbance	618 (11)	45 (15)	1.5 (1.04-2.04)	.057

(continued)

TABLE III. *(Continued)*

Reaction symptoms	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Withdrawal	771 (13)	65 (21)	1.8 (1.33-2.37)	5.7×10^{-04}
Other emotional manifestations	248 (4)	10 (3)	0.73 (0.38- 1.39)	.42
Autonomic	1365 (24)	89 (29)	1.4 (1.05-1.77)	.049
Abnormal sweating	532 (9)	34 (11)	1.2 (0.83-1.78)	.41
Dry skin	486 (8)	35 (11)	1.5 (1.03-2.14)	.07
Dehydration	348 (6)	20 (6)	1.1 (0.69-1.78)	.71
Fainting	281 (5)	22 (7)	1.5 (0.98-2.43)	.11
Sexual dysfunction	33 (1)	4 (1)	2.3 (0.79-6.61)	.20
Urinary dysfunction	74 (1)	5 (2)	1.3 (0.52-3.29)	.61
Uterine contractions	34 (1)	4 (1)	2.3 (0.80-6.52)	.21
Weight loss	177 (3)	20 (6)	2.3 (1.42-3.71)	.0030
Other autonomic manifestations	96 (2)	8 (3)	1.6 (0.74-3.25)	.34
Motor	391 (7)	34 (11)	1.8 (1.25-2.68)	.0065
Arm weakness	178 (3)	11 (4)	1.2 (0.65-2.29)	.61
Clawing of toes	48 (1)	4 (1)	1.7 (0.60-4.77)	.41
Leg weakness	237 (4)	22 (7)	1.9 (1.21-3.07)	.014
Muscle wasting	47 (1)	11 (4)	4.9 (2.49-9.72)	3.5×10^{-05}
Other motor manifestations	90 (2)	3 (1)	0.61 (0.19-1.96)	.48

FDR, False-discovery rate; *OR*, odds ratio.
Values are n (%) unless otherwise indicated.
*Adjusted for sex, age, race, ethnicity, and geographic location in multivariable logistic regression models.

higher rate of detected sensitization in those with EoE due to greater likelihood of empiric food allergy panels obtained or inclusion of EoE triggers in reported allergies. However, our finding is consistent with a previous report of increased risk of EoE in those with more than 1 food allergy from a large study with data verified by manual chart review.[3] Of note, our participants both with and without EoE reported allergies to the same 4 foods most frequently (peanut, tree nut, egg, and milk)—reflective of the most common food allergies in the general food allergy population—the top 2 of which are less common EoE triggers, potentially lending support to the data pertaining to true food allergy in this subset.[1,3,12,36,37]

The association between coexisting EoE and increased food-related allergic reaction frequency and severity measures may be a reflection of a truly more severe food allergy phenotype—potentially influenced and compounded by the shared T_H2 pathology.[11,15,17,18,21,38] However, it is also possible that participants/enrollees recalled reaction episodes and health care utilization for food-related EoE exacerbations rather than food-related allergic reactions. Although the reaction symptom data do suggest an increased rate of gastrointestinal and potentially related symptoms (ie, chest pain/tightening) in those with EoE, which could reflect EoE exacerbations, the increased rate of other systemic symptoms would be less consistent with an EoE exacerbation. It is of note that several of the increased systemic symptoms are more subjective in nature and some symptoms, such as chest pain, which was included in the survey as a respiratory or cardiovascular symptom, could also represent a gastrointestinal manifestation. In addition, some symptoms included in the original survey, such as weight loss and muscle wasting, would not be considered manifestations of acute allergic reactions but were retained in the interest of including all possible survey responses.

Of note, there were 169 (3%) participants who reported having food allergy but no previous history of food-related allergic reaction. These participants could have conceivably had food allergy testing in the absence of reaction history (ie, severe atopic dermatitis in children) that was suggestive of significantly high likelihood of reaction and could have consequently been diagnosed with food allergy, though the survey did not elicit this data.

After adjusting for age, race, ethnicity, and geographic location, male participants were 1.3 times as likely as females to report coexisting EoE. In the stratification by self-respondent versus non−self-respondent data, the noted male predominance in the non−self-respondent group and female predominance in the self-respondents are likely a function of age, because non−self-respondents likely represent minors, supported by their lower median age. This pattern of male predominance in children and female predominance in adults has been reflected in the food allergy literature.[3,4,39] Thus, the distribution of sex in the data set followed that expected for food allergy, rather than EoE even within the EoE subset—likely reflective of the biased focus of the survey on those with reported food allergy. There has also been a well-established response bias in survey data, with females being more likely to respond,[40,41] which may have contributed to these distributions, reflected in the self- and non−self-respondents.

The EoE literature demonstrates a strong White predominance, ranging from 62% to 94%.[3,8,9,24,34] With 88% White in the EoE subset, the racial composition of this cohort is consistent with previously reported rates. In addition, the proportion of those with EoE identifying as Hispanic or Latino (7%) is also reflective of previously published findings of 5% to 11%.[24,34]

Finding strong association with atopic diseases in those with EoE—specifically the high rates of comorbid asthma (62%), allergic rhinitis (52%), and atopic dermatitis (53%)—is consistent with previous EoE cohorts.[1,2,7,8,24,38] The significantly greater odds of EoE in those with asthma and allergic rhinitis though not atopic dermatitis are not surprising given the high rate of comorbid atopic dermatitis in those with food allergy in general.[42,43] This strong association provides support for use of more systemic targeting of the shared T_H2 pathology in EoE management.[11,15,17,18,21,38] It is notable that genetic susceptibility to EoE involves the interplay of genetic variants in atopy-associated genes, as well as EoE-specific genes, which likely contributes to the coenrichment of both diseases.[44]

Although previous EoE studies have focused primarily on comorbid asthma, allergic rhinitis, and atopic dermatitis, our study presents novel comparison of the likelihood of EoE in those with other comorbidities—both atopic and nonatopic—notably with higher odds of EoE in those with food protein−induced enterocolitis syndrome, oral allergy syndrome, hyper-IgE syndrome (though very small n and potentially skewed by self-report), inflammatory bowel disease, gluten sensitivity, arrhythmias, connective tissue disorder, and migraines. Previous literature has reported associations between EoE and oral allergy syndrome,[17,45−47] hyper-IgE syndrome,[48,49] inflammatory bowel disease,[50−53] connective tissue disorders,[54,55] mixed findings with food protein−induced enterocolitis syndrome,[56,57] and wheat (gluten) as a known trigger of EoE,[1,3,12,36,37] though an association specifically between EoE and arrhythmias or migraines has not been described. Of note, despite the association with gluten sensitivity, there was no significant association with reported celiac disease, which has been noted in previous literature.[58−60] The reasoning for this is unclear, although this could potentially reflect dietary wheat elimination in these participants.

The conclusions and generalizability of our findings are limited by the nature of the study's cross-sectional design and reliance on unvalidated self-reported data. The study is subject to recall bias and selection bias inherent to voluntary registry enrollment and completion of the surveys. In addition, the survey did not elicit data regarding oral food challenges or biomarkers for food allergy diagnosis, esophagoduodenoscopy for EoE diagnosis, or chronic treatments, which could have implications on the study data, particularly for those with EoE. Likewise, there was no information on disease activity of EoE or the other atopic comorbidities. Furthermore, given the interplay between EoE, food allergy, and other atopic comorbidities, such as asthma, it is possible that the measures of severity could be skewed by respondent inclusion of EoE exacerbations in recall, and that the combination of atopic disorders could be contributing to the observed results.

Overall, this study supports the conclusion that food-allergic patients with coexisting EoE have an increased number of food allergies, food-related allergic reactions, and some measures reflective of increased reaction severity, which could suggest a more severe food allergy phenotype. This information can be used by clinicians to inform their evaluation and management of patients with EoE, tailor their counseling of patients/families, anticipate potential increased health care needs, and ultimately optimize the medical care for this unique patient population.

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ONLINE REPOSITORY

METHODS

FARE Patient Registry

The FARE Patient Registry was developed for the purposes of conducting research on food allergy from self-reported data through an institutional review board–approved study protocol (Advarra, Protocol Pro00022715). Registry participants voluntarily elect to enroll in the FARE Patient Registry via a link on the FARE website (https://www.foodallergy.org). Enrollees were required to be 18 years or older, though adult caregivers can enroll on behalf of children with food allergy and provide information pertaining to their child. Before enrollment completion, enrollees review information on the FARE Patient Registry and its objectives as a research study and voluntarily provide informed assent and/or consent for enrollment.

Exclusions

Participants with demographic information but no additional survey questions completed (n = 19) or no current age (n = 11) were excluded. In addition, participants were excluded if they had no apparent food allergy (n = 35)—signified by selecting "None of the above" for the question, "Has the participant ever been diagnosed by a doctor as allergic to any of the following foods or food groups?" and/or not selecting any of the food allergen categories listed and also selecting "No" for "Does the participant have any food allergies not listed above?"

Statistical analyses

For the purposes of analysis, nominal age range values for ages less than 1 year and more than 80 years were converted to a representative numeric value. The option of "0 to 30 days old" was converted to 0.01, "1 to 3 months old" to 0.25, "4 to 7 months old" to 0.5, "8 to 11 months old" to 0.75, and "80 or more years old" to 80.

In the questionnaire section about symptoms that developed within 2 hours of eating the food or foods that produce an allergic reaction, the questions are grouped by main symptom categories (eg, skin and respiratory); however, the respondents were not directly asked about any of the main category symptoms. To be able to study the association of symptoms of the main categories with coexisting EoE, we counted everyone who selected at least 1 of the specific symptoms or "Other" within 1 main symptom category as having a symptom of that main category.

TABLE E1. Adjusted* odds of coexisting eosinophilic esophagitis for food-allergic registry participants with specific food allergies

Food allergens†	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted P value
Beans/legumes/peas	688 (12)	71 (23)	2.2 (1.67-2.91)	2.0×10^{-07}
Black beans	174 (3)	29 (9)	3.3 (2.18-4.99)	1.4×10^{-07}
Chickpea	403 (7)	33 (11)	1.6 (1.09-2.31)	.027
Green beans	189 (3)	22 (7)	2.2 (1.41-3.53)	.0015
Lentils	356 (6)	38 (12)	2.1 (1.49-3.04)	1.3×10^{-04}
Lima beans	195 (3)	25 (8)	2.5 (1.61-3.86)	1.4×10^{-04}
Navy beans	189 (3)	22 (7)	2.3 (1.42-3.56)	.0014
Red kidney beans	176 (3)	27 (9)	3.0 (1.95-4.56)	2.8×10^{-06}
Peas	439 (8)	55 (18)	2.6 (1.93-3.57)	1.1×10^{-08}
Pinto beans	179 (3)	30 (10)	3.3 (2.19-4.95)	1.1×10^{-07}
Other bean/pea	88 (2)	7 (2)	1.6 (0.71-3.39)	.31
Cereals/grains	416 (7)	56 (18)	3.0 (2.17-4.07)	2.0×10^{-10}
Barley	195 (3)	28 (9)	3.0 (1.94-4.51)	2.8×10^{-06}
Buckwheat	86 (1)	17 (6)	3.9 (2.29-6.78)	4.1×10^{-06}
Corn	169 (3)	22 (7)	2.6 (1.62-4.14)	2.3×10^{-04}
Gluten	156 (3)	22 (7)	2.9 (1.80-4.63)	4.3×10^{-05}
Hops	71 (1)	8 (3)	2.2 (1.03-4.65)	.060
Malt	97 (2)	13 (4)	2.7 (1.46-4.88)	.0031
Millet	54 (1)	10 (3)	3.9 (1.93-7.79)	4.3×10^{-04}
Oat	185 (3)	25 (8)	2.7 (1.77-4.25)	2.9×10^{-05}
Rapeseed	19 (<1)	5 (2)	5.2 (1.90-14.08)	.0029
Rice	73 (1)	16 (5)	4.2 (2.42-7.39)	2.5×10^{-06}
Rye	154 (3)	17 (6)	2.1 (1.27-3.62)	.0082
Spelt	65 (1)	16 (5)	5.1 (2.88-9.06)	2.0×10^{-07}
Wheat	279 (5)	44 (14)	3.4 (2.40-4.81)	9.5×10^{-11}
Other cereal/grain	38 (1)	4 (1)	2.1 (0.73-5.89)	.21
Egg	2405 (42)	189 (61)	2.5 (1.91-3.15)	3.7×10^{-11}
Finned fish	530 (9)	70 (23)	3.0 (2.23-3.95)	2.2×10^{-12}
Anchovies	188 (3)	17 (6)	1.8 (1.04-2.93)	.051
Bass	177 (3)	15 (5)	1.6 (0.94-2.80)	.11
Catfish	193 (3)	16 (5)	1.6 (0.93-2.69)	.12
Cod	284 (5)	33 (11)	2.3 (1.58-3.40)	7.6×10^{-05}
Eel	139 (2)	12 (4)	1.7 (0.90-3.02)	.14
Flounder	196 (3)	15 (5)	1.5 (0.84-2.49)	.21
Haddock	177 (3)	19 (6)	2.1 (1.26-3.38)	.0076
Hake	145 (3)	11 (4)	1.4 (0.76-2.69)	.30
Halibut	198 (3)	20 (6)	2.0 (1.21-3.17)	.011
Herring	159 (3)	13 (4)	1.6 (0.86-2.77)	.18
Mackerel	169 (3)	12 (4)	1.4 (0.75-2.49)	.35
Megrim	136 (2)	11 (4)	1.5 (0.82-2.90)	.21
Perch	165 (3)	13 (4)	1.5 (0.82-2.64)	.22
Plaice	136 (2)	11 (4)	1.5 (0.82-2.89)	.21
Pollock	165 (3)	14 (5)	1.6 (0.91-2.82)	.13
Salmon	304 (5)	36 (12)	2.5 (1.70-3.57)	8.8×10^{-06}
Sardine	169 (3)	11 (4)	1.3 (0.67-2.33)	.52
Snapper	157 (3)	13 (4)	1.6 (0.89-2.84)	.16
Swordfish	157 (3)	11 (4)	1.3 (0.70-2.47)	.43
Tilapia	202 (4)	21 (7)	2.1 (1.30-3.33)	.0046
Trout	193 (3)	15 (5)	1.5 (0.88-2.60)	.18
Tuna	273 (5)	33 (11)	2.5 (1.68-3.64)	2.0×10^{-05}
Whitefish	196 (3)	22 (7)	2.2 (1.39-3.50)	.0019
Other finned fish	77 (1)	9 (3)	2.2 (1.06-4.34)	.050

(continued)

TABLE E1. *(Continued)*

Food allergens†	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Fruit	970 (17)	80 (26)	1.8 (1.36-2.34)	1.2×10^{-04}
Apple	246 (4)	32 (10)	2.7 (1.79-3.98)	7.2×10^{-06}
Apricot	116 (2)	13 (4)	2.1 (1.18-3.87)	.020
Avocado	222 (4)	25 (8)	2.2 (1.45-3.48)	8.8×10^{-04}
Banana	296 (5)	28 (9)	1.8 (1.22-2.78)	.0075
Blackberry	66 (1)	8 (3)	2.3 (1.11-4.96)	.041
Blueberry	80 (1)	11 (4)	2.7 (1.41-5.17)	.0057
Carambola	14 (<1)	4 (1)	5.4 (1.74-16.48)	.0070
Cherry	145 (3)	14 (5)	1.9 (1.06-3.30)	.049
Coconut	152 (3)	18 (6)	2.4 (1.42-3.94)	.0021
Cranberry	40 (1)	6 (2)	2.9 (1.20-6.94)	.028
Currant	19 (<1)	5 (2)	4.8 (1.78-13.10)	.0042
Date	47 (1)	5 (2)	2.0 (0.79-5.12)	.18
Grape	68 (1)	19 (6)	5.5 (3.21-9.26)	4.4×10^{-09}
Grapefruit	89 (2)	8 (3)	1.7 (0.80-3.53)	.21
Guava	43 (1)	6 (2)	2.6 (1.10-6.30)	.046
Kiwifruit	226 (4)	27 (9)	2.4 (1.57-3.66)	1.8×10^{-04}
Lemon	78 (1)	5 (2)	1.2 (0.46-2.91)	.76
Lime	60 (1)	5 (2)	1.5 (0.59-3.77)	.43
Mandarin	63 (1)	6 (2)	1.8 (0.77-4.23)	.21
Mango	186 (3)	22 (7)	2.3 (1.46-3.71)	.0010
Melon	214 (4)	25 (8)	2.4 (1.51-3.66)	4.5×10^{-04}
Orange	167 (3)	12 (4)	1.4 (0.74-2.50)	.35
Papaya	75 (1)	8 (3)	2.0 (0.95-4.27)	.094
Passion fruit	54 (1)	7 (2)	2.5 (1.10-5.54)	.044
Peach	211 (4)	24 (8)	2.3 (1.45-3.54)	9.2×10^{-04}
Pear	127 (2)	16 (5)	2.5 (1.43-4.22)	.0028
Persimmon	30 (1)	4 (1)	2.6 (0.88-7.35)	.12
Pineapple	181 (3)	15 (5)	1.6 (0.90-2.69)	.14
Plum	112 (2)	13 (4)	2.3 (1.27-4.17)	.011
Raspberry	83 (1)	9 (3)	2.1 (1.03-4.24)	.059
Strawberry	235 (4)	24 (8)	2.0 (1.29-3.14)	.0042
Watermelon	196 (3)	24 (8)	2.4 (1.56-3.81)	3.0×10^{-04}
Other fruit	118 (2)	9 (3)	1.4 (0.72-2.87)	.35
Meat	412 (7)	60 (19)	3.1 (2.30-4.26)	8.2×10^{-12}
Beef	293 (5)	41 (13)	2.8 (1.95-3.98)	1.6×10^{-07}
Chicken	106 (2)	33 (11)	6.3 (4.13-9.46)	3.1×10^{-16}
Duck	27 (<1)	5 (2)	3.6 (1.37-9.53)	.016
Elk/moose	72 (1)	5 (2)	1.2 (0.47-3.06)	.71
Gelatin	88 (2)	7 (2)	1.4 (0.64-3.13)	.43
Horse	65 (1)	6 (2)	1.6 (0.68-3.84)	.31
Lamb	144 (2)	13 (4)	1.7 (0.91-2.98)	.13
Pork	179 (3)	31 (10)	3.5 (2.32-5.32)	2.9×10^{-08}
Rabbit	61 (1)	5 (2)	1.4 (0.57-3.67)	.47
Turkey	60 (1)	23 (7)	7.5 (4.53-12.33)	1.8×10^{-13}
Venison	84 (1)	5 (2)	1.0 (0.41-2.61)	.94
Milk	2027 (35)	189 (61)	3.0 (2.36-3.80)	2.0×10^{-17}
Peanut	3736 (65)	207 (67)	1.1 (0.87-1.47)	.38
Seeds	1106 (19)	89 (29)	1.7 (1.32-2.20)	1.6×10^{-04}
Fennel seed	54 (1)	6 (2)	2.2 (0.91-5.06)	.11
Flaxseed	119 (2)	20 (6)	3.3 (2.03-5.42)	8.8×10^{-06}
Mustard seed	182 (3)	20 (6)	2.1 (1.33-3.46)	.0039
Poppy seed	103 (2)	14 (5)	2.6 (1.45-4.56)	.0029
Pumpkin seed	91 (2)	14 (5)	3.0 (1.70-5.41)	5.3×10^{-04}

(continued)

TABLE E1. *(Continued)*

Food allergens†	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Sesame seed	911 (16)	77 (25)	1.8 (1.35-2.31)	1.3×10^{-04}
Sunflower seed	298 (5)	36 (12)	2.4 (1.67-3.50)	1.2×10^{-05}
Other seed	63 (1)	4 (1)	1.2 (0.43-3.31)	.75
Shellfish	1128 (20)	105 (34)	2.2 (1.74-2.89)	4.4×10^{-09}
Clam	493 (9)	38 (12)	1.6 (1.08-2.21)	.028
Crab	696 (12)	60 (19)	1.8 (1.36-2.48)	2.3×10^{-04}
Crayfish	397 (7)	28 (9)	1.4 (0.92-2.09)	.14
Lobster	663 (12)	63 (20)	2.1 (1.53-2.76)	9.1×10^{-06}
Octopus	282 (5)	17 (6)	1.2 (0.70-1.93)	.59
Oyster	455 (8)	31 (10)	1.3 (0.90-1.97)	.19
Scallop	478 (8)	39 (13)	1.6 (1.15-2.34)	.012
Squid	307 (5)	17 (6)	1.1 (0.64-1.77)	.81
Shrimp	866 (15)	73 (24)	1.8 (1.39-2.44)	8.2×10^{-05}
Other shellfish	133 (2)	15 (5)	2.1 (1.24-3.72)	.012
Soy	1095 (19)	115 (37)	2.6 (2.03-3.28)	5.8×10^{-13}
Tree nuts	3414 (59)	206 (67)	1.4 (1.09-1.79)	.016
Almond	2175 (38)	147 (48)	1.5 (1.20-1.90)	.0013
Brazil nut	1795 (31)	113 (37)	1.3 (1.01-1.62)	.066
Cashew	2585 (45)	148 (48)	1.1 (0.90-1.45)	.30
Chestnut	1225 (21)	96 (31)	1.7 (1.30-2.14)	1.9×10^{-04}
Coconut	546 (9)	42 (14)	1.5 (1.09-2.15)	.023
Hazelnut	2193 (38)	140 (45)	1.4 (1.07-1.70)	.019
Macadamia nut	1648 (29)	117 (38)	1.5 (1.20-1.94)	.0013
Pecan	2091 (36)	132 (43)	1.3 (1.04-1.66)	.035
Pine nut	1332 (23)	108 (35)	1.8 (1.41-2.29)	1.1×10^{-05}
Pistachio	2285 (40)	141 (46)	1.3 (1.03-1.64)	.045
Walnut	2381 (41)	152 (49)	1.4 (1.10-1.74)	.011
Other tree nut	157 (3)	9 (3)	1.1 (0.53-2.08)	.90
Vegetables	586 (10)	66 (21)	2.5 (1.87-3.40)	1.6×10^{-08}
Asparagus	37 (1)	6 (2)	3.1 (1.29-7.48)	.020
Broccoli	62 (1)	6 (2)	1.8 (0.78-4.28)	.21
Brussel sprouts	38 (1)	3 (1)	1.5 (0.45-4.84)	.55
Cabbage	50 (1)	5 (2)	1.9 (0.75-4.90)	.21
Carrot	148 (3)	19 (6)	2.5 (1.50-4.08)	.0010
Cauliflower	46 (1)	6 (2)	2.4 (1.01-5.74)	.066
Celery	110 (2)	16 (5)	2.8 (1.64-4.92)	5.5×10^{-04}
Cucumber	87 (2)	13 (4)	2.9 (1.61-5.37)	.0012
Eggplant	78 (1)	6 (2)	1.4 (0.60-3.30)	.46
Lettuce	45 (1)	13 (4)	5.9 (3.10-11.16)	4.5×10^{-07}
Onion	95 (2)	12 (4)	2.6 (1.37-4.80)	.0069
Parsley	24 (<1)	6 (2)	4.9 (1.96-12.09)	.0016
Pepper	90 (2)	6 (2)	1.2 (0.53-2.88)	.64
Sweet potato	42 (1)	12 (4)	5.7 (2.95-11.00)	1.5×10^{-06}
Spinach	41 (1)	7 (2)	3.3 (1.47-7.53)	.0077
Pumpkin, squash	73 (2)	8 (3)	2.1 (0.97-4.33)	.084
Tomato	194 (3)	25 (8)	2.6 (1.68-4.10)	9.6×10^{-05}
White potato	91 (2)	13 (4)	2.8 (1.54-5.17)	.0018
Other vegetable	187 (3)	24 (8)	2.6 (1.63-3.99)	1.6×10^{-04}
Wheat	962 (17)	102 (33)	2.6 (2.01-3.33)	3.4×10^{-12}
Other food allergy	1418 (25)	117 (38)	1.9 (1.51-2.47)	1.1×10^{-06}

EoE, Eosinophilic esophagitis; *FDR*, false-discovery rate; *OR*, odds ratio.
Values are n (%) unless otherwise indicated.
*Adjusted for sex, age, race, ethnicity, and geographic location in multivariable logistic regression models.
†Excluded carob, jackfruit, olive, other meat, bamboo, Brussels sprouts, and beets because of <1% of participants reporting these comorbidities in both subsets.

TABLE E2. Adjusted* odds of coexisting EoE based on reported outgrown food allergies

Outgrown food allergies	−EoE (n = 5765)	+EoE (n = 309)	aOR (95% CI)	FDR-adjusted *P* value
Any food allergies outgrown				
Yes	1682 (29)	104 (34)	1.3 (0.99- 1.65)	.056†
No	3448 (60)	167 (54)		
Unsure	635 (11)	38 (12)		
Outgrown food allergens				
Beans/legumes/peas	113 (2)	14 (5)	2.5 (1.39- 4.35)	.026
Cereals/grains	81 (1)	6 (2)	1.4 (0.61- 3.26)	.86
Egg	669 (12)	36 (12)	0.99 (0.69- 1.41)	.98
Finned fish	72 (1)	9 (3)	2.4 (1.17- 4.81)	.12
Fruit	188 (3)	13 (4)	1.3 (0.72- 2.28)	.86
Meat	85 (1)	15 (5)	3.4 (1.92- 5.95)	6.0×10^{-04}
Milk	478 (8)	28 (9)	1.1 (0.73- 1.62)	.98
Peanut	205 (4)	19 (6)	1.8 (1.08- 2.87)	.12
Seeds	110 (2)	12 (4)	2.0 (1.10- 3.72)	.12
Shellfish	109 (2)	9 (3)	1.5 (0.77- 3.08)	.57
Soy	310 (5)	22 (7)	1.4 (0.87- 2.15)	.49
Tree nuts				
Almond	622 (11)	33 (11)	0.98 (0.68- 1.43)	.98
Brazil nut	298 (5)	15 (5)	0.93 (0.55- 1.59)	.98
Cashew	343 (6)	18 (6)	0.98 (0.60- 1.60)	.98
Chestnut	270 (5)	13 (4)	0.89 (0.50- 1.57)	.98
Coconut	481 (8)	26 (8)	1.0 (0.66- 1.51)	>.99
Hazelnut	395 (7)	18 (6)	0.85 (0.52- 1.39)	.95
Macadamia nut	302 (5)	15 (5)	0.92 (0.54- 1.56)	.98
Pecan	367 (6)	19 (6)	0.96 (0.60- 1.55)	.98
Pine nut	340 (6)	15 (5)	0.80 (0.47- 1.37)	.86
Pistachio	337 (6)	19 (6)	1.1 (0.66- 1.71)	.98
Walnut	381 (7)	18 (6)	0.88 (0.54- 1.43)	.98
Vegetables	89 (2)	9 (3)	2.0 (1.00- 4.03)	.19
Wheat	219 (4)	18 (6)	1.6 (0.96- 2.60)	.23
Other	346 (6)	10 (3)	0.51 (0.27- 0.96)	.16

FDR, False-discovery rate; *OR*, odds ratio.
Values are n (%) unless otherwise indicated.
*Adjusted for sex, age, race, ethnicity, and geographic location in multivariable logistic regression models.
†"Yes" compared with "No" as reference. *P* value is not FDR-adjusted.

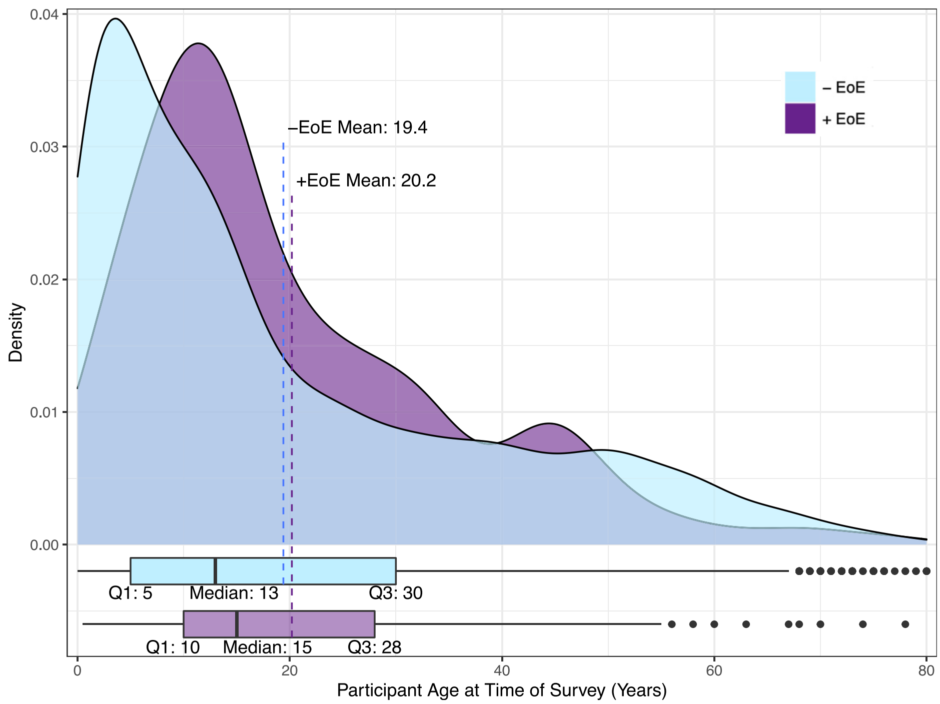

FIGURE E1. Distributions of ages of participants at time of survey by +EoE and -EoE subsets. The median age of participants in the +EoE subset was 15 years and 182 (58.9%) were 18 years or younger at the time of the survey. The median age for participants in the -EoE subset was 13 years with 3600 (62.4%) being 18 years or younger at the time of the survey.

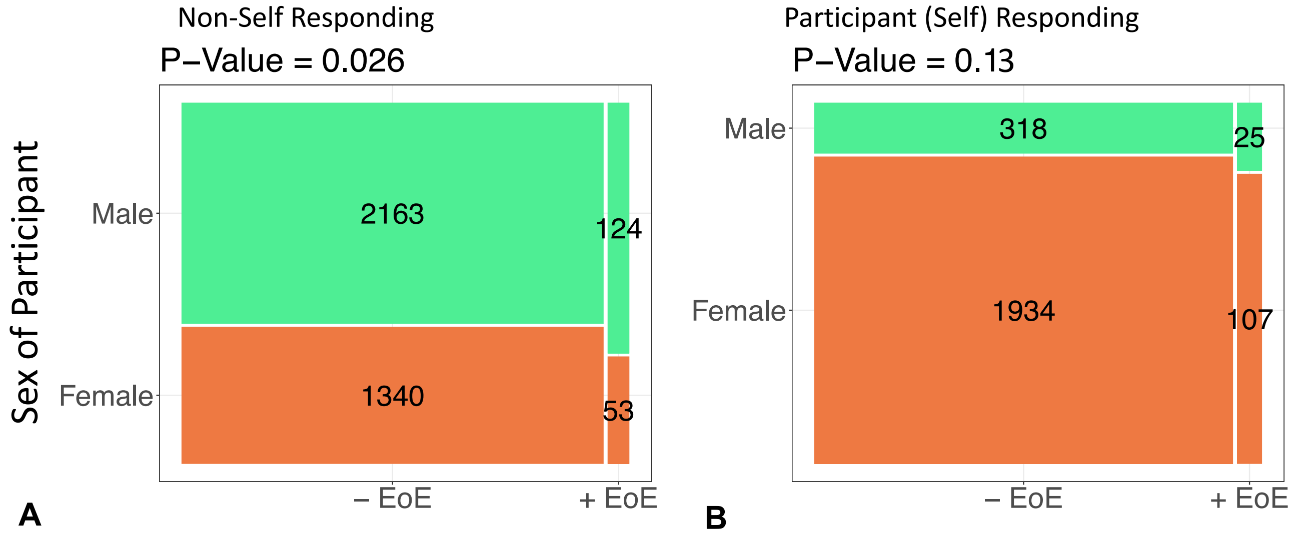

FIGURE E2. Analysis of participant sex based on "Who is completing this survey?" response by +EoE or -EoE subset. (a) Participants whose data was reported by non-self respondents. **(b)** Participants whose data was self-reported. N=6,064; 10 participants in the -EoE subset were removed due to lack of response. There was no significant difference in the percentage of participants with EoE between the self-reporting (5.86% +EoE) and non-self-reporting (5.04% +EoE) subsets (P-value: 0.2093). P-values obtained by Fisher's exact test.