



Relationship Between Housing Components and Development of Eosinophilic Esophagitis

S. RYANNE CORDER¹ · MANASWITA TAPPATA¹ · OLIVIA SHAHEEN¹ · CARY C. COTTON¹ · ELIZABETH T. JENSEN^{1,2} · EVAN S. DELLON^{1,3,4}

Received: 5 August 2019 / Accepted: 9 January 2020
© Springer Science+Business Media, LLC, part of Springer Nature 2020

Abstract

Background While the environment contributes to EoE pathogenesis, few environmental risk factors for EoE have been identified.

Aim To determine whether housing components such as exterior materials, heating systems, and house age are associated with EoE.

Methods This case–control study used the UNC EoE clinicopathologic database to identify newly diagnosed EoE patients. Controls were patients without EoE who underwent endoscopy during the study time frame. Housing data were collected from publicly available online sources, and cases and controls were compared. The primary analysis was restricted to those living at their provided address at the time of diagnostic endoscopy. Multivariable logistical regression estimated associations after adjusting for potential confounders.

Results Of 451 EoE cases and 2421 controls identified, the primary analysis included 158 cases and 769 controls. Compared to controls, EoE cases were more likely to have a house with a brick exterior (35% vs 26%; $p=0.04$), gas heating (14% vs 8%; $p=0.06$), or forced air (57% vs 45%; $p=0.009$). In adjusted analysis, brick exterior was positively associated with EoE diagnosis [aOR 1.83 (95% CI 1.11–3.02)]. The average duration a patient lived in their house before EoE diagnosis was 7.2 ± 5.9 years, while symptom duration prior to diagnosis was 6.8 ± 8.4 years.

Conclusion EoE patients were more likely to have houses with a brick exterior, forced air, or gas heating, and brick exteriors were independently associated with EoE. Since symptoms generally started after moving into a house, housing-related environmental exposures may contribute to EoE disease development.

Keywords Eosinophilic esophagitis · Exposures · Housing · Epidemiology · Risk factors

Introduction

Eosinophilic esophagitis (EoE) is a rare, chronic, allergic disease with significant morbidity and financial burden [1, 2]. It presents with symptoms of esophageal dysfunction. In children, this manifests as failure to thrive, abdominal pain, and emesis, while the primary symptoms in adults include dysphagia, food impaction, and heartburn [3, 4]. Endoscopic features of EoE include esophageal rings, strictures, linear furrows, and white plaques or exudates [4]. Treatments for EoE currently include topical steroids, proton-pump inhibitors, dietary therapies, and endoscopic dilation [5].

The epidemiology of EoE is rapidly evolving, with marked increases in incidence and prevalence over the past two decades that outpace any increases in diagnosis or detection [2, 6]. While some genetic predispositions have been identified [7],

✉ Evan S. Dellon
edellon@med.unc.edu

¹ Center for Esophageal Diseases and Swallowing, UNC-CH, Chapel Hill, NC, USA

² Department of Epidemiology and Prevention, Wake Forest School of Medicine, UNC-CH, Chapel Hill, NC, USA

³ Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, UNC-CH, Chapel Hill, NC, USA

⁴ UNC-CH, CB#7080, Bioinformatics Building, 130 Mason Farm Rd., Chapel Hill, NC 27599-7080, USA

the rising number of cases over a short period of time strongly implicates changing environmental factors as etiologic. In fact, this increase is also noted in other allergic conditions [8]. If these factors are identified and can be removed, this provides potential for treatment or prevention. For example, EoE is believed to be triggered by food allergens in most patients, allowing food elimination diets to serve as a non-pharmacological option for EoE treatment. While these diets can be effective for improving symptoms [9], this is not always the case, and response rates of symptoms, esophageal eosinophil counts, and esophageal fibrosis and remodeling are not universal [10], so other environmental allergens may be implicated. There are limited data on risk factors for EoE. While EoE is an allergic disorder frequently caused by food allergens, the inciting etiological trigger for EoE remains uncertain. Studies of the genetics of EoE have identified several genetic susceptibility loci [11–15], but familial studies suggest that heritability only accounts for a small proportion of disease development and environmental factors predominate [16]. Several prior studies have begun to examine this issue. One hypothesized environmental factor is geography, and a large case–control study found a strong inverse association between EoE and population density, with elevated odds of EoE in areas with lower population density [17]. Another study found that EoE prevalence differed between climate zones with the highest prevalence being found in cold and arid climate zones [18]. There is also seasonal variation in EoE diagnosis suggesting disease exacerbation from aeroallergens [19–21]. Early life exposures such as Cesarean section or early antibiotic use have also been hypothesized to contribute to the development of EoE [22, 23]. In contrast, exposure to the bacterium *Helicobacter pylori* has been inversely associated with EoE [8]. Specific environmental factors that could contribute to the increase in EoE remain unknown.

Because these prior studies have not disentangled the relationships between environmental allergens and EoE, further study in this area is needed to create both a better understanding of disease pathology as well as potentially guiding treatment decisions. One possible, though not yet investigated, source of allergen exposure is in the household. Building materials introduce the potential for chronic exposure to toxicants, heavy metals, and other risk factors such as mold in the home, but these have not been examined in EoE [24–27]. Therefore, the aim of this study was to determine whether there is an association with specific housing components such as exterior materials, heating systems, and house age with EoE.

Methods

Study Design and Population

This was a case–control study conducted using the University of North Carolina EoE Clinicopathologic database from 2001 to 2014, details of which have previously been reported [28–30]. The study was approved by the UNC Institutional Review Board. EoE cases were eligible if they had a new (incident) diagnosis of EoE per consensus guidelines at the time of this study design and conduct. The diagnostic criteria at the time of the study design included the following: symptoms related to esophageal dysfunction, eosinophilic inflammation on biopsy with ≥ 15 eosinophils per high-power field (2–4 biopsies both proximal and distal were recommended), persistent eosinophilia on biopsy after a trial with PPI, and exclusion of secondary causes of esophageal eosinophilia [3, 31]. Controls were patients undergoing endoscopy with esophageal biopsy during the same time frame, who did not have EoE. Of note, patients with Barrett's esophagus referred for ablation were also included in the overall control group to adequately reflect UNC's catchment area and specialty referral patterns for esophageal diseases throughout North Carolina.

Data Collection

Demographic data were extracted from the medical record. In particular, the recorded address at the time of endoscopy (which was the address used for both clinical and billing purposes) was considered the address of record. We extracted residential exposure data from several sources. Data regarding tax values of homes and length of residence were retrospectively extracted from public tax records. Other housing characteristics and exposures were collected from online publicly available resources (e.g., *Zillow*) using standardized case report forms. These exposures included exterior materials (brick, wood, stone, vinyl, or other), heating types (forced air, central, gas, electric, or heat pump), date of original construction (which was further dichotomized at 1978 when leaded household paint was banned), presence of a fireplace (gas or wood burning), and square footage. We were not able to accurately determine water source from publicly available resources, so this could not be included as an exposure. Also, apartments and properties listed as rentals were not included in the primary study as tax records did not provide information regarding time of residence for renters, so the primary analysis was primarily reflective of home owners.

Statistical Analysis

The population for the primary analysis included only subjects whose address listed on the electronic medical record was the address at the time of their EoE diagnostic endoscopy. This was defined by a date of purchase of the residence prior to the date of endoscopy and North Carolina property tax records were used as an aid to confirm residence. A secondary analysis used all cases and controls regardless of whether their current address was the same as their residence at the time of diagnostic endoscopy. Bivariate analysis was performed to identify differences between the case and control groups using the two-sample *t* test to compare means and the Chi-square test to compare proportions, as appropriate. Those variables in which the bivariate analysis demonstrated $p < 0.1$ were included in a multivariable logistic regression model to estimate odds ratios (ORs) and 95% confidence intervals (CIs) after adjusting for potential confounding factors. Analyses were performed using Stata (College Station, TX).

Results

The primary analysis restricted subjects to those living in their residence at the time of EoE diagnosis or endoscopy. There were 158 EoE cases and 769 controls identified who met this criterion. Of the EoE cases, 68% were male and 32% female. The average age of EoE cases was significantly less than that of the control group (30.9 vs 52.2 years; $p < 0.001$). A larger proportion of EoE cases had private health insurance than the control group (76% vs 54%; $p < 0.001$) (Table 1).

The proportion of houses built before 1978 was similar for cases and controls (23% vs 26%; $p < 0.37$). Houses for EoE cases were larger on average than endoscopy controls (2415 sqft $\pm$ 1090 vs 2244 sqft $\pm$ 1071), but this did not reach statistical significance ($p = 0.07$). There was no significant difference in lot size, tax-assessed value, or presence of a fireplace between EoE cases and controls (Table 1).

Compared to controls, EoE cases were more likely to have a house with a brick exterior (35% vs 26%; $p = 0.04$),

Table 1 Demographic and housing characteristic of EoE cases and non-EoE controls, limited to those subjects living at their current residence at the time of EoE diagnosis or endoscopy performance

Characteristic	EoE (<i>n</i> = 158)	Controls (<i>n</i> = 769)	<i>p</i>
Age (mean years $\pm$ SD)	30.9 $\pm$ 17.3	52.2 $\pm$ 15.6	< 0.001
Male (<i>n</i> , %)	108 (68)	309 (40)	< 0.001
White (<i>n</i> , %)	123 (79)	592 (77)	0.83
Insurance (<i>n</i> , %)			< 0.001
Private	116 (76)	417 (54)	
Medicare	3 (2)	202 (26)	
Medicaid	15 (10)	63 (8)	
Military	14 (9)	38 (5)	
Self-pay/uninsured	4 (3)	48 (6)	
House built before 1978 (<i>n</i> , %) (cases <i>n</i> = 157; control <i>n</i> = 750)	36 (23)	198 (26)	0.37
Square feet (mean $\pm$ SD) (cases <i>n</i> = 155; control <i>n</i> = 748)	2415 $\pm$ 1090	2244 $\pm$ 1071	0.07
Lot size in acres (mean $\pm$ SD) (cases <i>n</i> = 149; control <i>n</i> = 705)	1.3 $\pm$ 4.3	1.2 $\pm$ 2.7	0.72
Tax-assessed value (mean \$ $\pm$ SD) (cases <i>n</i> = 93; control <i>n</i> = 420)	320,167 $\pm$ 261,740	280,954 $\pm$ 261,029	0.19
Single family home (<i>n</i> , %) (cases <i>n</i> = 158; control <i>n</i> = 764)	151 (96)	691 (90)	0.38
Exterior type			
Wood (cases <i>n</i> = 126; control <i>n</i> = 542)	36 (29)	138 (25)	0.47
Brick (cases <i>n</i> = 128; control <i>n</i> = 552)	45 (35)	144 (26)	0.04
Stone (cases <i>n</i> = 124; control <i>n</i> = 537)	7 (6)	38 (7)	0.57
Vinyl (cases <i>n</i> = 126; control <i>n</i> = 538)	12 (10)	49 (9)	0.88
Heating type			
Gas (cases <i>n</i> = 125; control <i>n</i> = 542)	17 (14)	44 (8)	0.06
Electric (cases <i>n</i> = 125; control <i>n</i> = 535)	11 (9)	36 (7)	0.42
Forced air (cases <i>n</i> = 135; control <i>n</i> = 574)	77 (57)	258 (45)	0.009
Heat pump (cases <i>n</i> = 125; control <i>n</i> = 564)	27 (22)	145 (26)	0.34
Central (cases <i>n</i> = 124; control <i>n</i> = 554)	12 (10)	66 (12)	0.48
Fireplace (<i>n</i> , %) (cases <i>n</i> = 138; control <i>n</i> = 632)	15 (11)	76 (12)	0.70

gas heating (14% vs 8%; $p=0.06$), or forced air (57% vs 45%; $p=0.009$). In adjusted analysis, brick exterior was positively associated with EoE diagnosis [aOR 1.83 (95% CI 1.11–3.02)]. Gas and forced air heating were also positively associated with EoE after multivariable analysis, but the 95% confidence intervals crossed 1. [aOR 1.56 (95% CI 0.75–3.24) and 1.44 (95% CI 0.91–2.27), respectively; Table 2]. The average duration a patient lived in their house before EoE diagnosis was 7.2 years $\pm$ 5.9. The average length of symptoms a patient reported prior to diagnosis was 6.8 years $\pm$ 8.4.

Table 2 Multivariate logistic regression analysis, limited to those subjects living at their current residence at the time of EoE diagnosis or endoscopy performance

Characteristic	OR	95% CI	aOR ^a	95% CI
Brick	1.54	1.02–2.31	1.83	1.11–3.02
Gas	1.78	0.98–3.24	1.56	0.75–3.24
Forced air	1.65	1.13–2.41	1.44	0.91–2.27

^aAdjusted for age, sex, race, insurance, and house size (in square feet)

In the secondary analysis, which analyzed all cases regardless of whether they lived in their address provided by the medical record at the time of diagnosis, there were 451 EoE cases and 2411 controls. The proportion of houses built before 1978 was significantly less in EoE cases than controls (26% vs 34%; $p=0.002$), and the square footage of the houses was also significantly greater in EoE cases than controls (2307 $\pm$ 1024 sqft vs 2155 $\pm$ 1277 sqft; $p=0.04$) (Table 3). In this analysis, there was not a significant difference in the proportion of houses with brick exteriors from cases compared to controls. Gas (21% vs 12%; $p<0.001$), forced air (56% vs 46%, $p=0.002$), and central heating (20% vs 15%; $p=0.04$) were seen in a greater proportion of EoE cases than controls. Gas was positively associated with an EoE diagnosis in adjusted analysis [aOR 1.93 (1.24–3.01)]. Forced air and central heating were also positively associated with EoE after multivariable analysis but the 95% confidence intervals crossed 1 [aOR 1.27 (0.92–1.77) and 1.18 (0.76–1.83), respectively; Table 4].

Table 3 Secondary analysis of demographic and housing characteristic of the entire study population of EoE cases and non-EoE controls

Characteristic	EoE ($n=451$)	Controls ($n=2411$)	p
Age (mean years $\pm$ SD)	31.2 $\pm$ 18.0	53.6 $\pm$ 17.9	<0.001
Male (n , %)	317 (71)	952 (40)	<0.001
White (n , %)	343 (78)	1810 (75)	0.10
Insurance (n , %)			<0.001
Private	297 (69)	1113 (46)	
Medicare	16 (4)	720 (30)	
Medicaid	67 (16)	293 (12)	
Military	34 (8)	83 (3)	
Self-pay/uninsured	190 (9)	192 (8)	
House built before 1978 (n , %) (cases $n=324$; control $n=1645$)	83 (26)	564 (34)	0.002
Square feet (mean $\pm$ SD) (cases $n=325$; control $n=1651$)	2307 $\pm$ 1024	2155 $\pm$ 1277	0.04
Lot size in acres (mean $\pm$ SD) (cases $n=306$; control $n=1537$)	1.6 $\pm$ 4.1	2.4 $\pm$ 9.7	0.15
Tax-assessed value (mean \$ $\pm$ SD) (cases $n=172$; control $n=947$)	286,000 $\pm$ 228,000	251,445 $\pm$ 245,809	0.09
Single family home (n , %) (cases $n=335$; control $n=1708$)	310 (93)	1512 (89)	0.27
Exterior type			
Wood (cases $n=256$; control $n=1165$)	68 (27)	273 (23)	0.29
Brick (cases $n=264$; control $n=1196$)	78 (30)	359 (30)	0.88
Stone (cases $n=253$; control $n=1153$)	17 (7)	82 (7)	0.83
Vinyl (cases $n=258$; control $n=1163$)	35 (14)	134 (12)	0.36
Heating type			
Gas (cases $n=258$; control $n=1175$)	52 (21)	137 (12)	<0.001
Electric (cases $n=256$; control $n=1154$)	31 (12)	102 (9)	0.11
Forced air (cases $n=277$; control $n=1257$)	155 (56)	575 (46)	0.002
Heat pump (cases $n=255$; control $n=1204$)	61 (24)	307 (26)	0.60
Central (cases $n=260$; control $n=1190$)	53 (20)	181 (15)	0.04
Fireplace (n , %) (cases $n=281$; control $n=1340$)	242 (86)	210 (16)	0.45

Table 4 Secondary multivariate logistic regression analysis of the entire study population of EoE cases and non-EoE controls

Characteristic	OR	95% CI	aOR ^a	95% CI
Gas	2.01	1.41–2.84	1.93	1.24–3.01
Forced air	1.51	1.15–1.96	1.27	0.92–1.77
Central	1.43	1.02–2.01	1.18	0.76–1.83

^aAdjusted for age, sex, race, insurance, and house size (in square feet)

Discussion

The rapid increase in incidence of EoE is not solely due to increased detection and not easily explained by genetic changes [6, 32]. Environmental triggers are therefore strongly hypothesized to play a critical role in the increasing emergence of this disease. However, the relationship between EoE and potential etiologic environmental factors has not yet been fully elucidated. Our study aimed to examine the relationship between housing components and EoE diagnosis, hypothesizing that certain housing materials might predispose to EoE. We found that EoE patients were more likely to have houses with a brick exterior, forced air, or gas heating, and brick exteriors were independently associated with EoE. The secondary analysis, which consisted of a less restricted population, found that EoE patients were more likely to have houses with gas, forced air, and central heating, and gas heating was independently associated with EoE. Notably, the time a patient lived in a house was similar but slightly longer than patient-reported symptom duration prior to the time of diagnosis. This provides a possible temporal association between a new exposure and presumptive disease onset, suggesting that local housing-related environmental exposures could contribute to EoE disease development. Many of the negative findings in our study also contribute to the current body of knowledge regarding risk factors for EoE, as many of the housing components analyzed were similar between cases and controls.

While EoE is an allergic disorder frequently caused by food allergens, the inciting etiological trigger for EoE remains uncertain. Prior studies have shown links between EoE and pollen season, climate zones, and aeroallergens, population density, and early life exposures [17–21, 23, 33]. While other atopic diseases, such as asthma, are strongly linked to indoor environmental exposures such as mold, humidity, housing quality, smoking, and pets [34–37], our study is the first to assess aspects of household exposures in EoE. Though the results are preliminary and will require confirmation with more granular data such as direct collection of household samples and paired biosamples from EoE cases and controls, our results and the timing of symptoms in relation to living in a residence suggests that EoE triggers could be related to the household environment.

There are several limitations to this study. First is the potential for misclassification of data, specifically those collected from online databases. Since the accuracy of the data on public websites is not available, there is the potential that data collected about the housing exposures were misclassified. However, if misclassification did occur, this is likely to be non-differential with respect to case versus control and would bias our results toward the null. Secondly, there were limitations to the study design. It is a retrospective study and thus does not have the ability to control for a full spectrum of confounders as prospective study designs do. Additionally, by only including homeowners in this study, there could be some degree of socioeconomic selection bias. Interestingly, Franciosi et al. [38] showed that after controlling for race demographic data did not differ between EoE cases and controls, so this selection bias may not alter the results of the study. Another limitation is that our associations are somewhat ecologic and do not establish causality. While we have a sense of the general exposure, we do not know the specific building materials used, age of heating systems, whether these were maintained properly, if there were other factors that might influence household exposures, or if there were any changes made to the house that were not reflected in the publicly available data. We also did not have the ability to collect biosamples which would determine which specific components of brick, forced air, and gas heating are related to EoE and the mechanism through which they act. Future research in this area could also look at other household irritants such as mold, pests, and household humidity, as well as specific toxicants that might be contained in the building materials. The data presented in this study and the hypotheses generated here can help guide future study designs. External generalizability could also have limited the utility of this study, as patterns of construction materials and heating sources vary widely in different locations, and our sample was restricted to building patterns in North Carolina. However, the prevalence of EoE also differs geographically. Epidemiological studies have shown that the prevalence of EoE to be significantly lower in Japan than in Western countries [39]. Interestingly, the traditional Japanese house uses primarily wood as the construction material rather than the clay bricks that our study found to be independently associated with EoE. This raises another hypothesis to investigate in future studies.

This study also has significant strengths. An extensive and rigorously constructed database was used that allowed for analysis of a large group of cases as well as an appropriate control group. This study was also strengthened by limiting the primary analysis to those living at their houses at or before the time of EoE diagnosis, to have a temporally appropriate analysis. The secondary analysis did not require patients to currently live at the address in which they lived when their incident EoE diagnosis was made. The results

of the secondary analysis were intended to supplement and strengthen the primary analysis; however, given that it was a more inclusive population, it is not surprising that the secondary analysis did not produce the same results as the primary analysis. Future studies could examine residence at time of symptom onset providing an even more precise picture of environmental triggers.

In conclusion, this study is the first examining the relationship between housing components and EoE. We found that EoE risk is positively associated with gas and forced air heating systems and independently associated with brick exteriors. In addition, the length of time from symptom onset to diagnostic endoscopy was similar to but shorter than the average duration a patient lived in their house before EoE diagnosis, lending further strength and the appropriate temporality to these associations. Overall, this suggests that local housing-related environmental exposures may contribute to EoE disease development. Because housing components have not yet been investigated as risk factors for EoE, this study provides the basis for hypothesis generation for further research to more specifically elucidate the nature of this relationship.

Author's contribution SRC contributed to project conception, study design, data collection, data analysis/interpretation, manuscript drafting, and critical revision. CCC and MT collected data and critically revised the manuscript. ETJ contributed to data interpretation and critical revision. ESD contributed to project conception, study design, data collection, data analysis/interpretation, manuscript drafting, and critical revision. All authors approved the final manuscript.

Funding This study was supported, in part, by NIH T35 DK007386 (SRC; MT), T32 DK007634 (CCC), R01 DK101856 (ESD), and R01 AI39126 (ETJ).

Compliance with Ethical Standards

Conflict of interest None of the authors have relevant disclosures or potential conflicts of interest related to this study.

References

- Jensen ET, Kappelman MD, Martin CF, Dellon ES. Health-care utilization, costs, and the burden of disease related to eosinophilic esophagitis in the United States. *Am J Gastroenterol*. 2015;110:626–632.
- Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology*. 2018;154:e3.
- Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Am J Gastroenterol*. 2013;108:679–692. (quiz 693).
- Dellon ES, Liacouras CA. Advances in clinical management of eosinophilic esophagitis. *Gastroenterology*. 2014;147:1238–1254.
- Straumann A, Katzka DA. Diagnosis and treatment of eosinophilic esophagitis. *Gastroenterology*. 2018;154:346–359.
- Dellon ES, Erichsen R, Baron JA, et al. The increasing incidence and prevalence of eosinophilic oesophagitis outpaces changes in endoscopic and biopsy practice: national population-based estimates from Denmark. *Aliment Pharmacol Ther*. 2015;41:662–670.
- O'Shea KM, Aceves SS, Dellon ES, et al. Pathophysiology of eosinophilic esophagitis. *Gastroenterology*. 2018;154:333–345.
- Jensen ET, Dellon ES. Environmental factors and eosinophilic esophagitis. *J Allergy Clin Immunol*. 2018;142:32–40.
- Arias A, Gonzalez-Cervera J, Tenias JM, Lucendo AJ. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. *Gastroenterology*. 2014;146:1639–1648.
- Kagalwalla AF, Akhtar N, Woodruff SA, et al. Eosinophilic esophagitis: epithelial mesenchymal transition contributes to esophageal remodeling and reverses with treatment. *J Allergy Clin Immunol*. 2012;129:e7.
- Blanchard C, Wang N, Stringer KF, et al. Eotaxin-3 and a uniquely conserved gene-expression profile in eosinophilic esophagitis. *J Clin Invest*. 2006;116:536–547.
- Blanchard C, Wang N, Rothenberg ME. Eosinophilic esophagitis: pathogenesis, genetics, and therapy. *J Allergy Clin Immunol*. 2006;118:1054–1059.
- Rothenberg ME, Spergel JM, Sherrill JD, et al. Common variants at 5q22 associate with pediatric eosinophilic esophagitis. *Nat Genet*. 2010;42:289–291.
- Kottyan LC, Davis BP, Sherrill JD, et al. Genome-wide association analysis of eosinophilic esophagitis provides insight into the tissue specificity of this allergic disease. *Nat Genet*. 2014;46:895–900.
- Sleiman PM, Wang ML, Cianferoni A, et al. GWAS identifies four novel eosinophilic esophagitis loci. *Nat Commun*. 2014;5:5593.
- Alexander ES, Martin LJ, Collins MH, et al. Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis. *J Allergy Clin Immunol*. 2014;134:e1.
- Jensen ET, Hoffman K, Shaheen NJ, Genta RM, Dellon ES. Esophageal eosinophilia is increased in rural areas with low population density: results from a national pathology database. *Am J Gastroenterol*. 2014;109:668–675.
- Hurrell JM, Genta RM, Dellon ES. Prevalence of esophageal eosinophilia varies by climate zone in the United States. *Am J Gastroenterol*. 2012;107:698–706.
- Reed CC, Iglesia EGA, Commings SP, Dellon ES. Seasonal exacerbation of eosinophilic esophagitis histologic activity in adults and children implicates role of aeroallergens. *Ann Allergy Asthma Immunol*. 2019;122:296–301.
- Ram G, Lee J, Ott M, et al. Seasonal exacerbation of esophageal eosinophilia in children with eosinophilic esophagitis and allergic rhinitis. *Ann Allergy Asthma Immunol*. 2015;115:e1.
- Jensen ET, Shah ND, Hoffman K, et al. Seasonal variation in detection of oesophageal eosinophilia and eosinophilic oesophagitis. *Aliment Pharmacol Ther*. 2015;42:461–469.
- Jensen ET, Kappelman MD, Kim HP, Ringel-Kulka T, Dellon ES. Early life exposures as risk factors for pediatric eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr*. 2013;57:67–71.
- Jensen ET, Kuhl JT, Martin LJ, Rothenberg ME, Dellon ES. Prenatal, intrapartum, and postnatal factors are associated with pediatric eosinophilic esophagitis. *J Allergy Clin Immunol*. 2018;141:214–222.
- Zimmer AT, Ha H. People, planet and profit: unintended consequences of legacy building materials. *J Environ Manag*. 2017;204:472–485.
- Dodson RE, Udesky JO, Colton MD, et al. Chemical exposures in recently renovated low-income housing: influence of building materials and occupant activities. *Environ Int*. 2017;109:114–127.

26. Volchek K, Thouin G, Kuang W, et al. The release of lindane from contaminated building materials. *Environ Sci Pollut Res Int*. 2014;21:11844–11855.
27. Huang L, Mo J, Sundell J, Fan Z, Zhang Y. Health risk assessment of inhalation exposure to formaldehyde and benzene in newly remodeled buildings, Beijing. *PLoS ONE*. 2013;8:e79553.
28. Runge TM, Eluri S, Cotton CC, et al. Outcomes of esophageal dilation in eosinophilic esophagitis: safety, efficacy, and persistence of the fibrostenotic phenotype. *Am J Gastroenterol*. 2016;111:206–213.
29. Eluri S, Runge TM, Hansen J, et al. Diminishing effectiveness of long-term maintenance topical steroid therapy in PPI non-responsive eosinophilic esophagitis. *Clin Transl Gastroenterol*. 2017;8:e97.
30. Reed CC, Fan C, Koutlas NT, Shaheen NJ, Dellon ES. Food elimination diets are effective for long-term treatment of adults with eosinophilic oesophagitis. *Aliment Pharmacol Ther*. 2017;46:836–844.
31. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol*. 2011;128:e6. (quiz 21–2).
32. Dellon ES. Epidemiology of eosinophilic esophagitis. *Gastroenterol Clin North Am*. 2014;43:201–218.
33. Moawad FJ, Veerappan GR, Lake JM, et al. Correlation between eosinophilic oesophagitis and aeroallergens. *Aliment Pharmacol Ther*. 2010;31:509–515.
34. Jie Y, Ismail NH, Jie X, Isa ZM. Do indoor environments influence asthma and asthma-related symptoms among adults in homes? A review of the literature. *J Formos Med Assoc*. 2011;110:555–563.
35. Thacher JD, Gruzieva O, Pershagen G, et al. Mold and dampness exposure and allergic outcomes from birth to adolescence: data from the BAMSE cohort. *Allergy*. 2017;72:967–974.
36. Silverman RA, Hasegawa K, Egan DJ, et al. Multicenter study of cigarette smoking among adults with asthma exacerbations in the emergency department, 2011–2012. *Respir Med*. 2017;125:89–91.
37. Matsui EC, Abramson SL, Sandel MT, et al. Indoor environmental control practices and asthma management. *Pediatrics*. 2016;138:e20162589.
38. Franciosi JP, Tam V, Liacouras CA, Spergel JM. A case-control study of sociodemographic and geographic characteristics of 335 children with eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2009;7:415–419.
39. Shoda T, Morita H, Nomura I, et al. Comparison of gene expression profiles in eosinophilic esophagitis (EoE) between Japan and Western countries. *Allergol Int*. 2015;64:260–265.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.