

Risk factors for recurrent anaphylaxis-related emergency department visits in the United States



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ABSTRACT

Background: Anaphylaxis is a potentially life-threatening allergic reaction with a strong risk of recurrence.

Objective: To assess risk factors associated with recurrent anaphylaxis-related emergency department (ED) visits within 1 year of an ED visit for anaphylaxis in a large observational cohort study.

Methods: We used an administrative claims database to identify patients seen from 2008 through 2012 in the ED for anaphylaxis based on an *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code algorithm. Patients with at least 2 years of continuous enrollment in a health plan were included. Multivariable logistic regression analysis was used to determine associations with recurrence of anaphylaxis within 1 year.

Results: During the 5-year study period, 7,367 patients (median age, 42 years; <18 years old, 23.3%) met the inclusion criteria. The most common anaphylaxis trigger was unspecified (56.2%), followed by food (25.3%), medication (14.6%), and venom (3.9%). Overall, 3.0% of patients had an additional anaphylaxis-related ED visit within 1 year (3.61 episodes per 100 patient-years). On multivariable analysis, risk factors associated with anaphylaxis recurrence were food trigger (odds ratio [OR], 2.31; 95% confidence interval [CI], 1.34–3.99), history of asthma (OR, 1.30; 95% CI, 1.13–1.51), and intensive care unit admission at the index anaphylaxis event (OR, 1.95; 95% CI, 1.41–2.69).

Conclusion: In this contemporary cohort study, history of asthma, food trigger, and greater index anaphylaxis severity, as measured by intensive care unit admission, were associated with a higher likelihood of a recurrent anaphylaxis-related ED visit within 1 year.

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Introduction

Anaphylaxis is an acute systemic allergic reaction that may be life-threatening.¹ Patients with a history of anaphylaxis live with a chronic risk of relapse, with the subsequent event being unpredictable. In one of the earliest studies examining anaphylaxis recurrence, Mullins² reported that 1 in 12 patients with anaphylaxis will experience recurrence and 1 in 50 will require adrenaline or hospital attention.

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However, not all patients with anaphylaxis have the same risk for recurrence. As recent studies suggest,^{2–4} food-induced, exercise, and idiopathic anaphylaxis have been associated with a higher risk of relapse compared with drug-induced anaphylaxis. Defining risk factors associated with recurrence is important because it will identify those at highest risk to both patients and practitioners and may guide future interventions to reduce recurrence risk going forward.

To date, few studies have examined anaphylaxis recurrence, and those that have are based on small patient sizes. The objective of this study was to examine the rate of recurrent ED anaphylaxis visits, along with potential risk factors for recurrent ED anaphylaxis visits, within a large contemporary national cohort.

Methods

Data Source

This retrospective study used data from the OptumLabs Data Warehouse,⁵ as previously described.^{6,7} This study involved analysis of preexisting, deidentified data and was deemed exempt from

institutional review and ethics board approval by Mayo. The RECORD (Reporting of Studies Conducted Using Observational Routinely Collected Health Data)⁸ standardized reporting guidelines were followed.

Study Population

To identify the analytic cohort of ED visits for anaphylaxis from 2008 through 2012, we used a previously validated algorithm that includes 2 methods.⁹ Method 1 identified patients who had *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes for anaphylactic shock (995.60–995.69 and 995.0), and method 2 identified patients through a algorithm using ICD-9-CM codes of symptoms combinations necessary to make the diagnosis of anaphylaxis. ED visits identified by both methods were counted only once. Patients were required to have continuous medical insurance and pharmacy coverage for 12 months before and 12 months after the index event (anaphylaxis-related ED visit).

Outcomes and Variables

The primary outcome of interest was a recurrent anaphylaxis-related ED visit within 1 year of the index visit. Potential predictor variables included (1) patient characteristics (age, sex, race/ethnicity, census region); (2) trigger for the allergic reaction; (3) patient comorbid conditions; (4) disposition from the ED, including dismissal home, observation (in the hospital or ED observation unit), inpatient hospital admission to a general ward, and intensive care unit (ICU) admission (including coronary care unit and medical ICU); (5)

self-injectable epinephrine (SIE) dispensed; and 6) allergist/immunologist follow-up. Demographic characteristics, ED disposition, and triggers were obtained from the claim for the index event. Comorbid conditions and ED outcomes (ED discharge or observation within an ED observation unit or in the hospital, non-ICU hospital admission, and ICU admission) were identified by professional claims. Allergy/immunology visits were identified by *Current Procedural Terminology, Fourth Edition* (CPT-4) codes. All professional claims and CPT-4 codes used are listed in eTable 1.¹⁰ Epinephrine autoinjector prescription dispensing was identified by medication names and drug class.

Statistical Analysis

Patient characteristics, comorbid conditions, ED disposition, and follow-up care were reported as counts and percentages. Multivariable logistic regression was used to evaluate independent predictors of 1-year recurrence overall and by age group (children [<18 years old] and adults [≥ 18 years old]). Covariates included age, sex, race/ethnicity, region, trigger, comorbid conditions (cardiac disease, diabetes mellitus, asthma, eczema), ED disposition (discharged, inpatient admission, ICU admission), and follow-up care (office visit to allergist/immunologist, dispensed epinephrine). Sensitivity analyses were planned a priori and included analysis of patient visits identified by method 1 only because these are anaphylaxis-specific codes.

Odds ratios (ORs) are presented with 95% confidence intervals (CIs). All significance tests were 2-sided, and $P < .01$ was considered statistically significant. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc, Cary, North Carolina).

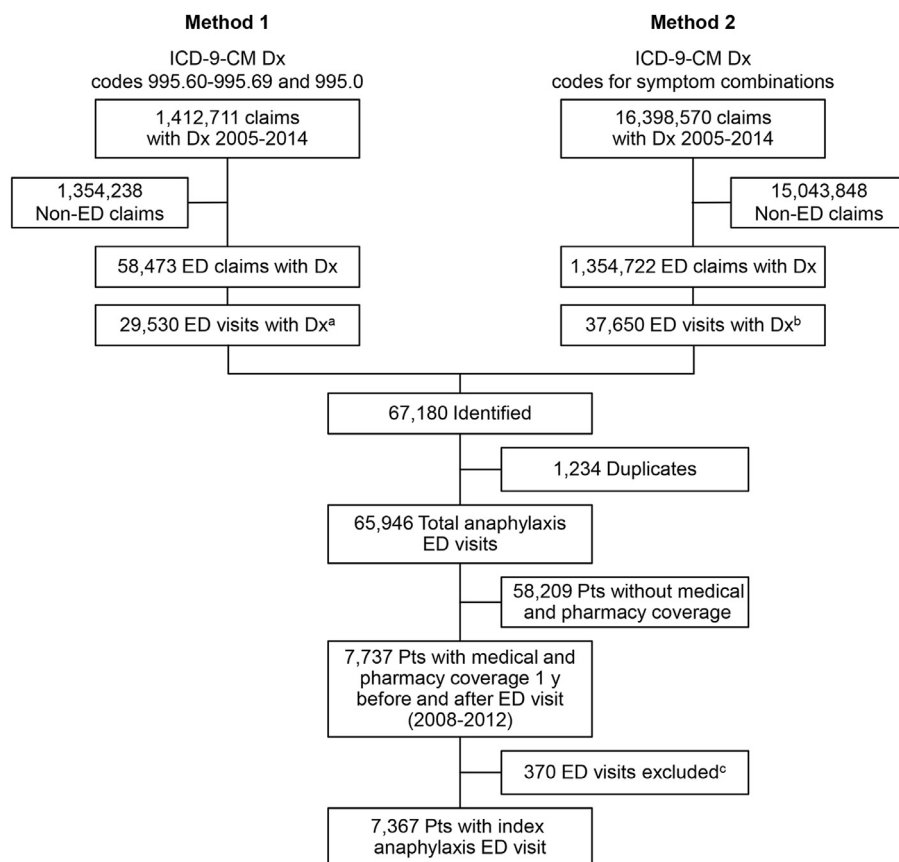


Figure 1. Flowchart of cohort identification. ED indicates emergency department; ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*. Modified from Motosue et al⁷ and used with permission.

^{a,b}More than 1 claim can be associated with a single ED visit.

^cA total of 370 ED visits were excluded because they were not the index ED visit.

Results

During the 5-year study period, among patients with medical and pharmacy coverage for 1 year before and after the index ED event, 7,367 patients had an index ED visit for anaphylaxis (Fig 1). The median age was 42 years (range, 1–87 years), and 22.3% were children and adolescents. More than two-thirds of the patients were white (67.5%), and more than half (58.3%) were female (Table 1). The largest percentage of patients was from the South (48.8%). The most common trigger was unspecified (56.2%), followed by food (25.3%), medication (14.6%), and venom (3.9%).

At the index ED visit for anaphylaxis, most patients (85.7%) were discharged from the ED or observed in the hospital or in ED observation units. The other 14.3% had anaphylaxis that required admission to a general medical unit (7.1%) or ICU level of care (7.2%). In terms of post-ED follow-up care, less than half (45.1%) had SIE dispensed, 28.3% had follow-up with an allergist, and 21% had both allergist follow-up and SIE dispensed (Table 1).

Recurrent Anaphylaxis-Related ED Visits

In the whole cohort, 220 patients (3.0%) had an additional anaphylaxis-related ED visit within 1 year after the index anaphylaxis event. Thus, the rate of first recurrent anaphylaxis-related ED visits was 3.61 episodes per 100 patient-years. The rate was 3.5% in patients younger than 18 years and 2.8% among adults (Table 1). Overall, 10% of recurrences took place within the first week, and 52% had an additional ED visit at least 4 months after the index ED visit (Fig 2).

Risk Factor Analysis

On multivariable logistic regression analysis of the overall cohort, including adults and children, food trigger (OR, 2.31; 95% CI, 1.34–3.99; $P = .003$), history of asthma (OR, 1.30; 95% CI, 1.13–1.51; $P < .001$), and ICU admission during the index anaphylaxis visit (OR, 1.95; 95% CI, 1.41–2.69; $P < .001$) were associated with increased odds of a recurrent anaphylaxis-related ED visit within 1 year (Table 2). Similar findings were observed when adults were analyzed as a separate cohort. However, among children, none of the risk factors examined were significantly associated with recurrent anaphylaxis, although the directionality of the ORs was similar.

Sensitivity Analyses

A sensitivity analysis of patient visits identified by method 1 (anaphylaxis-specific codes) only showed similar significant associations of recurrent anaphylaxis-related ED visit with asthma (eTable 2).

Discussion

In this study examining risk factors for recurrent visits among more than 7,300 index ED visits for anaphylaxis, 3.0% of patients had a recurrent anaphylaxis-related ED visit within 1 year, and the rate was higher in children than in adults. In addition, food trigger, history of asthma, and ICU admission during the index anaphylaxis visit were associated with increased odds of a recurrent anaphylaxis-related ED visit within 1 year.

Our rate of first recurrent anaphylaxis ED visits of 3.61 episodes per 100 patient-years was similar to that published by Lee et al¹¹: a recurrence rate of 2.6 episodes per 100 patient-years from their population-based study in Olmsted County, Minnesota. This rate is also similar to that reported by Tejedor-Alonso et al⁴ (3.2 episodes per 100 patient-years) in their questionnaire-based study sent to patients retrieved from databases of EDs, hospitalized patients, and primary care centers. However, these rates are substantially lower than the calculated rate observed by Mullins² in 2003, who reported a

recurrence rate of 54 episodes per 100 patient-years overall and 10 serious recurrences per 100 patient-years. We suspect this discrepancy is attributable to issues related to referral and sampling bias because the data from the study by Mullins² were based on a questionnaire limited to patients referred to a single allergy/immunology practice and included episodes in which the patient did not seek medical care.

Of the identifiable triggers, food was associated with a higher likelihood of recurrent ED anaphylaxis visits. Similar results were reported in a Spanish questionnaire-based study⁴ of adults and children and 2 prior pediatric based studies.^{3,12} In their pediatric-based study, Gold and Sainsbury³ reported that food-induced anaphylaxis was 4 times as likely to experience anaphylaxis recurrence than children with insect venom anaphylaxis. This finding may reflect the risk of constant exposure associated with a food trigger compared with potentially more limited exposure to other triggers, such as certain venoms that are associated with seasonal exposure and drugs.

Table 1

Demographic and Clinical Characteristics of ED Patients With Anaphylaxis^a

Characteristic	All patients (N=7,367)	Children (Age <18 y) (n = 1,646)	Adults (Age ≥ 18 y) (n = 5,721)
Recurrent anaphylaxis ED visit within 1 year	220 (3.0)	58 (3.5)	162 (2.8)
Total No. of recurrent ED visits	266	66	200
Rate per 100 patient-years	3.61	4.01	3.50
Age, y			
0–4	488 (6.6)	488 (29.6)	NA
5–17	1,158 (15.7)	1,158 (70.4)	NA
18–34	1,269 (17.2)	NA	1,269 (22.2)
35–64	3,218 (43.7)	NA	3,218 (56.2)
≥ 65	1,234 (16.8)	NA	1,234 (21.6)
Race/ethnicity			
Asian	266 (3.6)	108 (6.6)	158 (2.8)
Black	1,123 (15.2)	198 (12.0)	925 (16.2)
Hispanic	723 (9.8)	172 (10.4)	551 (9.6)
White	4,970 (67.5)	1,079 (65.6)	3,891 (68.0)
Unknown	285 (3.9)	89 (5.4)	196 (3.4)
Sex			
Female	4,296 (58.3)	682 (41.4)	3,614 (63.2)
Male	3,071 (41.7)	964 (58.6)	2,107 (36.8)
Census region			
Midwest	1,894 (25.7)	407 (24.7)	1,487 (26.0)
Northeast	924 (12.5)	279 (17.0)	645 (11.3)
South	3,598 (48.8)	707 (43.0)	2,891 (50.5)
West	951 (12.9)	253 (15.4)	698 (12.2)
Trigger			
Food	1,865 (25.3)	854 (51.9)	1,011 (17.7)
Medication	1,076 (14.6)	85 (5.2)	991 (17.3)
Venom	289 (3.9)	44 (2.7)	245 (4.3)
Unspecified	4,137 (56.2)	663 (40.3)	3,474 (60.7)
Charlson comorbidity index			
0	3,510 (47.6)	1,052 (63.9)	2,458 (43.0)
1	1,484 (20.1)	496 (30.1)	988 (17.3)
≥ 2	2,373 (32.2)	98 (6.0)	2,275 (39.8)
Comorbid conditions			
Cardiac disease	2,573 (34.9)	NR ^b	NR ^b
Diabetes mellitus	846 (11.5)	38 (2.3)	808 (14.1)
Asthma	1,732 (23.5)	528 (32.1)	1,204 (21.0)
Eczema	997 (13.5)	385 (23.4)	612 (10.7)
ED disposition			
ED discharge or observation	6,312 (85.7)	1,550 (94.2)	4,762 (83.2)
Inpatient (non-ICU) admission	523 (7.1)	80 (4.9)	443 (7.7)
ICU admission	532 (7.2)	16 (1.0)	516 (9.0)
SIE dispensed ^c	3,322 (45.1)	1,192 (72.4)	2,130 (37.2)
A/I follow-up ^c	2,087 (28.3)	805 (48.9)	1,282 (22.4)
SIE dispensed and A/I follow-up ^c	1,550 (21.0)	701 (42.6)	849 (14.8)

Abbreviations: A/I, allergy/immunology; ED, emergency department; ICU, intensive care unit; NA, not applicable; NR, not reported; SIE, self-injectable epinephrine.

^aData are presented as number (percentage) of patients unless otherwise indicated.

^bCells had 10 or fewer observations; data have been suppressed to protect patient confidentiality.

^cAfter index anaphylaxis ED visit.

Table 2
Multivariable Predictors of Recurrent Anaphylaxis

Predictor ^a	Overall		Children		Adults	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age, y						
0–4	1.30 (0.84–1.99)	.24	1.11 (0.83–1.50)	.49	NA	NA
5–17	1.04 (0.75–1.44)	.80	1 [Reference]		NA	NA
18–34	1 [Reference]	NA	NA		1 [Reference]	NA
35–64	0.79 (0.61–1.01)	.06	NA		0.86 (0.69–1.07)	.17
≥ 65	0.70 (0.46–1.06)	.09	NA		0.80 (0.58–1.10)	.17
Race/ethnicity						
White	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Asian	0.79 (0.40–1.55)	.49	0.78 (0.29–2.08)	.62	0.80 (0.31–2.07)	.64
Black	1.02 (0.71–1.49)	.90	0.78 (0.36–1.67)	.52	1.12 (0.71–1.76)	.63
Hispanic	0.98 (0.63–1.50)	.91	1.14 (0.56–2.31)	.72	0.93 (0.54–1.62)	.80
Unknown	1.10 (0.62–1.96)	.73	1.38 (0.57–3.34)	.47	0.97 (0.45–2.10)	.95
Female sex	1.08 (0.94–1.25)	.27	1.12 (0.86–1.47)	.39	1.06 (0.90–1.26)	.47
Census region						
Midwest	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Northeast	0.93 (0.68–1.28)	.68	0.93 (0.53–1.62)	.79	0.98 (0.66–1.44)	.92
South	1.08 (0.87–1.34)	.48	1.14 (0.75–1.72)	.54	1.10 (0.85–1.43)	.45
West	1.02 (0.75–1.39)	.89	1.42 (0.87–2.34)	.16	0.85 (0.56–1.28)	.43
Trigger						
Unspecified	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Food	2.31 (1.34–3.99)	.003	23.17 (<0.001–>999.99)	.95	2.19 (1.24–3.87)	.007
Venom	0.23 (0.05–1.02)	.05	0 (<0.001–>999.99)	.95	0.25 (0.06–1.09)	.07
Medication	1.05 (0.56–1.94)	.89	8.40 (<0.001–>999.99)	.96	1.06 (0.56–2.00)	.87
Cardiac disease	1.08 (0.89–1.32)	.41	0 (<0.001–>999.99)	.99	1.10 (0.90–1.34)	.35
Diabetes mellitus	1.14 (0.93–1.42)	.21	1.79 (0.96–3.35)	.07	1.11 (0.88–1.38)	.38
Asthma	1.30 (1.13–1.51)	<.001	1.20 (0.91–1.59)	.19	1.37 (1.15–1.63)	<.001
Eczema	0.98 (0.80–1.19)	.82	1.07 (0.78–1.46)	.67	0.92 (0.71–1.20)	.56
ED disposition						
ED discharge or observation	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Inpatient (non-ICU) admission	0.77 (0.53–1.13)	.18	1.16 (0.44–3.07)	.77	0.70 (0.45–1.09)	.12
ICU admission	1.95 (1.41–2.69)	<.001	1.36 (0.33–5.62)	.67	2.07 (1.47–2.93)	<.001
SIE dispensed ^b	1.10 (0.92–1.32)	.30	0.67 (0.45–0.99)	.04	1.24 (1.01–1.52)	.04
A/I follow-up ^b	0.98 (0.74–1.30)	.88	0.83 (0.47–1.47)	.53	0.99 (0.71–1.37)	.94
SIE dispensed and A/I follow-up ^b	1.00 (0.71–1.41)	.99	1.28 (0.66–2.49)	.47	0.99 (0.66–1.48)	.95

Abbreviations: A/I, allergy/immunology; CI, confidence interval; ED, emergency department; ICU, intensive care unit; NA, not applicable; OR, odds ratio; SIE, self-injectable epinephrine.

^aReference groups were chosen arbitrarily for purpose of calculating an OR.

^bAfter index anaphylaxis ED visit.

The role of atopy with regard to anaphylaxis recurrence is unclear because the findings from prior studies have been inconsistent. In our study, history of asthma was associated with a higher risk for recurrent anaphylaxis and agrees with a prior pediatric-based study.¹² However, Gonzalez-Perez et al¹³ reported lower rates of recurrent anaphylaxis in their adult and pediatric patients with severe (5.5 per 100 patient-years) and nonsevere asthma (8.2 per 100 patient-years) compared with those with no asthma (10.7 per 100 patient-years). It is unclear what risk for recurrence asthma poses in those with a

history of anaphylaxis, and we suspect there are confounding factors, including level of asthma control, that should also be considered.

In this study, we did not find that eczema was associated with an increased risk of relapse, although this has been reported by others.¹¹ In the study by Mullins,² asthma and atopic dermatitis were not associated with increased recurrence. Atopy is a risk factor for anaphylaxis severity¹⁴ and via sensitization and cross-reactivity atopy may in theory predispose patients to recurrent reactions. Future studies are needed to clarify the role of atopy on the risk of relapse.

ICU admission at the time of the index reaction was also associated with risk of a recurrent anaphylaxis ED visit. Anaphylaxis remains a clinical diagnosis.¹⁵ Consequently, patients with more severe reactions are likely to have a true underlying hypersensitivity, in contrast to those with vague reactions for whom the diagnosis of anaphylaxis is unclear. One study¹⁰ has reported administration of epinephrine during the index event to be a risk factor; this can also be seen as a marker of more severe reactions. ICU admission at the time of the index event as a risk factor for recurrence is a novel finding that has not been previously reported, perhaps because recurrent anaphylaxis and ICU admission are uncommon and studies of primary data have insufficient power to detect the association because of smaller sample sizes. Additional studies are needed to validate and explain this finding.

In our cohort study, fewer than half the patients (45.1%) had an SIE dispensed at their index ED visit, and this factor was not significantly associated with recurrent anaphylaxis ED visits. Pre-index event SIE dispensing and allergist/immunologist visits have been associated with a lower risk of severe anaphylaxis requiring hospitalization,¹⁶

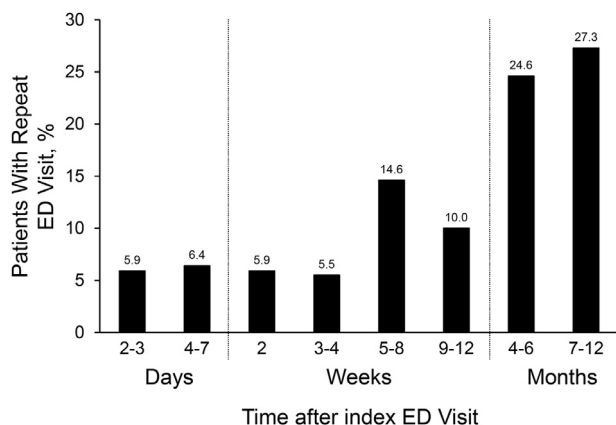


Figure 2. Time to additional anaphylaxis-related emergency department (ED) visit.

but the effect of prior SIE dispensing and allergist/immunologist visits on the risk of a recurrent event is unclear. Interestingly, Vetander et al¹⁷ reported that the prescription of SIE before the index event was associated with ED revisit for anaphylaxis (relative risk, 2.09; 95% CI, 1.17–3.49). Although SIE is meant to be a protective measure against future episodes of anaphylaxis, Cummings et al¹⁸ demonstrated that SIE prescriptions were associated with reduced vigilance and poor adherence with medical management because it may have decreased the anxiety of both food allergic children and their parents. Addressing this and other barriers to anaphylaxis care from the patient, practitioner, and system perspective will be vital in improving adherence with current guidelines.¹⁹

There were several limitations of our study. First, our study was based on ED visits; thus, recurrent episodes of anaphylaxis not managed in the ED setting could not be captured. Second, our study used administrative claims data that have the potential for coding errors and a possibility of underreporting of cases. Third, our study was limited to persons with private insurance and those with Medicare Advantage. Those without health insurance or with Medicaid were not part of the data source and may explain why our sample population (median age, 42 years) was slightly older than previous studies by Lee et al¹¹ (median age, 31 years) and Mullins² (median age, 27.4 years). Fourth, most of our cohort was white, and nearly half the patients were from the South. Although this reflects the overall geographic distribution of patients in the OptumLabs database, anaphylaxis rates are higher in northern latitudes,^{20,21} so this study may underestimate anaphylaxis rates. Fifth, 5.9% of recurrences occurred within 2 to 3 days of the index ED visit, and the possibility that some of these reactions were biphasic reactions cannot be ruled out in these patients.

Regardless of these limitations, this is the first study, to our knowledge, to examine recurrent anaphylaxis ED visits in a large national cohort. Large population-level studies such as this one are necessary for studying the epidemiology of anaphylaxis. Recurrent anaphylaxis has received little attention in the past decade, which may be related to difficulties in data collection and methods. We agree with Tejedor-Alonso et al²² that future studies should establish how to best define and study anaphylaxis recurrence. For example, it is unclear whether it is better to define recurrence by studying the first episode vs subsequent episodes and whether only new episodes with the same trigger are considered recurrences or whether episodes caused by a trigger that is cross-reactive with a trigger of the first or prior episodes can be considered a recurrence. From a research standpoint, answering these questions will be helpful and may provide a much-needed level of methodologic uniformity that will facilitate useful comparisons among studies.

In summary, with the use of a large contemporary patient database, the results of our study suggest that a history of asthma and food trigger may be associated with anaphylaxis recurrence. Given that many of our findings agree with smaller observational studies, our study suggests that administrative claims data may be a useful data source to study anaphylaxis on a larger population scale. In addition, our study is the first, to our knowledge, to suggest that a history of a ICU admission related to the index event may be associated with a higher risk of anaphylaxis recurrence. Going forward, additional studies are needed to expand

our understanding of recurrent anaphylaxis and its associated risk factors.

Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.anai.2018.08.021>.

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eTable 1
Professional Claims^a

Description of Diagnosis	Professional Claims
Triggers	
Food	693.10, 995.6x, and 995.7
Medication	693.0, 995.2x, 995.4, E930.x, and E931.x
Venom	989.5, E905.3, E905.5, E905.8, and E905.9
Unspecified	Not categorized in above 3 groups
Cardiac disease	
Hypertensive disease	401.x, 402.xx, 404.xx, and 405.xx
Coronary atherosclerosis	414.00–414.05
Congestive heart failure	428.x
Asthma	493.xx except 493.93
Eczema	691.8, 692.xx except 692.97
Allergy/immunology visit before index event	CPT codes 99201–99205, 99211–99215, and 99241–99245 and practitioner specialty
ICU admission	
Intensive care	Revenue codes 20x
Coronary care	Revenue codes 210, 211, 212, 214, and 219

Abbreviations: CPT, Current Procedural Terminology; ICU, intensive care unit.

^aUsed with permission from Motosue et al.¹⁰**eTable 2**
Multivariable Predictors of Recurrent Anaphylaxis-Related ED Visit Based on Patients Identified by Method 1 Only

Predictor ^a	Overall		Children		Adults	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age, y						
0–4	1.32 (0.80–2.17)	.27	1.22 (0.87–1.72)	.25	NA	NA
5–17	0.94 (0.62–1.42)	.77	1 [Reference]		NA	NA
18–34	1 [Reference]	NA	NA	NA	1 [Reference]	NA
35–64	0.92 (0.65–1.29)	.63	NA	NA	0.96 (0.69–1.34)	.82
≥ 65	0.66 (0.34–1.29)	.23	NA	NA	0.75 (0.43–1.28)	.29
Race/ethnicity						
White	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Asian	0.73 (0.32–1.69)	.46	0.74 (0.22–2.47)	.62	0.83 (0.25–2.72)	.75
Black	1.24 (0.75–2.05)	.41	0.87 (0.36–2.10)	.76	1.44 (0.75–2.76)	.28
Hispanic	0.72 (0.38–1.35)	.31	1.05 (0.45–2.46)	.91	0.48 (0.18–1.29)	.15
Unknown	1.42 (0.72–2.78)	.31	1.40 (0.49–3.95)	.53	1.50 (0.60–3.71)	.38
Female sex	1.03 (0.85–1.24)	.79	1.17 (0.85–1.61)	.35	0.94 (0.74–1.19)	.60
Census region						
Midwest	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Northeast	0.89 (0.58–1.35)	.57	0.93 (0.49–1.76)	.81	0.88 (0.50–1.56)	.67
South	1.08 (0.80–1.44)	.63	1.24 (0.75–2.04)	.39	1.05 (0.72–1.52)	.81
West	1.32 (0.91–1.92)	.15	1.57 (0.88–2.82)	.13	1.19 (0.72–1.97)	.49
Trigger						
Unspecified	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Food	1.76 (0.96–3.22)	.07	257.05 (<0.001–>999.99)	.95	1.60 (0.85–3.00)	.14
Venom	0.33 (0.07–1.51)	.15	0.01 (<0.001–>999.99)	.98	0.33 (0.07–1.51)	.15
Medication	0.98 (0.39–2.43)	.96	0 (<0.001–>999.99)	.98	1.13 (0.45–2.82)	.80
Cardiac disease	0.96 (0.72–1.28)	.76	0 (<0.001–>999.99)	.98	0.97 (0.72–1.29)	.82
Diabetes mellitus	1.24 (0.92–1.68)	.16	1.98 (1.03–3.81)	.04	1.17 (0.83–1.65)	.38
Asthma	1.39 (1.14–1.70)	.001	1.23 (0.88–1.73)	.22	1.54 (1.19–1.98)	<.001
Eczema	0.86 (0.65–1.12)	.26	0.86 (0.59–1.26)	.43	0.85 (0.57–1.28)	.44
ED disposition						
ED discharge or observation	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Inpatient (non-ICU) admission	1.11 (0.67–1.85)	.68	53.70 (<0.001–>999.99)	.97	1.05 (0.57–1.92)	.88
ICU admission	1.31 (0.78–2.18)	.30	0 (<0.001–>999.99)	.97	1.44 (0.84–2.47)	.18
SIE dispensed ^b	1.04 (0.81–1.33)	.76	0.53 (0.33–0.84)	.008	1.30 (0.97–1.73)	.07
A/I follow-up ^b	1.29 (0.88–1.90)	.19	1.08 (0.58–2.04)	.80	1.25 (0.75–2.06)	.39
SIE dispensed and A/I follow-up ^b	0.77 (0.49–1.21)	.26	1.00 (0.47–2.10)	<.99	0.80 (0.45–1.43)	.45

Abbreviations: A/I, allergy/immunology; CI, confidence interval; ED, emergency department; ICU, intensive care unit; OR, odds ratio; NA, not applicable; SIE, self-injectable epinephrine.

^aReference groups were chosen arbitrarily for purpose of calculating an OR.^bAfter index anaphylaxis ED visit.