

Changes in Emergency Department Concordance with Guidelines for the Management of Food-Induced Anaphylaxis: 1999-2001 versus 2013-2015



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What is already known about this topic? Emergency department (ED) visits for food-induced anaphylaxis have been increasing. Concordance with guideline recommendations has been described, but little is known about whether there have been improvements in concordance with these guidelines.

What does this article add to our knowledge? We found increased concordance with guideline recommendations over 15 years (1999-2001 vs 2013-2015). Pre-ED/ED treatment with epinephrine increased, documentation for referral to an allergist/immunologist, and prescriptions for an epinephrine autoinjector at discharge all increased, but practice variability remained.

How does this study impact current management guidelines? Future work should focus on barriers to implementation of recommendations, improvements in education for patients and providers, and strategies, such as decision support tools in electronic medical records, to remind providers about evidence-based anaphylaxis guidelines.

BACKGROUND: Awareness about food allergy and food-induced anaphylaxis (FIA) has increased dramatically over the past decade. It remains unclear, however, whether concordance with guidelines for FIA management has improved over time. **OBJECTIVE:** Our objective was to describe changes in emergency department (ED) concordance with guidelines for FIA management.

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METHODS: We analyzed data from 2 multicenter retrospective studies of patients with food-related acute allergic reactions seen in 1 of 17 EDs during 2 time periods: 1999 to 2001 and 2013 to 2015. Visits were identified similarly across years—for example, using International Classification of Diseases, Ninth Revision, Clinical Modification codes 693.1, 995.60, 995.61-995.69, 995.0, and 995.3. Anaphylaxis was defined as an acute allergic reaction with involvement of 2+ organ systems or hypotension. We compared concordance between time periods for 4 guideline recommendations: (1) treatment with epinephrine, (2) discharge prescription for an epinephrine autoinjector (EAI), (3) referral to an allergist/immunologist, and (4) instructions to avoid offending allergen. **RESULTS:** We compared 290 patients with FIA during 1999 to 2001 and 459 during 2013 to 2015. Any treatment with epinephrine (pre-ED or in the ED) for patients with FIA increased over time (38% vs 56%; $P < .001$). Prescriptions for EAI at discharge (24% vs 54%; $P < .001$) and documentation for referral to an allergist/immunologist (14% vs 24%; $P = .001$) approximately doubled, whereas instructions to avoid the offending allergen did not change significantly (37% vs 43%; $P = .08$). Receipt of 3+ guideline recommendations remained low but almost quadrupled over the study interval (6% vs 23%; $P < .001$).

CONCLUSIONS: Over the nearly 15-year study interval, we observed clinically and statistically significant increases in ED concordance with epinephrine-related guidelines for FIA. Management gaps remain and interventions to standardize care still appear warranted. © 2019 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2262-9)

Key words: Food allergy; Anaphylaxis; Emergency department

Abbreviations used

CI- Confidence interval
EAI- Epinephrine autoinjector
ED- Emergency department
EMNet- Emergency Medicine Network
EMR- Electronic medical record
FAAN- Food Allergy and Anaphylaxis Network
FIA- Food-induced anaphylaxis
ICD-9- International Classification of Diseases, Ninth Revision
MARC- Multicenter Airway Research Collaboration
NIAID- National Institute of Allergy and Infectious Disease
OR- Odds ratio

Food-induced anaphylaxis (FIA) is a severe and potentially life-threatening reaction. Earlier work by our group estimated that there are 203,000 emergency department (ED) visits for food-related acute allergic reactions annually in the United States, of which 90,000 are classified as FIA.¹ A recent study reported an overall 124% increase in ED visits for FIA between 2005 and 2014, and a 285% increase among children,² the group most likely to also be hospitalized.³

National and international guidelines recommend that patients treated for anaphylaxis receive epinephrine as first-line therapy.⁴⁻¹⁰ In addition to the use of epinephrine as first-line therapy for anaphylaxis, guidelines recommend a prescription for an epinephrine autoinjector (EAI), referral to an allergist/immunologist, and an allergy action plan at ED discharge.⁴⁻¹⁰

Concordance with guideline recommendations for the emergency management of FIA has been described. In 2 studies conducted at Boston-area EDs during 2001 to 2006, 44% of children¹¹ and 34% of adults¹² with FIA were treated with epinephrine, whereas in a 2007 study in Stockholm, 71% of children with FIA were treated with epinephrine.¹³ With respect to discharge guideline recommendations, both Boston-area studies found that approximately 40% of patients with FIA received a prescription for EAI at ED discharge.^{11,12} Documentation of referral to an allergist/immunologist at ED discharge varied from 18%¹² to 71%.¹³

Despite increasing frequency of anaphylaxis and awareness among patients and physicians, it remains unclear whether concordance with guidelines for the management of FIA has improved over time. Our objective was to describe changes in ED concordance with guidelines for the management of FIA.

METHODS

Study design

Data from 2 retrospective studies were compared. Both studies were conducted as part of the Multicenter Airway Research Collaboration (MARC), a division of the Emergency Medicine Network (EMNet). The first study, MARC-8, was conducted at 21 EDs in the United States and Canada during 1999 to 2001.¹⁴ The current study, MARC-38, was conducted at 20 EDs, including 17 of the 21 originally participating EDs, but focused on 2013 to 2015 data. Both studies used similar methodology, as described in detail elsewhere for MARC-8,¹⁴ and as summarized briefly below, with emphasis on the new MARC-38 study.

A standardized protocol and data abstraction forms were used. All data abstractors were required to participate in a webinar training

and satisfactorily ($\geq 80\%$ correct) complete abstraction from 2 practice charts. Investigators at 20 EDs examined ED visits for food allergy. More specifically, sites performed chart reviews for randomly selected patients presenting to the ED during a 12- to 36-month period between January 1, 2013, and December 31, 2015, with a physician-diagnosed, food-related acute allergic reaction. The following International Classification of Diseases, Ninth Revision (ICD-9) or Tenth Revision, Canada (ICD-10-CA) codes were used for inclusion in the current study: 693.1/L27.2 (dermatitis due to food), 995.60/T78.09 (allergy due to unspecified food), and 995.61/T78.00 to 995.69/T78.08 (allergy due to specified food). For sites with less than 50 cases with the above food allergy codes, site investigators were asked to screen patients with less specific codes (ie, 995.0/T78.2 [other anaphylactic shock] and 995.3/T78.4 [allergy, unspecified]) to identify additional food allergy cases up to 50 patients per site. A list of all patients with the relevant ICD-9/ICD-10-CA codes was submitted to the EMNet Coordinating Center, and a random number generating macro in Excel (Microsoft Corp, Redmond, Wash) was used to rank the list with the first 50 patients being those randomly identified to undergo chart review. The same approach was used in the earlier MARC-8 study.¹⁴ The Institutional Review Board at each of the 20 participating hospitals approved the study.

Data collection

The structured chart review was performed to collect patients' demographic characteristics, allergy history, and details of their food-related acute allergic reaction, including prehospital, ED, and hospital management. Symptoms and signs were extracted from all available sources (ie, prehospital, ED, and inpatient records), and any positive findings were counted. Discharge instructions were recorded for patients sent home from the ED.

Definitions

FIA was defined based on a slightly modified version of the Food Allergy and Anaphylaxis Network and the National Institute of Allergy and Infectious Disease (FAAN/NIAID) clinical criteria.¹⁵ Briefly, anaphylaxis was defined as allergic reaction involving 2 or more organ systems or hypotension before arrival to or in the ED. Hypotension was defined as systolic blood pressure less than $(70 + (\text{age} \times 2))$ for children aged <10 years, a systolic blood pressure less than 90 mm Hg for children aged 10 to 17 years, and a systolic blood pressure less than 100 mm Hg for adults aged 18+ years. The same definition was used in the earlier MARC-8 study.¹⁴

A known allergy to the offending food was determined with the following question: "Does the patient have a known allergy to this food exposure?" Other known allergic problems include allergic reactions to other foods, allergic reactions to other sources (eg, medications, insects/spiders, latex), asthma, allergic rhinitis, atopic dermatitis, idiopathic urticaria, angioedema, and other. Pre-ED treatment included self-treatment or treatment by emergency medical services/prehospital providers.

Outcomes

The outcomes of interest were in concordance with 4 recommended guidelines: (1) pre-ED or ED treatment with epinephrine; (2) discharge prescription for an EAI, (3) referral to an allergist/immunologist, and (4) an allergy action plan at ED discharge. In addition to each individual recommendation, we also analyzed the number of recommended guidelines followed.

TABLE I. Characteristics of patients presenting to the emergency department with food-induced anaphylaxis, according to the study period

Characteristics	1999-2001 (n = 290)	2013-2015 (n = 459)	P value
Demographic characteristics			
Age, median (IQR)	29.8 (20.4-40.6)	24.0 (13.0-35.0)	.001
Age (%)			<.001
<18 y	18%	32%	
≥18 y	82%	68%	
Sex (%)			.82
Female	61%	62%	
Male	39%	38%	
White race/ethnicity	52%	38%	<.001
Allergy history			
Known allergy to offending allergen (%)	42%	56%	<.001
Other known allergic problems (%)*	68%	52%	<.001
Presentation and clinical course			
Offending food			
Peanuts (%)	13%	18%	.08
Tree nuts (%)	11%	22%	<.001
Fruits and vegetables (%)	11%	9%	.22
Crustaceans (%)	18%	15%	.29
Fish (%)	9%	9%	.84
Food additives (%)	1%	1%	.50
Milk (%)	5%	3%	.16
Eggs (%)	2%	3%	.88
Other food (%)	36%	24%	<.001
Time since exposure (%)			
<1 h	36%	30%	
1-3 h	39%	49%	
4-6 h	12%	7%	
7-12 h	8%	3%	
>12 h	4%	10%	
Signs and symptoms			
Respiratory (%)	79%	73%	.06
Cutaneous (%)	97%	99%	.048
Gastrointestinal (%)	24%	47%	<.001
Cardiovascular (%)	14%	9%	.06
Arrived to ED by ambulance (%)	23%	29%	.11
Received pre-ED epinephrine (%)†	17%	24%	.02
Received epinephrine in ED (%)	26%	37%	.002
Received epinephrine pre-ED or in ED (%)†	38%	56%	<.001
Received Benadryl in ED (%)	67%	62%	.17
Received systemic steroids in ED (%)	54%	79%	<.001
Admitted to ICU (%)	2%	4%	.09
Discharged home from ED (%)	92%	86%	.03
Discharge management			
	n = 266	n = 397	
Prescription for epinephrine autoinjector (%)	24%	54%	<.001
Documentation of referral to an allergist (%)	14%	24%	.001
Instructions to avoid offending allergen (%)	37%	43%	.08

ED, Emergency department; ICU, intensive care unit; IQR, interquartile range.

*Other known allergic problems include allergic reactions to other foods, allergic reactions to other sources (eg, medications, insects/spiders, latex), asthma, allergic rhinitis, atopic dermatitis, idiopathic urticaria, angioedema, and other.

†Pre-ED treatment included self-treatment or treatment by emergency medical services/prehospital providers.

Statistical analysis

Data were collected at each site and transferred without patient identifiers to the Coordinating Center. All analyses were performed using Stata 14.0 (Stata Corp, College Station, Tex). Data

are presented as proportions, means with standard deviations, and medians with interquartile ranges. Comparisons between the 2 time periods (1999-2001 vs 2013-2015) were done using χ^2 , Fisher's exact test, Student's *t* test, and Kruskal-Wallis test, as

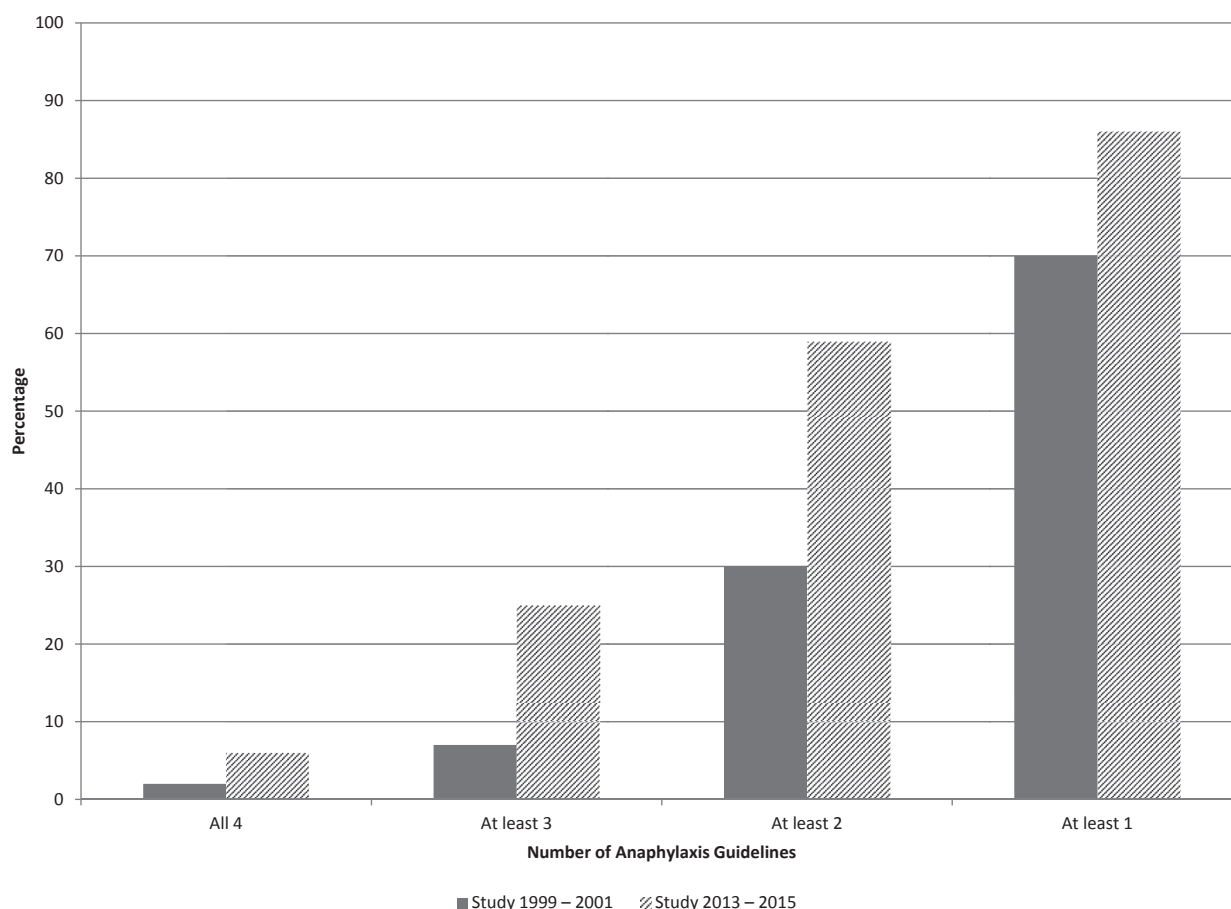


FIGURE 1. Number of guideline recommendations implemented for food-induced anaphylaxis, according to the study period. Proportion of concordance with all 4, at least 3, at least 2, and at least 1 of guideline recommendations (1. treatment with epinephrine, 2. discharge prescription for an epinephrine autoinjector, 3. referral to an allergist/immunologist, and 4. instructions to avoid offending allergen) for the emergency management of food-induced anaphylaxis during 2 study periods (1999-2001 and 2013-2015).

appropriate. To account for the potential lack of independence within sites, differences between the 2 time periods for pre-ED or ED treatment with epinephrine and discharge prescription for an EAI were analyzed using multilevel logistic regression. Results are reported as odds ratios (OR) and 95% confidence intervals (CIs). Secondary analyses stratified results for primary outcomes by age. All *P* values are 2-tailed, with *P* < .05 considered statistically significant.

RESULTS

Among the 678 patients identified during 1999 to 2001, 567 were enrolled at sites participating in both MARC-8 and MARC-38. Among these 567 patients, 290 (51%) had anaphylaxis according to FAAN/NIAID clinical criteria and were included in the current analysis. Among the 1000 patients identified during 2013 to 2015, 850 were enrolled at sites participating in both studies. Of these, 459 (54%) had anaphylaxis and were included in the current analysis. Patients in the 2013 to 2015 cohort were younger and less likely to be white than those in the 1999 to

2001 cohort, but the 2 groups did not differ with respect to sex. The 2 cohorts also did not differ with respect to offending food allergen, and were equally likely to arrive to the ED by ambulance (Table I).

Patients in the 2013 to 2015 cohort were more likely to receive care concordant with guideline recommendations for the emergency management of anaphylaxis (Table I). Any treatment with epinephrine (pre-ED or in the ED) for these patients with FIA increased approximately 50% over time (38% vs 56%; *P* < .001). Although prescriptions for EAI (24% vs 54%; *P* < .001) and documentation for referral to an allergist/immunologist (14% vs 24%; *P* = .001) at discharge approximately doubled, documentation of instructions to avoid the offending allergen did not differ significantly across the 2 time periods (14% vs 24%; *P* = .08). Receipt of 3+ guideline recommendations remained low (25%) in 2013 to 2015 but increased almost 4-fold over the study interval (7% vs 25%; *P* < .001) (Figure 1).

Although variation in care across sites was observed during both time periods (9%-68% in 1999-2001 and 8%-90% in 2013-2015), 60% of sites showed an improvement in treatment

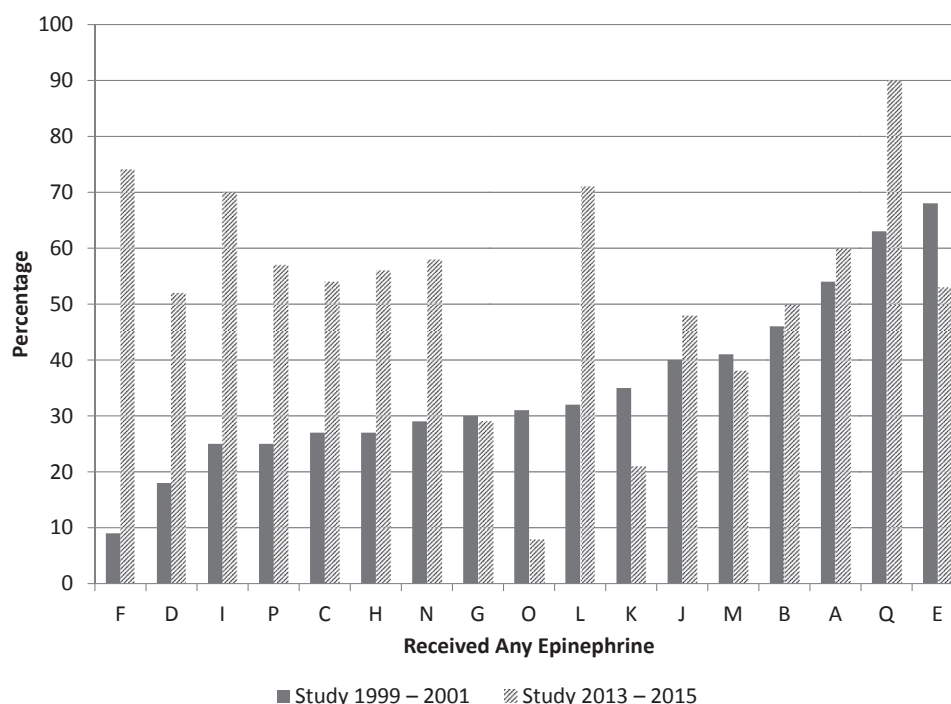


FIGURE 2. Site variation in treatment with epinephrine before or during an emergency department visit for food-induced anaphylaxis, according to the study period. Variation in treatment with epinephrine before or during an emergency department visit for food-induced anaphylaxis during 2 study periods (1999-2001 and 2013-2015).

with epinephrine pre-ED or in the ED (Figure 2). Similarly, 100% had an increase in prescriptions for EAI at discharge and 70% of sites showed increases in documentation of referral to an allergist/immunologist (Figure 3).

Multilevel logistic regression accounting for potential clustering by site revealed robust results for improvements in any treatment with epinephrine (OR, 2.16; 95% CI, 1.58-2.96; $P < .001$) and discharge prescriptions for EAI (OR, 4.07; 95% CI, 2.83-5.86; $P < .001$).

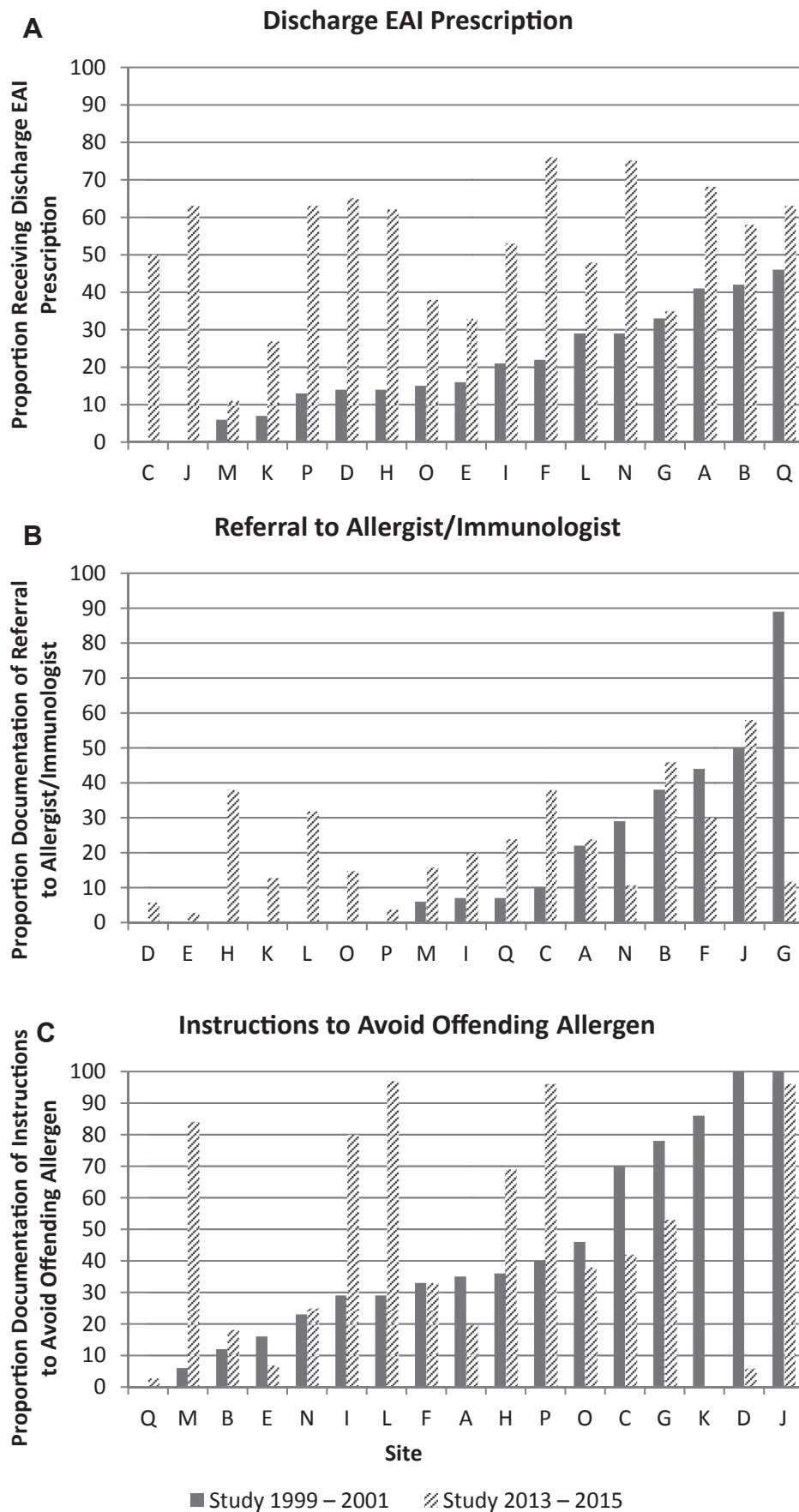
Next, we examined the primary outcomes stratified by age. Among children (age <18 years, $n = 197$), any treatment with epinephrine for patients with FIA increased from 42% to 63% ($P = .008$). Similarly, prescriptions for EAI (32% vs 61%; $P < .001$) and documentation for referral to an allergist/immunologist (15% vs 33%; $P = .02$) at discharge both approximately doubled. With a limited statistical power, instructions to avoid the offending allergen nonsignificantly improved (32% vs 47%; $P = .08$). Among adults (age ≥ 18 years, $n = 552$), any treatment with epinephrine for patients with FIA also increased from 37% to 53% ($P < 0.001$). Although prescriptions for EAI more than doubled (22% vs 51%; $P < .001$), neither documentation for referral to an allergist/immunologist (13% vs 19%; $P = .11$) nor instructions to avoid the offending allergen (38% vs 42%; $P = .38$) significantly improved.

DISCUSSION

Comparing FIA management in 20 North American EDs during 1999 to 2001 versus 2013 to 2015, we not only found improvements in concordance with guideline recommendations,

but also observed continued variability in care across study sites. Treatment with epinephrine before or during an ED visit for FIA significantly increased over the approximately 15-year study period. Documentation of discharge prescriptions for EAI and referral to an allergist/immunologist both approximately doubled, and patients receiving 3 or more of the guideline recommendations remained low but increased by almost 4-fold. To our knowledge, this is the first study to examine the trends in the ED management of FIA,¹¹⁻¹³ and others have described temporal changes in and the effectiveness of educational interventions on changes in the management of anaphylaxis due to any cause,¹⁶⁻¹⁹ we are unaware of recent literature describing trends in ED management for FIA.

Two observational studies of FIA management in the ED conducted during the early 2000s report results similar to those we observed during 1999 to 2001, whereas a third observed higher guideline concordance than we observed during either time period. Rudders et al¹¹ examined FIA management in children in 2 Boston-area EDs during 2001 to 2006 and found that nearly half of children with FIA received treatment with epinephrine. In the same cohort, but among adults, Banerji et al¹² also found that one-third of adults with FIA received treatment with epinephrine. Another study of children treated in the ED for food-related acute allergic reaction in Stockholm during 2007 found that 43% of children received epinephrine, and when restricting to those coded as having anaphylaxis, 71% were treated with epinephrine.¹³ Data gathered as part of the European Anaphylaxis Registry during 2007 to 2015 showed that among children referred to tertiary referral centers specializing in pediatric allergy across Europe, 41%



were treated with epinephrine during the ED visit during which the tertiary referral was made, and that epinephrine use increased over time.²⁰ Although these studies highlight variability in the management of FIA, they also may reflect international differences in access and patient education, as well as provider and institutional variations in care.

We found significant increases in 2 of the 3 discharge recommendations. Patients with FIA were nearly twice as likely to receive a prescription for an EAI and to have documentation for referral to an allergist/immunologist in 2013 to 2015 compared with 1999 to 2001, though concordance with both recommendations remained low. Although the observed improvement in concordance with guideline recommendations is still low, it does represent an improvement in the emergency management in FIA described in other observational studies on the management of FIA. Both Rudders et al¹¹ and Banerji et al¹² found that approximately 40% of children and adults received prescriptions for EAI at ED discharge. Documentation of referral to an allergist/immunologist at ED discharge was low in both Boston-area studies at 22% for children¹¹ and 18% of adults,¹² whereas the results from the study in Stockholm, Sweden, showed that 71% of children with FIA received referral to an allergist/immunologist.¹³ These geographic differences may reflect both variations in practice patterns and access to health insurance and specialty providers across countries, and further represent the need to better understand differences in the management of anaphylaxis and to identify improvements in emergency care.

Despite these improvements, and similar to treatment with epinephrine before or during the ED visit, we observed site-to-site variability in both discharge prescriptions for EAI and documentation of referral to an allergist/immunologist. The reasons for the observed variability in concordance with guideline recommendations may be multifactorial and related to provider practice patterns, patient preferences, and availability of allergy/immunology specialists. Future work should focus on reasons for this variability and potential solutions for continued improvements in emergency care of FIA.

Limitations

Limitations of our study include reliance on medical records, which are documents created for clinical care and billing and not for research purposes. Although reliance on medical records may lead to underestimates of important outcomes because of poor documentation, the same methodology was used during both study periods, mitigating an effect on differences observed between the 2 time periods. Second, medication administration is recorded diligently by nursing staff, ensuring the validity of the epinephrine data. Third, it is possible that the introduction of electronic medical records (EMRs) may have changed documentation practices, with some observed improvements in concordance with guidelines being due to better documentation when using an EMR. Fourth, the range of interventions to

improve allergy care applied across the participating centers over the study period is unknown. Finally, most participating sites are voluntary academic medical centers that may limit the generalizability of our results to other settings (eg, rural settings, community hospitals).

CONCLUSIONS

In this analysis of the data from 2 multicenter observational studies, improvements in the ED management of FIA were observed over the nearly 15-year study period. Among the 17 participating EDs, treatment with epinephrine before or during the ED visit, a prescription for self-injectable epinephrine, and referral to an allergist/immunologist at ED discharge all improved. Despite these improvements, concordance for guidelines remains low and variability across sites continues to be seen. Further improvement is needed. Future work might focus on current barriers to implementation of the guideline recommendations, improvements in education for both patients and providers,²⁰ and potential new strategies, such as decision support tools in EMRs, to remind busy ED providers about the evidence-based anaphylaxis guidelines.²¹

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FIGURE 3. Site variation in concordance with guideline recommendations for discharge from the emergency department after a visit for food-induced anaphylaxis, according to the study period. Variation in concordance with guideline recommendations for the management of food-induced anaphylaxis and emergency department discharge during 2 study periods (1999-2001 and 2013-2015). **A**, Receipt of a discharge prescription for epinephrine autoinjector (EAI). **B**, Documentation of referral to an allergist/immunologist. **C**, Documentation of instructions to avoid the offending allergen.

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