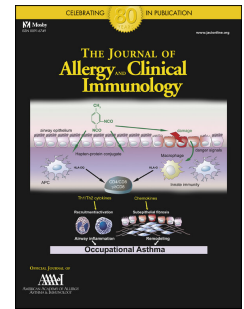


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Trends, Characteristics and Incidence of Anaphylaxis in 2001-2010: A Population Based Study

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TRENDS, CHARACTERISTICS AND INCIDENCE OF ANAPHYLAXIS IN 2001-2010: A
POPULATION BASED STUDY

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ABSTRACT**Background**

Anaphylaxis is a potentially life-threatening systemic allergic reaction.

Objective

We aimed to determine the incidence rate and causes of anaphylaxis during a 10-year period in Olmsted County, Minnesota.

Methods

Using the resources of the Rochester Epidemiology Project, a comprehensive records linkage system, we performed a population-based incidence study in Olmsted County, Minnesota, from 2001 through 2010. All cases with a diagnosis of anaphylactic shock and 20% of cases with related diagnoses were manually reviewed. The relationships of age group, sex, and year of anaphylaxis with incidence rates were assessed by fitting Poisson regression models.

Results

Six hundred and thirty-one cases of anaphylaxis were identified. Median age was 31 years (interquartile range 19-44). The overall age- and sex-adjusted incidence rate was 42 (95% CI 38.7-45.3) per 100,000 person-years. There was a significant increase in the overall incidence of anaphylaxis during the study period with an average increase of 4.3% per year ($P < 0.001$). In addition, there was a 9.8% increase per year in the incidence rate for food-related anaphylaxis. Food-related anaphylaxis was most common in children aged 0-9 years, venom related

anaphylaxis was most common in those 20-39 years of age, and medication-related anaphylaxis was most common in those 30-39 years of age.

Conclusion

The overall incidence rate of anaphylaxis was 42 per 100,000 person-years from 2001-2010 in Olmsted County, Minnesota. The incidence of anaphylaxis increased over time, and several inciting triggers were uniquely associated with different age groups.

Key messages

1. The incidence rate of anaphylaxis has increased from 2001 to 2010 in Olmsted County, MN
2. Food-related anaphylaxis has increased during the study period and was most common in children aged 0-9 years.
3. The venom-related anaphylaxis was most common in those 20-39 years of age and medication related anaphylaxis was most common in those 30-39 years of age.

Capsule summary

We found an increased incidence of anaphylaxis over time, especially food-related anaphylaxis in a population-based cohort from 2001 to 2010.

Key words

Anaphylaxis, food allergy, venom allergy, medication allergy, epidemiology, incidence rate

Abbreviations

REP: Rochester Epidemiology Project

REDCap: Research Electronic Data Capture

ICD: International Classification of Diseases

NIAID/FAAN: National Institutes of Allergy and Infectious Disease/Food Allergy and

Anaphylaxis Network

IQRs: interquartile ranges

CI: Confidence interval

ED: Emergency department

INTRODUCTION

Anaphylaxis has been defined as a serious allergic reaction that has a rapid onset and can be fatal.¹ Epidemiological studies of anaphylaxis related conditions, such as food allergy and asthma have demonstrated concerning increases.^{2,3} Studies of anaphylaxis also suggest that the incidence may be increasing.⁴⁻⁷

Two prior epidemiological studies of residents of Olmsted County, Minnesota have been conducted utilizing the resources of the Rochester Epidemiology Project (REP), a comprehensive records linkage system, to study the incidence of anaphylaxis.^{5,7} Yocum et al. reported an average annual incidence rate of anaphylaxis in residents of Olmsted County between 1983 and 1987 of 21 per 100,000 person years.⁷ Decker et al. reported an incidence rate in residents of the city of Rochester from 1990 to 2000 of 49.8 per 100,000 person years.⁵ Although the two geographic regions are not directly comparable, these findings suggest that anaphylaxis may be increasing in the population. Studies of anaphylaxis related hospitalizations have demonstrated increases as well.^{8,9}

Trends in anaphylaxis incidence have important public health implications. We sought to evaluate contemporary temporal trends of anaphylaxis in Olmsted County, Minnesota using the REP research infrastructure from 2001 to 2010.

METHODS

Data collection

We accessed the medical record linkage system of the REP to obtain a list of all Olmsted County residents who had diagnostic codes related to anaphylaxis from January 1, 2001 to December 31, 2010.¹⁰⁻¹⁴ The infrastructure of the REP captures 98.7% of the population in Olmsted County. St.Sauver et al. reported that age, sex, and ethnic characteristics of Olmsted County were similar to those of the state of Minnesota and the Upper Midwest; however, Olmsted County was less ethnically diverse than the entire US population, more highly educated, and wealthier.¹² The main providers in the area during our study period included Mayo Clinic and its two affiliated hospitals (Saint Marys Hospital and Rochester Methodist Hospital), the Olmsted Medical Center, Olmsted Medical Center branch offices and affiliated hospital (Olmsted Medical Center Hospital), and the Rochester Family Medicine Clinic (a private medical care practice in Olmsted County), all of which were included in the REP. Importantly, the REP captures virtually the entire Olmsted County population and there are no restrictions based on age, sex, ethnicity, disease status, socioeconomic status, or insurance status.¹³

The study was approved by the Institutional Review Boards of both Mayo Clinic and Olmsted Medical Center. Residents of Olmsted County who had granted permission for their medical records to be reviewed were included in the study.

With the assistances of data retrieval specialists, we divided the list of potential anaphylaxis cases into four sublists by diagnosis:

a) Diagnoses of anaphylactic shock; anaphylactic shock caused by food; anaphylactic shock not elsewhere classified; and anaphylactic shock after sting (ICD9 codes: 995.60-995.69, 999.41-999.42, 999.49, 995.0, V13.81).

b) Diagnosis of venom or bee sting related toxic effects (ICD-9 codes: V15.06, E905.0-E905.9, 989.5).

c) Diagnosis of allergy, foodstuff; adverse effect, food; dermatitis caused by food taken internally; or toxic effect of specific food (ICD-9 codes: 477.1, 692.5, 693.1, 995.7, V15.01-V15.05, 988.0-988.2, 988.8-988.9).

d) Diagnosis of medication reactions (ICD-9 codes: 995.20-995.21, 995.27).

All patients in sub-list (a) were manually reviewed, and random samples of 20% of patients from the remaining sub-lists were manually reviewed for potentially eligible cases. Our sampling method was previously undertaken by Decker et al.⁵ For the sampling, a random number was assigned to each patient, the patients were sorted by this random number, and the first 20% were selected.

Health records were independently reviewed and abstracted by the principle investigator and three trained abstractors (an undergraduate student, a medical student, and a physician research fellow): data were extracted in duplicate for a sample of 60 charts to ensure quality and consistency and to reduce the risk of bias. A calibration of the abstractors was performed after the duplicate abstraction, and inter-rater agreement was determined.

The abstractor fully reviewed the complete inpatient and outpatient medical records of each eligible subject to confirm Olmsted County residency and to collect relevant information on demographics, presenting signs and symptoms, inciting triggers, treatments, and outcomes of the

anaphylaxis episode. All episodes of anaphylaxis were collected initially and were subsequently examined to identify incident cases.

For those cases who granted permission for their records to be used for research, Study data regarding demographics, signs and symptoms, treatment, diagnosis of anaphylaxis and disposition were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Mayo Clinic.¹⁵ REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for importing data from external sources.

Anaphylaxis diagnostic criteria

Cases were identified as anaphylaxis if they met the National Institutes of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network (NIAID/FAAN) anaphylaxis criteria shown in **Appendix Table**.¹⁶ The NIAID/FAAN criteria have been shown to be highly sensitive for the diagnosis of anaphylaxis and have been widely adopted by numerous professional allergy organizations.¹⁷⁻¹⁹

Statistical analysis

Continuous variables were summarized as means, medians, interquartile ranges (IQRs), and ranges as appropriate for the distribution of the data. Categorical variables were summarized as frequencies and percentages.

Age- and sex-specific incidence rates were calculated using the cases that met NIAID/FAAN diagnostic criteria as the numerator and the population counts of Olmsted County as the denominator. The denominators were obtained from a complete enumeration of the Olmsted County population provided by the REP.¹⁴ Because the population of Olmsted County is nearly all white, incidence rates were age- and sex-adjusted to the structure of the 2010 US white population. Incident cases were grouped by age into 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, and 60+ years old. The relationships of age group, sex, and year of anaphylaxis with incidence rates were assessed by fitting Poisson regression models using the SAS procedure GENMOD. Age group and sex were analyzed as categorical terms and year of anaphylaxis was analyzed as a linear term in the Poisson regression models. Statistical analyses were conducted using version 9.3 of the SAS software package (SAS Institute; Cary, NC).

RESULTS

Inter-rater agreement

Inter-rater agreement between reviewers was measured at the beginning of chart review. After review of 60 charts, there was agreement on 93% of the observations, yielding a kappa of 0.80 (95%CI 0.62 - 0.99).

Participants

We reviewed the records of 2386 Olmsted County, MN residents with diagnoses of anaphylaxis between January 1, 2001, and December 31, 2010 (**Appendix Figure**). Of these, 613 were diagnosed with anaphylactic shock, 928 were diagnosed with venom/bee sting or food allergy, and 845 were diagnosed with adverse effects related to medication. The 613 with anaphylactic shock represented all patients with this diagnosis during the study period, of whom 312 (50.9%) met NIAID/FAAN criteria for anaphylaxis. The 928 patients with venom/bee sting or food allergy represented a random sample of 20% of records with these diagnoses, of whom 49 (5.3%) met NIAID/FAAN criteria for anaphylaxis. The 845 patients with adverse effects related to medication represented a random sample of 20% of patients with these diagnoses, of whom 14 (1.7%) met NIAID/FAAN criteria for anaphylaxis. Based on these data, we estimated that if all 4668 patients with venom/bee sting or food allergy initially identified prior to the random sampling had been reviewed, 247 (0.053×4668) would have met criteria for anaphylaxis. Likewise, if all 4242 patients with adverse effects related to medication initially identified prior to the random sampling had been reviewed, we would anticipate that 72 (0.017×4242) would have met criteria for anaphylaxis. As such, the incident cohort comprised 631 (312 + 247 + 72) patients (**Appendix Figure**).

Descriptive data

Demographics, inciting triggers and allergy history for the 631 incident cases of anaphylaxis are summarized in Table I. Mean age at first occurrence of anaphylaxis was 32.1 years [median 31; IQR 19-44; range 0-98]. The majority of the cases (74%) of anaphylaxis were treated in the ED. As shown in Table I, among 626 patients who were evaluated for the acute anaphylactic event, most (74%) were discharged home or observed in the ED observation unit (11%). Fifteen percent required hospitalization. There were no anaphylaxis-related deaths.

Presenting signs and symptoms and patient disposition are also shown in Table I. Biphasic reactions, defined as any recurrent symptoms after resolution of the initial symptoms of anaphylaxis without re-exposure to the inciting allergen, occurred in 16 (3%) patients. Among the patients evaluated for the acute anaphylactic reaction, epinephrine was administered for treatment in 285 (45%) patients (Table I). There was a significant increase in epinephrine administration over the study period ($p=0.031$). Forty-two percent of the patients diagnosed early in the study (2001-2002) were treated with epinephrine compared with 57% of the patients diagnosed late in the study (2009-2010).

Main results

The overall age- and sex-adjusted incidence of anaphylaxis was 42 per 100,000 person-years (95% CI: 38.7- 45.3). The incidence rate of anaphylaxis increased significantly during the study period, as summarized in Table II and illustrated in Figure I. The incidence rate ratio was 1.043 (95% CI 1.015-1.072), indicating that there was a 4.3% increase per year in the incidence rate of anaphylaxis ($p < 0.001$).

Incidence rates based on inciting triggers are summarized in Table II and illustrated in Figure I. Food related anaphylaxis increased significantly during the study period, ($p < 0.001$) with an incidence rate ratio of 1.098 (95% CI 1.048-1.150), indicating that there was a 9.8% increase per year in the incidence rate for patients with food as the suspected trigger.

Table III and Figure II summarize the incidence of anaphylaxis based on age at diagnosis and inciting trigger. Incidence rates varied significantly by age group overall and within each inciting trigger. Overall, the highest incidence of anaphylaxis occurred in the 30-39 year old age group. Food-related anaphylaxis was most common in children aged 0-9 years. Venom related anaphylaxis was most common in those 20-39 years of age, and medication-related anaphylaxis was most common in those 30-39 years of age. When trends in incidence rates over time were evaluated with each age group, there was evidence that the overall incidence of anaphylaxis increased over the study period in patients 20-49 years of age ($p = 0.007$). There was not a statistically significant change in incidence over time for the other age groups.

Overall, across all ages and years of diagnosis, incidence rates were similar for men and women ($p = 0.15$). However, there were differences in rates of anaphylaxis between men and women within particular age groups (Table III, Figure III). There was a trend towards increased incidence in boys aged 0-9 years ($p = 0.056$) compared to girls in this age group. A statistically significant increased incidence rate was noted for males aged 10-19 ($p = 0.024$) and 30-39 ($p = 0.002$) compared to women in these age groups. In contrast, women aged 40-49 years were more likely to experience anaphylaxis than men in this age group ($p = 0.011$) (Figure III). There was not a statistically significant difference in the rate of anaphylaxis between men and women aged 20-29 years, 50-59 years, or 60 years or older.

DISCUSSION

Statement of principle findings

The overall age- and sex-adjusted incidence of anaphylaxis was 42 (95%CI 38.7 - 45.3) per 100,000 person-years. The incidence rate increased significantly during the study period. Overall, the peak incidence in anaphylaxis occurred between 30-39 years of age. Food-related anaphylaxis increased significantly during the study period and was more common in children aged 0-9 years. Venom-related anaphylaxis was most common in those 20-39 years of age, and medication-related anaphylaxis was most common among patients 30-39 years of age. The use of epinephrine for anaphylaxis management increased during the study period.

Strengths and limitations

The primary strength of our study is the ability to obtain a population-based estimate of the incidence of anaphylaxis over a 10-year period. Through the REP, we were able to identify nearly all cases of anaphylaxis, the treatments received, and outcomes in a geographically-defined community from 2001-2010. With the use of a record linkage system and standardized chart review, we were able to ascertain a rigorous estimate of the incidence of anaphylaxis in the population.

It is also noteworthy that we used the NIAID/FAAN criteria to define anaphylaxis.¹⁶ As the diagnosis of anaphylaxis remains clinical, our study used these criteria to identify the cases of anaphylaxis. This enabled chart reviewers to elucidate the diagnosis of anaphylaxis and achieve very good concordance.

The study also has some potential limitations. First, this was a retrospective cohort study, and the incidence of anaphylaxis was estimated based on chart review of a stratified random

sample of potential cases, raising the possibility of selection bias. Study findings were dependent on the accuracy of the medical record, particularly regarding the inciting triggers, signs and symptoms, and outcomes. Particularly, it is possible that additional patients had received epinephrine prior to ED arrival that was not documented. Second, the study was conducted in a predominantly white community, and the study findings may not generalize to other more diverse settings. Third, there is no universal agreement on the definition of anaphylaxis and implementation of a different definition could alter the estimation of the incidence. Despite this, the NIAID/FAAN criteria have been widely accepted by national and international allergy organizations and have been extensively used in the contemporary literature.^{18, 20} In addition, they are closely aligned with the definitions used in prior studies.^{5, 7, 17}

Despite these potential limitations, our patient cohort was very similar to previously studied cohorts with regard to patient demographics, presenting signs and symptoms, inciting triggers, incidence of biphasic reactions, and ED disposition^{5, 7, 21-25}, indicating that our cohort consists of a representative sample of patients with anaphylaxis in the population of Olmsted County and other geographic areas.

Interpretation of findings

Our study found that the incidence rate of anaphylaxis was 42 (95% CI 38.7-45.3) per 100,000 person-years. Yocum et al. studied the anaphylaxis incidence rate in Olmsted County from 1983-1987 and reported an average annual incidence rate of 21 per 100,000 person-years (95% CI 17-25) using the REP resources (adjusted to the 1980 US white population).⁷ The definition of anaphylaxis implemented was one symptom of generalized mediator release and one additional symptom involving the oral, respiratory, cardiovascular, or gastrointestinal

system.⁷ Decker et al. subsequently identified cases of anaphylaxis in the city of Rochester using the REP linkage system from 1990-2000.⁵ Initially, the Decker et al. study used the same definition as Yocum et al. but subsequently applied NIAID/FAAN criteria, concluding that there were only three cases that did not meet NIAID/FAAN criteria, and this did not affect the overall results.⁵ The overall age- and sex-adjusted incidence rate (adjusted to the 2000 total US population) reported in the Decker et al. study was 49.8 (95% CI 45.0-54.5) per 100,000 person-years.⁵ In addition, the Decker study reported an increasing incidence of anaphylaxis between 1990 and 2000 among the residents of Rochester, Minnesota.^{5, 7} Our study population included a county-wide cohort similar to the Yocum et al. study, applied the NIAID/FAAN criteria for the definition of anaphylaxis, and reports rates adjusted to the 2010 US white population. Thus, we are unable to directly compare our study to the Decker et al. study given that our cohort is geographically different. Nevertheless, our findings suggest that anaphylaxis has been increasing over the past quarter century in Olmsted County.

We found a nearly 10% increase in the incidence of food-related anaphylaxis per year. In addition, we found that food-related anaphylaxis was most common in children. These findings are consistent with other recent reports demonstrating increases in hospitalizations associated with food anaphylaxis, particularly in young patients.^{9, 26, 27}

Our study also showed that venom-related anaphylaxis is most common in 20-39 years of age and medication-related anaphylaxis is more common in 30-39 years of age. Hospitalizations for venom-induced anaphylaxis were also found to be more common in middle aged patients with lower rates noted in young and elderly patients.⁹ In addition, medication-induced anaphylaxis hospitalizations and fatalities have been shown to be most common among older

patients.^{9, 28} These findings likely reflect the risks of trigger exposure among patients of various ages.

Finally, we found an increasing rate of epinephrine administration by patient or caregiver over the study period. Multiple previous studies have demonstrated low rates of epinephrine administration among ED anaphylaxis patients.^{29, 30} However, more recent report have demonstrated increased rates of epinephrine administration.^{31, 32} The overall increased use of epinephrine in our study suggests increased anaphylaxis guideline adherence.

Implications for clinicians or policymakers

Our study indicates that the incidence of anaphylaxis overall and, more specifically, food-related anaphylaxis, increased during the study period. In addition, food-related anaphylaxis was most common in children aged 0-9 years, venom-related anaphylaxis was most common in 20-39 years of age, and medication-related anaphylaxis was most common in 30-39 years. Even if an episode of anaphylaxis was self-limited, previous study indicated that future reactions might be more severe.³³ Clinicians must be cognizant of these trends in the epidemiology of anaphylaxis, provide education to the patients at risk and supply epinephrine auto-injectors to mitigate the effects of recurrent reactions. Although not all patients may require epinephrine for anaphylaxis, increased access to epinephrine in public settings will help reduce complications of anaphylaxis. The access to epinephrine auto-injectors is vitally important in public settings, such as restaurants, daycares, schools, and workplaces.³⁴ Policymakers should be made aware of the risks of anaphylaxis in various age groups and the effectiveness of epinephrine for the management of acute anaphylaxis.

Unanswered questions and future research

Although this and other recent studies have demonstrated an increase in the incidence of anaphylaxis, it remains unknown if this is truly due to an increase in the disease or if it could be due to improved recognition and diagnosis.^{5, 35, 36} The disproportionate increase in food-related anaphylaxis observed in this and other studies would favor a true increase in anaphylaxis,^{27, 37, 38} as a trend in increase in anaphylaxis related to all triggers as might be expected if improved recognition was the driving factor.

CONCLUSIONS

Our study reveals several important findings. First, the incidence of anaphylaxis and specifically food-related anaphylaxis increased in Olmsted County during the study period from 2001-2010. Second, the highest incidence of anaphylaxis occurred in the 30-39 year age group, and the increasing incidence observed over time was limited to those aged 20-49. Third, food-related anaphylaxis was most common in children aged 0-9 years, venom related anaphylaxis was most common in 20-39 years of age, and medication-related anaphylaxis was most common in 30-39 years of age. Fourth, there was an increase in epinephrine use for acute management of anaphylaxis over time. Healthcare providers must be cognizant of these trends in the epidemiology of anaphylaxis, provide education to patients at risk and provide epinephrine auto-injectors to avoid morbidity and mortality.

393 **Tables**394 **Table I: Features of incident cases of anaphylaxis, N=631****General characteristics**

Age at diagnosis in years

0-9 72 (11)

10-19 91 (14)

20-29 132 (21)

30-39 135 (21)

40-49 82 (13)

50-59 62 (10)

60+ 57 (9)

Sex

Women 309 (49)

Men 322 (51)

Race/ethnicity (N=580)

White 493 (85)

Asian/Pacific Islander 38 (7)

Black 18 (3)

Hispanic 1 (<1)

Other	30 (5)
Inciting trigger	
Food	231 (37)
Venom	158 (25)
Medication	130 (21)
Contrast	6 (1)
Latex	1 (<1)
Other	36 (6)
Unknown	69 (11)
Disposition (N=626)	
Home	463 (74)
ED observation unit	71 (11)
Hospital ward	56 (9)
Intensive care unit	36 (6)
Past medical history	
Asthma	103 (16)
Allergic rhinitis	59 (9)
Atopic dermatitis	20 (3)
Hives	27 (4)

Signs and symptoms

Mucocutaneous system	608 (96)
Diffuse urticarial	248 (39)
Local angioedema	142 (23)
Oral pruritus	6 (1)
Pruritus	89 (14)
Flushing	88 (14)
Local urticarial	187 (30)
Conjunctivitis	4 (1)
Oropharyngeal edema	48 (8)
Diffuse angioedema	24 (4)
Diaphoresis	7 (1)
Chemosis/edema ocular conjunctiva	30 (5)
Tightness or fullness of throat	224 (36)
Rhinitis	15 (2)
Gastrointestinal system	118 (19)
Emesis	66 (10)
Nausea	46 (7)
Abdominal cramping	32 (5)

Diarrhea	21 (3)
Cardiovascular system	223 (35)
Pre-syncope/lightheadedness	91 (14)
Chest pain	104 (16)
Hypotension	49 (8)
Arrhythmia	1 (<1)
Syncope	34 (5)
Orthostatic hypotension	5 (1)
Respiratory system	485 (77)
Dyspnea/difficulty breathing	414 (66)
Wheezing/bronchospasm	92 (15)
Cough	28 (4)
Hoarseness/raspy voice	46 (7)
Cyanosis	13 (2)
Stridor	8 (1)
Aphonia	3 (<1)
Biphasic reaction	16 (3)
Treatment	
Steroid provided as therapy	401 (64)

Epinephrine provided as therapy 285 (45)

395 Sample sizes for features with missing data are indicated in italics in parentheses.

396 The values are N (%)

Table II: Incidence of anaphylaxis in Olmsted County, Minnesota 2001-2010 by year of diagnosis and inciting trigger

	Food		Venom		Medication		Total[†]	
Year	<i>N</i>	<i>Rate*</i>	<i>N</i>	<i>Rate*</i>	<i>N</i>	<i>Rate*</i>	<i>N</i>	<i>Rate*</i>
2001	10	7.2	24	16.2	6	3.8	54	36.8
2002	26	20.9	15	11.9	17	11.1	64	48.0
2003	11	7.3	25	15.2	14	9.7	61	39.2
2004	23	16.6	8	5.4	9	8.5	48	35.9
2005	11	7.2	3	1.9	8	5.6	28	19.1
2006	15	9.6	24	14.1	11	7.2	60	37.9
2007	42	24.6	5	3.0	25	18.4	83	53.0
2008	31	20.4	16	10.2	13	7.5	74	47.3
2009	28	16.8	36	24.0	8	5.5	88	57.2
2010	34	22.1	2	1.4	19	13.2	71	46.6
p-value**	<0.001		0.11		0.25		<0.001	

*Incidence per 100,000 person-years age- and sex-adjusted to 2010 US white population.

**p-value for the trend in incident rates over time (2001-2010).

[†]Includes patients with other and unknown inciting triggers.

Table III: Incidence of anaphylaxis in Olmsted County, Minnesota 2001-2010 by age at diagnosis, sex and inciting trigger

	Women		Men		Food		Venom		Medication		Total ^{††}	
Age at Diagnosis	N	Rate*	N	Rate*	N	Rate*	N	Rate*	N	Rate*	N	Rate*
0-9	27	26.4	45	42.0	44	21.0	10	4.8	15	7.2	72	34.4
10-19	34	34.2	57	55.9	37	18.4	26	12.9	10	5.0	91	45.2
20-29	74	60.5	58	56.3	43	19.1	41	18.2	23	10.2	132	58.6
30-39	51	50.0	84	84.9	38	18.9	41	20.4	31	15.4	135	67.2
40-49	54	48.9	28	27.0	29	13.5	24	11.2	12	5.6	82	38.3
50-59	39	44.0	23	28.4	26	15.3	12	7.1	12	7.1	62	36.5
60+	30	24.5	27	28.1	14	6.4	4	1.8	27	12.4	57	26.1
Total	309	40.1 [†]	322	43.8 [†]	231	15.2 [‡]	158	10.2 [‡]	130	9.1 [‡]	631	42.0 [‡]
p-value**	<0.001		<0.001		0.006		<0.001		0.004		<0.001	

*Incidence per 100,000 person-years.

**p-value for differences in incidence rates among age groups (2001-2010).

[†]Incidence per 100,000 person-years age-adjusted to 2010 US white population.

[‡]Incidence per 100,000 person-years age- and sex-adjusted to 2010 US white population.

^{††}Includes patients with other and unknown inciting triggers.

Figure I. Age and sex adjusted incidence rate of anaphylaxis by year of diagnosis and inciting trigger, 2001-2010

Figure II. Incidence rate anaphylaxis by age group and inciting triggers

Figure III. The incidence rate of anaphylaxis by age group and sex

Appendix Figure. Patient selection process

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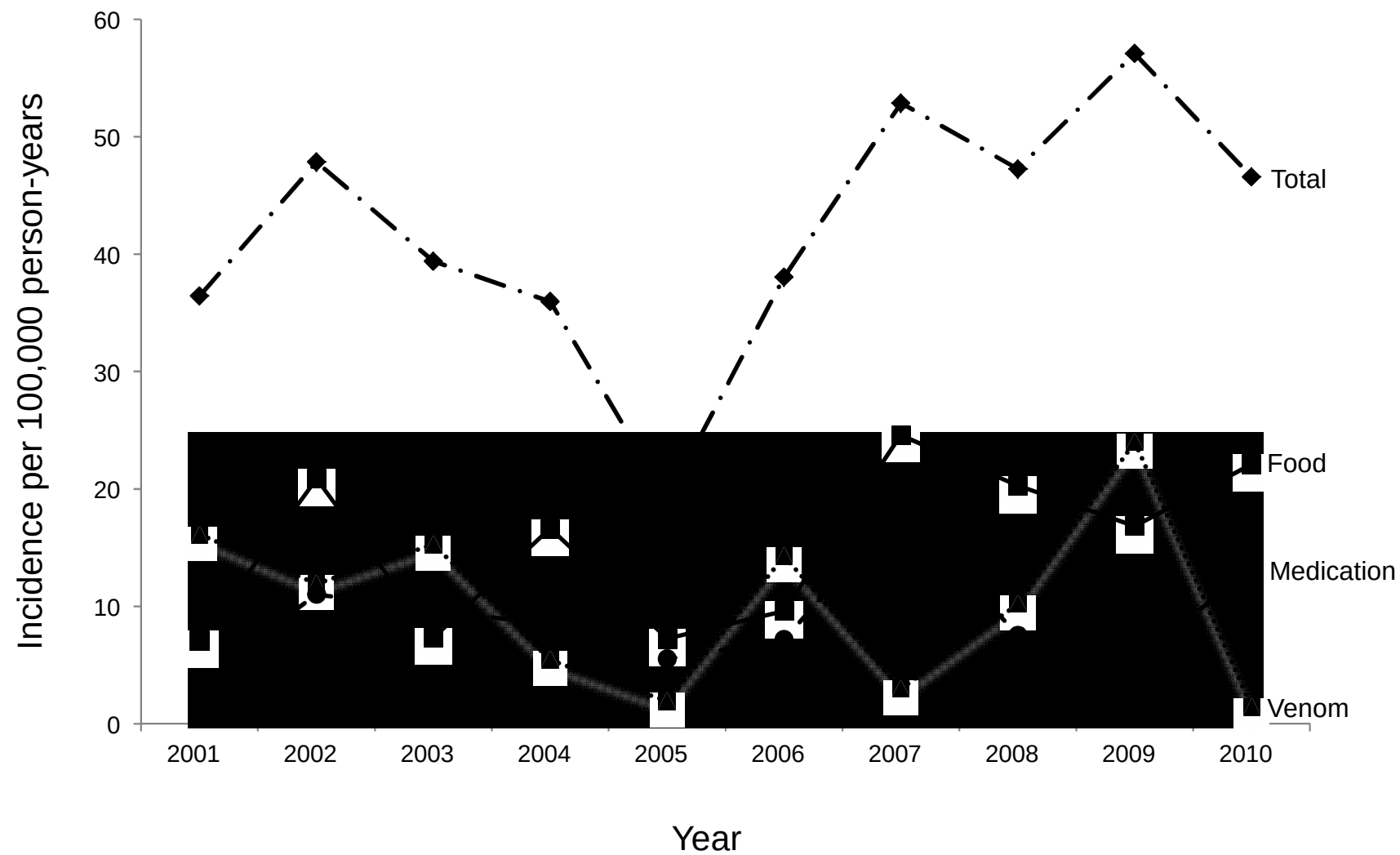
Reference

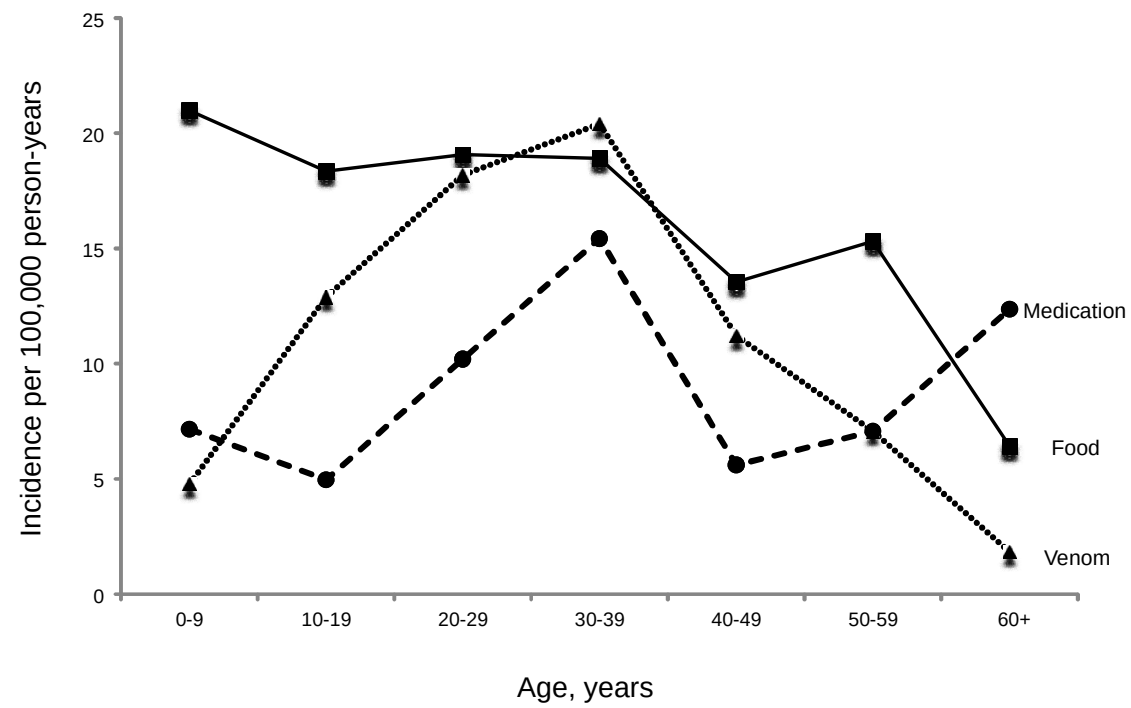
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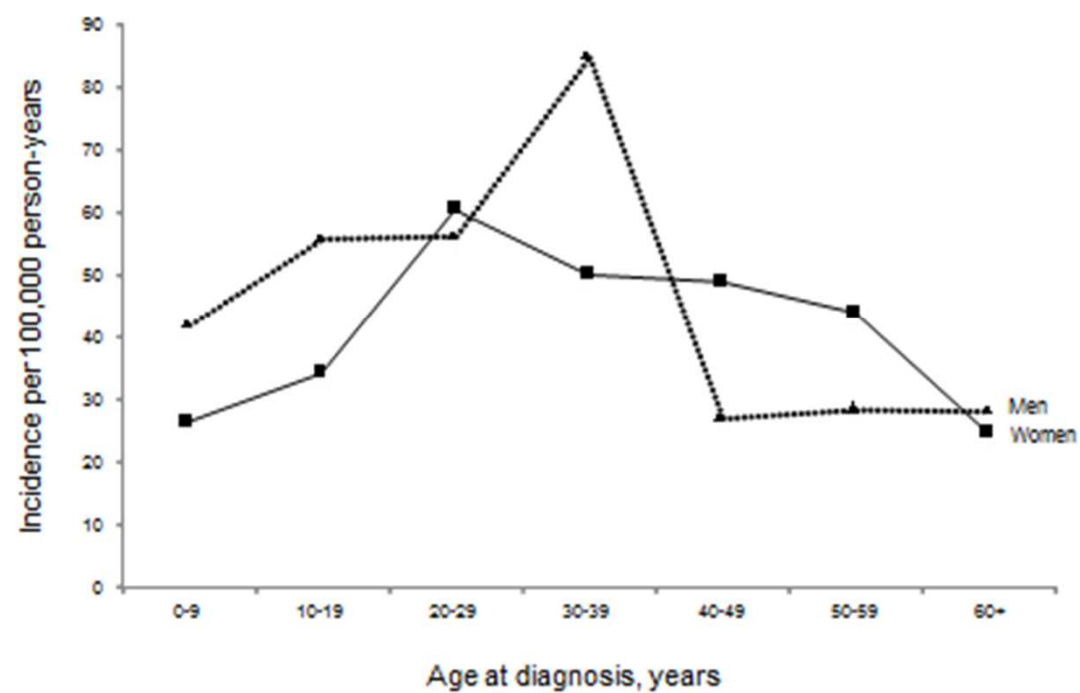
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Appendix Table. NIAID/FAAN criteria

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (generalized hives, pruritus or flushing, swollen lips-tongue-uvula) AND AT LEAST ONE OF THE FOLLOWING:
 - a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced Peak Expiratory flow [PEF], hypoxemia)
 - b. Reduced blood pressure [BP] or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a *likely* allergen for that patient (minutes to several hours)
 - a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
 - b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP after exposure to known allergen for that patient (minutes to several hours)
 - a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP
 - b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline³⁶

