

Prevalence and triggers of anaphylactic events in schools

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ABSTRACT

Background: Prevention and management of anaphylaxis in schools is an area of active interest as allergy and asthma rates in children continue to increase. A greater understanding of the prevalence and characteristics of anaphylaxis can help guide preventive and management strategies both within and outside of the school setting, with the goal of reducing morbidity and mortality.

Objective: This study was performed to elucidate the epidemiology of and management strategies for anaphylaxis in the school setting.

Methods: A cross-sectional, Web-based survey was administered to schools that participated in an initiative that provides stock epinephrine autoinjectors (EAI) to qualifying U.S. schools. Representatives from participating schools completed a questionnaire regarding anaphylactic reactions that occurred during the 2014–2015 school year. Weighted analyses were performed to account for differential responses between schools that completed the survey and those that did not.

Results: A total of 12,275 of the 45,819 invited schools responded to the survey. The occurrence of one or more anaphylactic events was reported by 1358 schools. Most events (89.8% [1803/2008]) occurred in students. High school students accounted for the largest proportion of anaphylactic reactions among students (40.1% [723/1802]). Food was the most commonly identified anaphylaxis trigger across grade levels, seasons, and geographic regions. The trigger was unknown to the individual who experienced anaphylaxis in 21.8% of the events (436/1998). No known history of allergy or asthma was present in 24.5% (491/2001) and 51.3% (1026/2000) of affected individuals, respectively. Transportation to the hospital or clinic for further treatment and/or management was reported for 72.6% of the individuals with anaphylactic events (1450/1997). Results from the weighted analyses were similar to those of the unweighted analyses.

Conclusion: Anaphylaxis occurred across grade levels and in individuals with or without known risk factors, which reinforced the need for school preparedness in both management of anaphylaxis and stocking of EAI.

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Anaphylaxis is a considerable and growing health concern in the United States. Rates of anaphylaxis seem to be on the rise in the general population,¹ with notable increases in the incidence of food-related anaphylaxis reported by pediatric emergency depart-

ments (ED) in recent years.^{1–3} School administrators have also noted increases in students who self-report severe allergies (particularly elementary-school-age children) and more frequent anaphylactic events occurring in the school setting.⁴ Despite these observations, there remains a lack of adequate information regarding the epidemiology of and triggers for anaphylactic events.⁵ Understanding the factors associated with anaphylaxis can help guide preventive and management strategies both within and outside of the school setting.

Since 2012, the EpiPen4Schools program (Mylan Specialty, L.P., Canonsburg, PA) has provided anaphylaxis training materials and epinephrine autoinjectors (EAI) to participating U.S. schools. EAI are provided at no cost, and free replacement products are offered in the event that a stock EAI is used to respond to an allergic reaction. To date, >60,000 schools have participated in the EpiPen4Schools program. By using this sample of public and private schools, an exploratory pilot survey was conducted at the completion of the 2013–2014 school year to gain insights into the prevalence of anaphylaxis and how anaphylactic events were managed in the school setting.^{6–9} This report presented data from an updated survey of schools for the 2014–

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Table 1 The 2014–2015 EpiPen4Schools survey questions

1. Is a report (electronic or paper) required to document anaphylactic events and/or use of epinephrine autoinjectors (EAI) at your school?
Where are those reports maintained?
2. Is there a school nurse at this school?
3. Who in your school is trained to recognize the signs and symptoms of anaphylaxis?
4. Which school members are permitted to administer epinephrine?
How are these school members trained to administer epinephrine?
5. When there is an anaphylaxis event at your school, what is your standard initial (*i.e.*, first-line) treatment?
6. Which of the following are components of your school or school district policy on the management of life-threatening allergies?
7. Please provide the total number of EAIs stocked during the 2014–2015 school year; include all EAIs, including those prescribed to individuals, those received through the EpiPen4Schools program, those received through other school programs, and any that were purchased or sourced by the school or school system.
8. Were any other forms of epinephrine (such as vials or nebulizer solution) stocked at the school during the 2014–2015 school year?
9. Have there been any anaphylactic events (life-threatening allergic reactions) that have occurred in your school during the 2014–2015 school year?
10. For each event, please answer the following questions.
 - a. Who had an anaphylactic attack?
 - b. What is the gender of the individual who had the anaphylactic attack?
 - c. What is the ethnicity of the individual who had the anaphylactic attack?
 - d. What is the race of the individual who had the anaphylactic attack?
 - e. When did the event occur?
 - f. Did the individual have a known allergy?
 - g. Did the individual have a diagnosis or history of asthma?
 - h. What was the trigger for the anaphylactic event?
 - i. Location where symptoms developed?
 - j. Was the individual administered epinephrine on school property or at a school-sponsored event?
 - k. Was a second epinephrine injection administered after the first while the individual was on school grounds or at a school-sponsored event?
 - l. Who administered the epinephrine injection(s)?
 - m. Was a treatment other than epinephrine given as an alternative or in addition to epinephrine?
 - n. Were emergency medical services called?
 - o. Was the individual transported to a hospital or clinic?
 - p. Did the individual survive the allergic reaction?
 - q. Were parents or guardians advised to follow up with student's or minor's medical provider?
 - r. Were arrangements made to restock epinephrine after this event?

2015 school year that built on previous findings to obtain more detailed data and to gather responses from a broader cross-section of schools.

METHODS

Study Design

A cross-sectional, Web-based survey was conducted between May 8, 2015, and August 14, 2015. Schools that were registered in the EpiPen4Schools program and for which contact information was available ($N = 45,819$) were invited to participate in a brief online questionnaire regarding anaphylactic reactions that occurred during the 2014–2015 school year. The survey consisted of 29 questions, 18 of which were repeated for each anaphylactic event reported (Table 1). Surveys

were to be completed by the individual best suited to respond (*e.g.*, school nurse, other health staff, school administrator). The study was submitted to the RTI Institutional Review Board for approval, which determined that the research activity did not constitute research that involved human subjects as defined by the U.S. Code of Federal Regulations (45 CFR 46.102).¹⁰ The approval of these activities by the RTI Institutional Review Board was not necessary; therefore, an exemption was granted.

Sample preparation and contact with schools that participated in the EpiPen4Schools program was performed as previously described.⁶ Of the 60,448 schools registered in the EpiPen4Schools program, 56,622 (94%) could be matched to the U.S. Department of

Education, National Center for Education Statistics Common Core of Data (CCD), and Private School Universe Survey (PSS) data bases, from which demographic information was obtained. The 3826 schools without entries in the CCD or PSS data bases were not included in the sample. In addition, 10,872 records were found to be duplicates and were excluded from the sample. The effective sample for this survey included 45,750 schools with CCD or PSS data and contact information (mail or e-mail address) available at the school or contact level. Another 69 schools that were not part of the effective sample (but were confirmed to be participating in the EpiPen4Schools program) also responded to the survey, for a final total of 45,819 schools.

Data Analysis

Data were presented primarily as unweighted descriptive statistics. Completed surveys were not required to have all questions answered; therefore, denominators for percentage calculations were based on the number of schools that responded to the associated question. "Unknown" responses were included in the denominator, but missing responses were excluded from the analyses. A weighted analysis was conducted to account for differential responses from schools that participated in the survey versus schools that did not. Only schools with CCD or PSS data were considered. The SUDAAN® procedure WTADJUST (RTI International, Research Triangle Park, NC) was used to calculate nonresponse analysis weights at the school level after first investigating the terms for bias between the responders and nonresponders. This procedure used a constrained logistic model to predict responses based on known terms (including region, school grade configuration, total student population, racial or ethnic makeup, type of school [private or public], and free or reduced-price lunch) in the CCD and PSS files. Although weights were created at the school level, they also were used for analyses conducted at the event level because each weighted event essentially represented events at other similar schools.

RESULTS

Survey Responses

Data were collected from 12,275 of the 45,819 schools that were invited to participate in the survey, which yielded a 26.8% overall response rate. All but 23 of the submitted surveys indicated the position of the survey respondent. Of these, 63.9% (7823/12,252) were completed by the school nurse, 12.6% (1542/12,252) by administrative staff at the district or school level, 12.5% (1534/12,252) by the principal or other school administrator, 8.9% (1085/12,252) by other school staff, and the remaining 2.2% (268/12,252) by other health staff. Schools from all four major U.S. census regions con-

tributed survey responses: 29.9% (3673/12,275) were from the Northeast, 27.9% (3429/12,275) were from the Midwest, 26.9% (3304/12,275) were from the South, and 15.2% (1869/12,275) were from the West. Elementary schools had the greatest representation in the overall sample (36.3%), followed by elementary/middle schools (23.2%), high schools (17.0%), middle schools (12.1%), middle/high schools (5.9%), and elementary/middle/high schools (5.2%).

Characteristics of Anaphylactic Events

A total of 2191 anaphylactic reactions were reported by 1358 schools who reported one or more events during the 2014–2015 school year. Of these events, none were reported to be fatal. The majority of schools (88.9% [10,823/12,181]) reported that no anaphylactic events had occurred during the school year. The regional breakdown of schools that reported no anaphylactic events was comparable with that of the overall survey population. Among the schools that described an anaphylactic event, 67.3% (914/1358) reported a single event, 19.6% (266/1358) reported two events, and 13.1% (178/1358) reported three or more events. Event rates were highest in the West (0.53 events per 1000 schools) and lowest in the Midwest (0.29 events per 1000 schools).

Demographic data for individuals with a reported anaphylactic event are described in Table 2. Anaphylactic events generally occurred in students (89.8% [1803/2008]). Staff, adult visitors, and minor visitors accounted for 9.3% (186/2008), 0.5% (10/2008), and 0.4% (9/2008) of anaphylactic reactions, respectively. High school students accounted for the largest proportion of anaphylactic reactions among students (40.1% [723/1802]); more female than male individuals experienced anaphylaxis: 56.3% (1107/1968) versus 41.7% (820/1968), respectively. Among those who experienced an anaphylactic attack, 24.5% (491/2001) had no known allergy and 51.3% (1026/2000) had no known history of asthma (Fig. 1).

Triggers of Anaphylactic Events

Food was reported as the most common putative trigger for anaphylaxis and accounted for 54.0% of events (1079/1998) for which responses were available (Table 3). Among foods linked to anaphylaxis, nuts were the most frequently cited trigger (40.9% [440/1077]), followed by fruit (13.0% [140/1077]). In a large proportion of events, the specific food involved could not be identified (32.8% [353/1077]). When parsed by grade level, food remained the predominant trigger, which ranged in prevalence from 53.5% (386/722 events in high school students) to 57.5% (235/409 events in middle school students) (Fig. 2). For 21.8% of reported events (436/1998), the trigger was unknown

Table 2 Demographic characteristics of individuals who experienced an anaphylactic event

Characteristic	Event, no. (%) (N = 2191)*
Classification, total no.	2008
Student	1803 (89.8)
Staff	186 (9.3)
Adult visitor	10 (0.5)
Minor visitor	9 (0.4)
Grade level, total no.	1802
Pre-kindergarten to 5th grade	643 (35.7)
6th to 8th grade	411 (22.8)
9th to 12th grade	723 (40.1)
Unknown	25 (1.4)
Sex, total no.	1968
Female	1107 (56.3)
Male	820 (41.7)
Unknown	41 (2.1)
Race, total no.	2003
American Indian or Alaskan native	17 (0.8)
African American	319 (15.9)
Asian	95 (4.7)
Native Hawaiian or other Pacific Islander	10 (0.5)
White	1236 (61.7)
Other	50 (2.5)
Unknown	290 (14.5)
Ethnicity, total no.	1996
Hispanic or Latino	186 (9.3)
Non-Hispanic or Latino	1484 (74.3)
Unknown	326 (16.3)

*Missing responses were excluded from the analyses.

to the individual who experienced anaphylaxis (Table 3). Unknown trigger prevalence was highest among high school students (26.9% [194/722]) and lowest among elementary school students (17.7% [113/638]) (Fig. 2).

Seasonal variations were observed in trigger distribution (Fig. 3). Food remained a leading trigger throughout the year; however, a higher relative percentage of food-triggered anaphylactic events was reported in winter (254/405 [62.7%]) than in spring (399/695 [57.4%]), fall (303/592 [51.2%]), or summer (34/74 [45.9%]). As would be expected, insect bite or sting and environmental triggers (e.g., pollen and mold) increased in the spring (41/695 [5.9%] for both insect bite or sting and environmental triggers), peaked in the summer (13/74 [17.6%] and 8/74 [10.8%], respectively), and decreased again in the fall (75/592 [12.7%] and 37/592 [6.3%], respectively), with their nadir in the winter (6/405 [1.5%] and 22/405 [5.4%], respectively). A

considerably larger proportion of anaphylactic events triggered by food allergies was reported in schools located in the Northeast (411/660 [62.3%]) than in the West (133/255 [52.2%]), South (344/692 [49.7%]), or Midwest (191/391 [48.8%]). Insect bites or stings were reported at slightly higher percentages by schools in the Midwest (45/391 [11.5%]) and West (26/255 [10.2%]) versus the Northeast (43/660 [6.5%]) and South (62/692 [9.0%]).

Additional Care Administered Outside the School and/or School-Sponsored Event

At the time of the event, parents or guardians were advised to follow up with a medical provider in 92.0% (1657/1801) of reported events that occurred in minors. Of the events with available data on hospital transport, 72.6% (1450/1997) were transported to a hospital or clinic by an ambulance or by a parent, guardian, or other individual. In 13.6% of the events (271/1997), the reason given for not transporting the individual was that the symptoms resolved or were deemed not to be severe.

Additional Analyses

To ensure that responding schools were representative of the broader EpiPen4Schools program, a weighted analysis was conducted wherein school demographics (e.g., region, grade configuration, student population, racial or ethnic makeup, private versus public, and free or reduced-price lunch) were used in a nonresponse adjustment model to account for differential school responses. No extreme weights that could cause a large unequal weighting effect were identified in these analyses. Overall, findings from the weighted analyses were similar to those of the unweighted analyses.

DISCUSSION

EpiPen4Schools survey data from both the initial pilot study and the subsequent larger-scale survey reported herein provided important insights into anaphylactic events that occurred in the U.S. school setting. A better understanding of the epidemiology of anaphylaxis in school-age children can build awareness, bolster preventive efforts, and inform school policy decisions. The results of the 2014–2015 survey, which included responses from 12,275 schools that participate in the EpiPen4Schools program, expanded on previous findings from the 2013–2014 pilot survey, both in terms of information gathered and the number of participants. The veracity and generalizability of the initial exploratory survey results were affirmed by consistency with findings from the current survey with regard to the anaphylactic event rate and distribution.^{6,8} In each school year, at least one anaphylactic

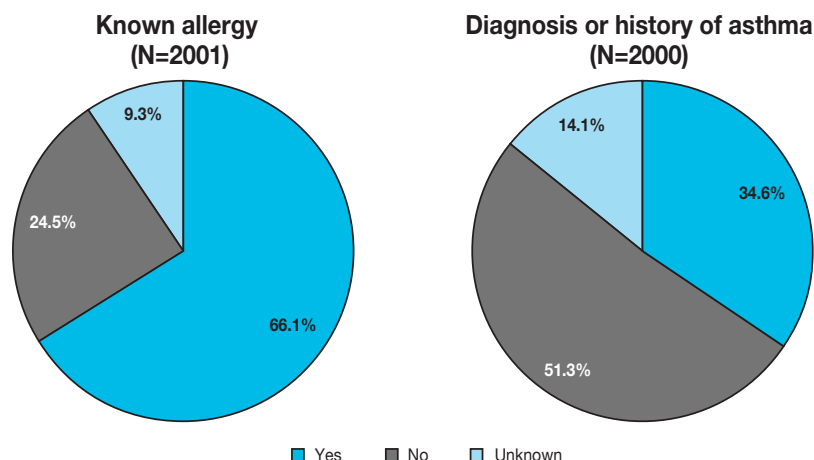


Figure 1. History of allergy or asthma among individuals who experienced an anaphylactic event.

Table 3 Triggers for reported anaphylactic reactions

Trigger	Event, no. (%) (N = 2191)*
Food	1079 (54.0)
Nuts	440 (40.9)
Fruit	140 (13.0)
Fish	50 (4.6)
Dairy	28 (2.6)
Egg	21 (1.9)
Other	45 (4.2)
Unknown	353 (32.8)
Missing	2
Insect bite or sting	176 (8.8)
Bee	130 (76.0)
Wasp or hornet	15 (8.8)
Ant	14 (8.2)
Other or unknown	12 (7.0)
Missing	5
Environmental	125 (6.3)
Medication	60 (3.0)
Exercise	30 (1.5)
Latex	10 (0.5)
Other	0
Unknown to individual	436 (21.8)
having event	
Unknown or information not	82 (4.1)
documented	
Missing	193

*Missing responses were excluded from the analyses.

event was reported by 11% of participating schools.⁶ In addition, both surveys found that the vast majority of anaphylactic events (89–90%) occurred among students rather than staff or visitors.

A notable dichotomy between the EpiPen4Schools surveys was in the distribution of anaphylaxis triggers.

In the 2013–2014 survey, anaphylactic reactions were attributed to food in 62.5% of the events,⁶ whereas, in the 2014–2015 survey, food accounted for 54.0% of the anaphylaxis triggers. The lower incidence of food as a trigger seemed counterintuitive given the observed rise in food-induced anaphylaxis in recent years.^{1–3} However, the proportion of food triggers from the 2014–2015 survey aligned with the 55.3% reported by DeSantiago-Cardenas *et al.*¹¹ in their assessment of anaphylactic reactions in Chicago public schools during the 2012–2013 school year.

Both EpiPen4Schools surveys found that a substantial proportion of anaphylactic events occurred in people with no known history of allergy (21.9% in 2013–2014 and 24.5% in 2014–2015). These observations were consistent with a previous report from Massachusetts in which approximately one-fourth of the anaphylactic events in the school setting occurred in individuals with no known allergies.¹² The 2014–2015 EpiPen4Schools survey also queried respondents about a history or a diagnosis of asthma among those who had experienced an anaphylactic event. The reported prevalence of asthma (34.6%) was on par with other studies in children treated for anaphylaxis in the ED.^{13–15} Taken together, the large subset of anaphylactic events that occurred in the absence of a known allergy or asthma supported the need for awareness of anaphylaxis symptoms and management among school personnel and reinforced the need to keep a supply of undesignated EAI on hand for general use in the treatment of these life-threatening events.

Both EpiPen4Schools surveys consistently found higher anaphylactic event rates among high school students compared with younger grade levels.⁸ High school students also experienced the greatest proportion of events in which the trigger was unknown to the individual. High school students may benefit the most from health care provider counseling because they are at the greatest risk of anaphylactic events. Older stu-

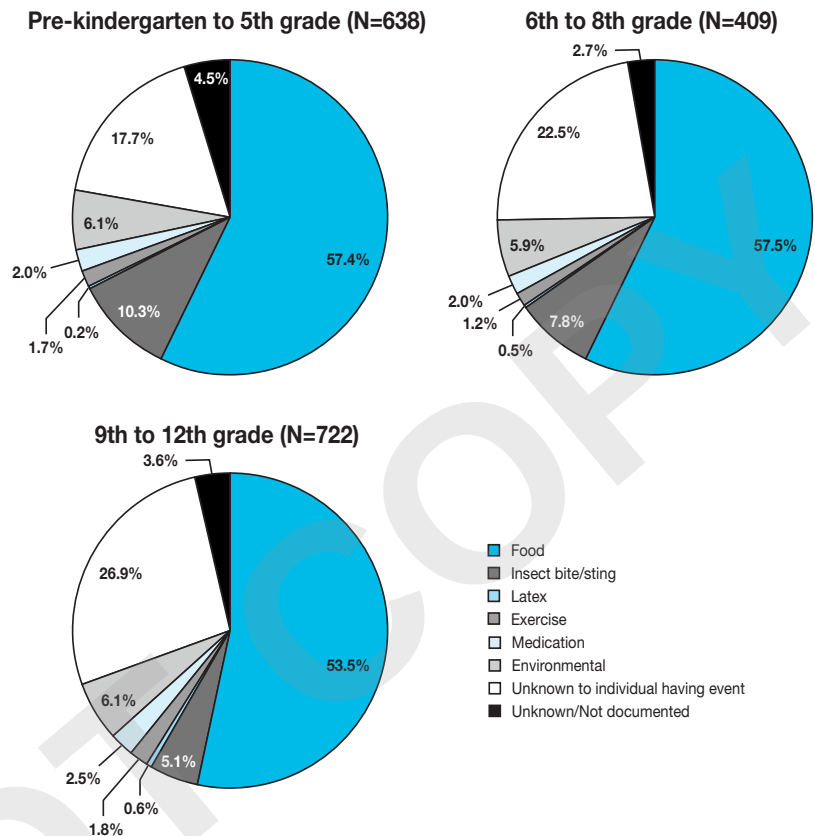


Figure 2. Anaphylaxis triggers by grade level for students. This includes data from 1769 anaphylactic events; the grade level was unknown for 24 events, and responses were missing for 10 of the 1803 reported student events.

dents are often in unsupervised situations in which peer pressure can lead them to engage in risky behaviors, *e.g.*, consuming known allergens, with >50% of high school students with known food allergies admitting to eating allergens.¹⁶ The degree of education regarding anaphylaxis and allergen avoidance in this group could not be determined from this study. However, in a recent survey of U.S.-based clinicians, most emergency medicine and family practitioners ($\geq 64\%$) expressed a lack of awareness regarding the heightened risk of fatal anaphylaxis in teenagers,¹⁷ which indicated that the need for instruction on anaphylaxis prevention and management among adolescents may be underestimated in clinical practice.

Most schools (92.0%) that participated in the 2014–2015 survey reported that they advised parents and guardians to follow up with a health care provider after an anaphylactic event, which is consistent with guidelines from major medical organizations.^{18,19} However, the 23.5% rate of nontransport to a hospital or clinic was concerning. Individuals are at risk of a biphasic reaction even after administration of epinephrine. Those who experience anaphylaxis are encouraged to seek immediate medical attention,²⁰ and delay in presentation to the ED has been identified as an independent predictor of biphasic reactions in children.²¹ For 13.6% of events in the 2014–2015 EpiPen4Schools survey,

the reason given for not transporting the individual was that the symptoms resolved or were deemed not to be severe; however, the onset of symptoms of anaphylaxis can be delayed, and the onset of food-related anaphylaxis is slower than drug- or insect-induced anaphylaxis.¹⁸ Professional guidelines advocate that the duration of medical supervision after an anaphylactic event be tailored to the individual, with a longer observation period (*i.e.*, 4–8 hours) for patients who have experienced moderate-to-severe anaphylaxis or who have risk factors for severe anaphylaxis.^{22,23}

The interpretation of these findings was subject to the limitations inherent to a survey instrument. Moreover, the data available for each event were limited by the level of detail recorded by the school or district at the time of occurrence. A strength of the larger sample size in the 2014–2015 study was that the effect of missing data points for an individual survey had less of an impact on the overall findings. Although the survey response rate was 26.8%, the weighted analyses provide reassurance that the results were representative of schools that participated in the EpiPen4Schools program. Nonetheless, by virtue of their participation in the program, the surveyed schools may be more proactive in anaphylaxis management than U.S. schools in general. Consistency in findings between the EpiPen4Schools surveys and those of other independent investigations (as

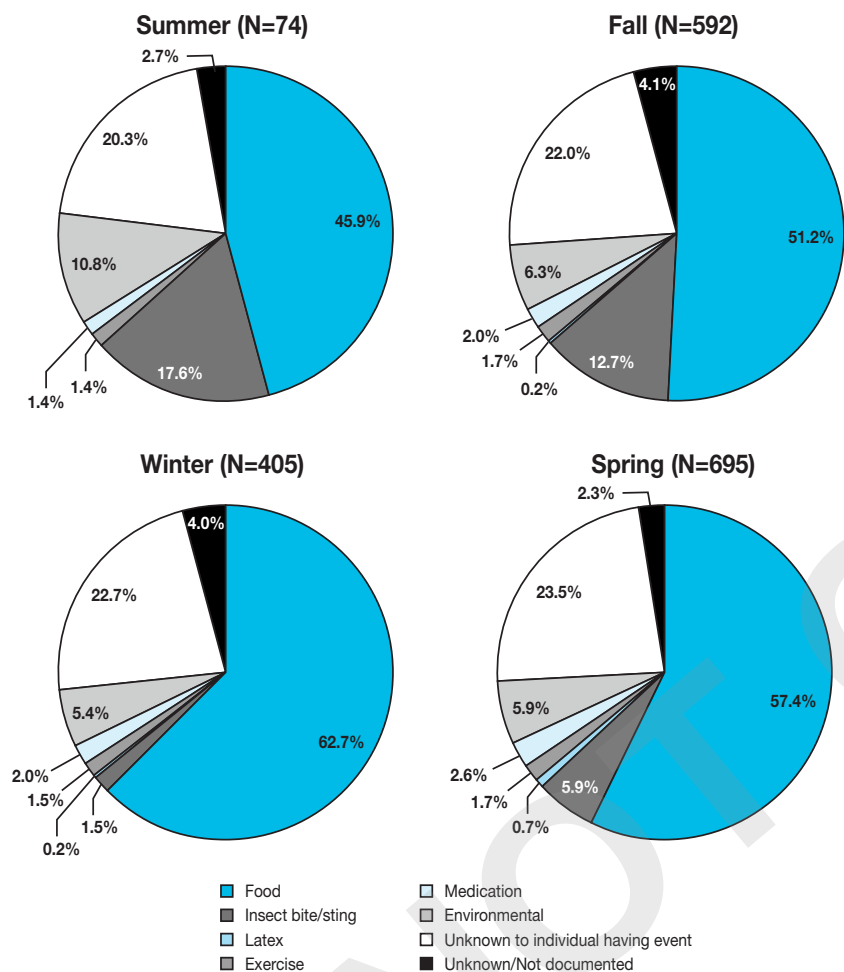


Figure 3. Anaphylaxis triggers by season for students. This includes data from 1766 anaphylactic events; responses were missing for 37 of the 1803 reported student events.

described above) supports the generalizability of the EpiPen4Schools survey beyond the scope of the participating schools. Further verification through independent assessments is warranted.

CONCLUSION

The EpiPen4Schools surveys demonstrated that schools were the setting for an appreciable number of anaphylactic events, many of which occurred in individuals without known risk factors for anaphylaxis. Although nearly 90% of schools did not report any anaphylactic events during the 2014–2015 school year, the results of this survey demonstrated that anaphylaxis was unpredictable and could occur in students of any grade level and across all regions. Thus, all schools need to be prepared to treat anaphylactic events with the prompt administration of epinephrine *via* an EAI in accordance with accepted guidelines.^{19,23} Awareness and preparedness (including stocking undesignated EAIs for general use) are needed to prevent adverse sequelae, including mortality, which can result from delayed or inappropriate management of anaphylactic reactions.

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