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Epinephrine treatment of food-induced and other cause anaphylaxis in United States and Canadian Emergency Departments: a systematic review and meta-analysis

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Abstract

Introduction: Studies from more than 10 years ago showed epinephrine treatment of food-induced anaphylaxis in the emergency department (ED) was unacceptably low. We investigated whether epinephrine treatment of food-induced and other cause anaphylaxis in United States and Canadian EDs has changed over time.

Methods: Guided by a health sciences librarian, we performed a systematic search in Medline, Embase and Web of Science on January 11, 2023. We included observational studies that reported epinephrine use to treat anaphylaxis in the ED. We stratified by anaphylaxis etiology (food-, venom-, medication-induced, any cause). Associations between year and epinephrine use were tested using Spearman correlation, and proportional meta-analysis.

Results: Of 2,458 records identified in our initial search, 40 met inclusion criteria. Of these, 14 examined food-induced, 4 venom-induced, 0 medication-induced, and 24 any cause anaphylaxis. For epinephrine treatment of food-induced anaphylaxis in the ED, among studies using similar definition of anaphylaxis, meta-analysis showed a pooled value of 20.7% (95% CI 17.8, 23.8) for studies performed >10 years ago, and 45.1% (95% CI 38.4, 52.0) from those in the last 10 years.

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Author contributions

G Mehta designed the study, performed review of articles and data extraction, carried out the statistical analyses, drafted the initial manuscript, critically reviewed and revised the manuscript. I Baroni, J El Zein, and M Qadir performed review of articles and data extraction, and critically reviewed and revised the manuscript. C Mita designed the search strategy, drafted the search strategy portion of the methods section and critically reviewed and revised the manuscript. R Cash supervised the statistical analysis and critically reviewed and revised the manuscript. C Camargo conceptualized and designed the study, supervised data collection and analysis, and critically reviewed and revised the manuscript. All authors read and approved the final version of the manuscript for publication.

Reviewer disclosures

One peer reviewer is a provincial lead for C-CARE. Peer reviewers on this manuscript have no other relevant financial relationships or otherwise to disclose.

Declaration of interest

Over the past 30 years, C Camargo has done paid consultation for several companies that make epinephrine auto-injectors (Mylan, Kaleo) or that are developing new modes of epinephrine delivery (Hikma, Bryn). He also has served on scientific advisory boards for these same companies. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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For anaphylaxis of any cause, there was no change over time, with a pooled value of 45.0% (95% CI 39.8, 50.3) over the last 10 years.

Discussion: Epinephrine treatment of food-induced anaphylaxis in the ED has increased over time. There was no clear change for anaphylaxis of any cause. Over the last 10 years, approximately 45% of ED patients with anaphylaxis received epinephrine. A limitation of the evidence is heterogeneity in anaphylaxis definitions.

Keywords

anaphylaxis; epinephrine; food-induced anaphylaxis; meta-analysis; proportion; systematic review; treatment

1.0 Background

Anaphylaxis is a serious allergic reaction that is rapid in onset and can be life-threatening.[1] It is relatively common, with lifetime prevalence of anaphylaxis from all triggers estimated to be 0.05% to 5%.[2,3] The incidence of anaphylaxis appears to be rising and food-induced anaphylaxis is the leading cause of anaphylactic reactions treated in the emergency department (ED).[4,5] Although use of adjunctive medications (e.g., antihistamines, glucocorticoids) to treat anaphylaxis is common, epinephrine administration is most clearly associated with decreased morbidity and mortality and is the single first-line management strategy.[6–8] Early studies showed that real world use of epinephrine to treat food-induced and other cause anaphylaxis in the ED was lower than expected.[9,10] Over the last two decades there seems to be increasing awareness about the primacy of epinephrine in anaphylaxis management by ED healthcare providers primarily due to increased emphasis of this principal in anaphylaxis management guidelines.[1,11–16] However, there have been no systematic reviews that have investigated this topic.

Our objective was to examine whether epinephrine use to treat food-induced and other cause anaphylaxis in United States and Canadian EDs has changed over time. Secondarily, we examined pre-ED epinephrine use, any epinephrine use (pre-ED or ED), prescription for epinephrine, and referral to allergy clinic on discharge from the ED.

2.0 Methods

We prospectively registered this study in the international prospective register of systematic reviews (PROSPERO) under the registration number: CRD42023389616. This can be accessed at crd.york.ac.uk/prospero. Amendments to the protocol are listed in Supplement Table 1. We adhered to Preferred Reporting Items of Systematic Review and Meta-Analyses (PRISMA) for reporting of this systematic review and meta-analysis.[17] This systematic review did not involve human subjects and therefore Institutional Review Board approval was waived.

2.1 Search strategy

We identified studies reporting the use of epinephrine to treat anaphylaxis in the ED by searching Medline/PubMed (National Library of Medicine, NCBI); Embase (Elsevier,

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embase.com), and Web of Science Core Collection (Clarivate). Controlled vocabulary terms (i.e., MeSH, Emtree) were included when available and appropriate. The search strategies were designed and carried out by a health sciences librarian (CM). A language limit was applied to include studies published in English and French due to the geographic region of interest. No publication date restrictions were applied. The search was conducted on January 11, 2023. The exact search terms used for each of the databases are provided in Supplement Table 2. To reduce the risk of missing any related citation, we also manually searched the reference list of included original articles.

2.2 Study selection

We included studies that reported the frequency of epinephrine treatment in the ED for anaphylaxis in a population of people who presented to the ED for anaphylaxis (food-induced, venom-induced, medication-induced, any cause) in the United States or Canada. Other inclusion criteria were observational study design, English or French language and report was a published manuscript. We excluded studies that did not report the sample size of the anaphylaxis population or the timeframe of data collection, surveys of patients and case reports/case series. Studies of interventions, reviews, systematic review and meta-analyses were also excluded.

Four reviewers performed title/abstract screening using Covidence, a web-based collaboration software platform that streamlines production of systematic and other literature reviews (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). As a calibration exercise, all reviewers screened the same 50 titles and abstracts and discussed questions/discrepancies prior to moving on to the formal reviewing phase. Each title/abstract was screened to meet the inclusion/exclusion criteria by two reviewers, independently. For titles/abstracts where there was disagreement, a third senior reviewer adjudicated. Each full text was screened to meet the inclusion/exclusion criteria by two reviewers, independently. For full texts where there was disagreement, a third senior reviewer adjudicated.

2.3 Data extraction and quality assessment

Three reviewers performed data extraction from included full texts. Two reviewers independently extracted data from each full text and consensus was reached on any discrepancies. We contacted corresponding authors for data clarification as needed. For each selected full text manuscript, we extracted the following primary outcome data: number of participants with anaphylaxis, number of participants treated with epinephrine in the ED, and etiology of anaphylaxis. We also extracted the following variables: lead author name, year of publication, study design, country of data collection, study period, age of participants, definition of anaphylaxis (Supplement Table 3), number of participants treated with epinephrine pre-ED (defined as self/parent/school/other administration or emergency medical services [EMS] administration), number of participants treated with epinephrine pre-ED or in the ED, number of participants prescribed epinephrine on discharge, and number of participants who received allergy clinic referral on discharge. Studies of anaphylaxis of any cause were examined for sub-analysis reporting of epinephrine use in

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the ED for food-, venom- and medication-induced anaphylaxis. Food-induced anaphylaxis was our primary diagnosis of interest.

To assess risk of bias among the full texts included, we used the Joanna Briggs Institute Prevalence Critical Appraisal Tool.[18–20] This tool uses nine questions with four standard answer options yes/no/unclear/not applicable. Two reviewers independently evaluated each article and consensus was reached on any discrepancy.

2.4 Data analysis

Interrater reliability was assessed using Cohen's kappa statistic. For studies that collected data over multiple years, the median year of the study period was used for data analysis. To assess for change in epinephrine treatment of anaphylaxis over time, we first examined the data qualitatively using scatter plots (x-axis = median year, y-axis = percent of patients with anaphylaxis treated with epinephrine in the ED). If there were sufficient number of studies, we used Spearman correlation and meta-analysis stratified by time period to quantitatively assess the relationship. We performed meta-analysis using a user-written Stata command called *metaprop* to calculate pooled proportions and 95% CI overall and for two time periods, 2013–2022 (last 10 years) and prior to 2013.[21,22] Pooled proportions are presented as percentages for clarity. Heterogeneity was determined by I^2 values. Given concern for bias, we excluded from the Spearman correlation and meta-analysis studies with overlapping cohorts or where the number treated with epinephrine was not stated. For overlapping cohorts, we selected those with shorter time frames, that included multiple timeframes within the study, or that increased total number of studies in the meta-analysis, and excluded the others. Secondary outcomes were not meta-analyzed due to concern for incomplete capture of relevant literature as our systematic search was optimized for capture of our primary outcome. Analyses were performed using Stata 15.1 (Stata Corp, College Station, TX, USA).

3.0 Results

3.1 Literature search and study selection

We identified 2,442 records though our systematic database search and then an additional 16 records by manual search of references from included articles (Figure 1). There were 1,639 records after removal of duplicates. Title/abstract review excluded 1,511 records, the remaining 128 were assessed for eligibility. Of these, 88 were excluded and a total of 40 were included in the systematic review. A sample of studies that may have appeared to meet the inclusion criteria, but which were excluded are available in Supplement Table 4.

Of 1639 titles/abstracts, there was disagreement on 61 (3.7%). Of 128 full texts, there was disagreement on 15 (12%). The interrater reliability of the title/abstract screening ranged from 0.61–0.80 among reviewers who reviewed >10 of the same titles/abstracts.

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3.2 Characteristics of eligible studies

Of the 40 eligible studies reporting epinephrine treatment of anaphylaxis in the ED, 14 reported on food-induced anaphylaxis, four venom-induced anaphylaxis, and 25 anaphylaxis of any cause (Table 1).

No included studies examined medication-induced anaphylaxis. Most studies were retrospective (n = 28), though some were prospective (n = 4), or a combination of the two (n = 8). Most studies used the National Institute of Allergy and Infectious Diseases/ Food Allergy and Anaphylaxis Network (NIAID/FAAN) definition of anaphylaxis (n = 27). Fewer studies used International Classification of Disease, Ninth Revision or Tenth Revision (ICD-9 or ICD-10) codes for anaphylaxis (n = 5), ICD-9 or ICD-10 codes for anaphylaxis followed by application of the NIAID/FAAN definition (n = 4), or other definitions of anaphylaxis (n = 4). There was a mix of studies that examined pediatric (n = 20), adult (n = 5) or both age groups (n = 15). There were 9 publications that reported on overlapping cohorts/timeframes: excluding three of these studies removed all potentially overlapping cases.[29,32,43] Gaeta 2007 only reported a percentage for epinephrine use in the ED, but not the number treated with epinephrine and therefore was also excluded from further analyses.[46]

3.3 Bias assessment

Overall, the quality of the studies included was good. Potential bias mainly came from differences in sample size, differences in the definition of anaphylaxis, and lack of reporting of important clinical factors (e.g., number of participants who received epinephrine before arriving to the ED [pre-ED]). Supplement Table 5 summarizes the potential for bias of each study.

3.4 Food-induced anaphylaxis

Of the 14 studies examining food-induced anaphylaxis, the median year of study period ranged from 2000 to 2016. The percentage of ED patients who received epinephrine treatment ranged from 17 to 63% (Table 2). There appeared to be a trend toward increase in epinephrine use in the ED over time ($r = 0.49$, $p=0.07$) (Figure 2A); excluding the three studies that used a non-NIAID/FAAN definition of anaphylaxis led to a stronger association ($r = 0.72$, $p = 0.009$) (Figure 2A). Meta-analysis of studies stratified by time period (prior to 2013 vs 2013–2022) showed trend toward an improvement in epinephrine use over time (prior to 2013: pooled 27.6% [95% CI 15.8, 41.1], $I^2 = 98.7\%$, $p < 0.001$; 2013–2022: pooled 45.1% [95% CI 38.4, 52.0], $I^2 = 85.1\%$, $p < 0.001$); however, heterogeneity was high (Supplement Figure 1). Sensitivity analysis examining only studies using the NIAIAD/ FAAN definition of anaphylaxis, stratified by time period, showed an improvement over time with a pooled value of 20.7% (95% CI 17.8, 23.7; $I^2 = 57.9$; $p = 0.04$) for studies performed prior to 2013, and a pooled value of 45.1% (95% CI 38.4, 52.0; $I^2 = 85.1$; $p < 0.001$) from those performed from 2013–2022 (Figure 3).

Many studies included participants of all ages. When restricting the analysis to studies that included only children (n = 8) the primary finding remained the same. There was an improvement in use of epinephrine in the ED for treatment of food-induced anaphylaxis

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(prior to 2013: 25.6% [95% CI 11.2, 43.5]; 2013–2022: 51.0% [95% CI 47.5, 54.4]). There were an insufficient number of studies that included only adults (n = 1) to examine this subgroup.

Examination of pre-ED epinephrine use over time did not show a clear improvement, with rates ranging between 17% and 55% (Figure 2B). However, when examining pre-ED or ED epinephrine use there appeared to be an improvement over time, with studies in the last 10 years ranging between 56% and 80% compared to studies prior to 2013 with range of 31% to 61% (Figure 2C). Qualitative examination of epinephrine prescription and allergy clinic referral on discharge from the ED also showed improvement (Figure 4A, B). These secondary outcomes were not meta-analyzed due to possible incomplete capture of data in the literature.

3.5 Venom-induced anaphylaxis

Of the four studies examining venom-induced anaphylaxis, the median year of study period ranged from 2000 to 2014. The percentage of ED patients who received epinephrine treatment ranged from 6% to 50% (Table 2). Given the low sample size, we were not able to assess for changes in ED epinephrine use over time in this group. We also were not able to assess for changes in pre-ED or pre-ED and/or ED epinephrine use over time.

3.6 Anaphylaxis of any cause

Of the 25 studies examining anaphylaxis of any cause, the median year of study period ranged from 1995 to 2019. The percentage of ED patients who received epinephrine treatment ranged from 6% to 72% (Table 2). There did not appear to be an increase in epinephrine use in the ED over time ($r = 0.08$, $p = 0.71$) (Figure 5A). This finding did not change when we excluded studies that used a non-NIAID/FAAN definition of anaphylaxis. Meta-analysis stratified by time period also showed no significant change; a pooled value of 38.3% (95% CI 19.8, 58.6; $I^2 = 99.9\%$; $p < 0.001$) for studies performed prior to 2013, and a pooled value of 45.0% (95% CI 39.8, 50.3; $I^2 = 92.4$; $p < 0.001$) for those performed from 2013–2022 (Supplement Figure 2). The overall pooled value was 41.0% (95% CI 27.1, 55.6, $I^2 = 99.9\%$, $p < 0.001$). This finding was similar when we excluded studies that used a non-NIAID/FAAN definition of anaphylaxis (Supplement Figure 3).

When restricting the analysis to studies that include only children (n = 13) the primary findings remain the same. There was no change over time for use of epinephrine in the ED for treatment of any cause anaphylaxis (prior to 2013: 46.7% [95% CI 38.4, 55.1]; 2013–2022: 44.7% [95%CI 37.4, 52.2]). There were an insufficient number of studies that included only adults (n = 4) to examined this subgroup.

There did appear to be qualitative improvement in pre-ED use of epinephrine and pre-ED and/or ED use of epinephrine over time (Figure 5B,C). These secondary outcomes were not meta-analyzed due to possible incomplete capture of data in the literature.

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4.0 Discussion

We performed a systematic review and meta-analysis to examine whether use of epinephrine in the ED for treatment of food-induced and other cause anaphylaxis, in the United States and Canada, has changed over time. We found that for food-induced anaphylaxis, the pooled percentage of ED patients treated with epinephrine in the ED improved from 21% for studies performed >10 years ago (prior to 2013), to 45% for those from the last 10 years (2013–2022), among studies who use the NIAID/FAAN definition of anaphylaxis. We did not find a change over time for anaphylaxis of any cause, but noted a similar frequency of treatment (45%) for studies performed over the last 10 years. There were not enough studies to analyze changes for venom- or medication-induced anaphylaxis.

4.1 Food-induced and any cause anaphylaxis

We have shown that the use of epinephrine for treatment of food-induced anaphylaxis in the ED has improved over time. Although the same cannot be said about any cause anaphylaxis, the frequency of epinephrine treatment started higher than for food-induced anaphylaxis -- and usage was similar (45%) for both food-induced and any cause anaphylaxis over the last 10 years. However, an important question remains: is 45% high enough or is there continued room for improvement in ED administration of epinephrine?

Although ED treatment is a key part of the care of a patient who experiences anaphylaxis, the pre-ED management, including self/parent/school/other and emergency medical services (EMS) administration of epinephrine will influence ED management. A recent systematic review and meta-analysis showed that only 8% of patients with anaphylaxis require more than a single dose of epinephrine.[61] Therefore, if a patient receives epinephrine prior to ED arrival, on most occasions the ED would not need to administer an additional dose. Further, since early administration of epinephrine is an important predictor of morbidity and mortality associated with epinephrine use,[26,62] preferably there would be increased pre-ED use of epinephrine which would necessarily and appropriately result in decreased need for ED use of epinephrine. Our secondary outcome, rate of pre-ED epinephrine use for treatment of anaphylaxis did not appear to improve over time for food-induced anaphylaxis, but it did appear to improve for any cause anaphylaxis. For any cause anaphylaxis, more pre-ED epinephrine use over the last 10 years may explain why we do not see an increase in ED epinephrine use over the same time frame.

Although we did not include studies from outside the United States or Canada in the present study, it appears that treatment of any cause anaphylaxis by a health professional in Europe may have improved over time. Using data from the European Anaphylaxis Register, Grabenhenrich and colleagues found that over the last decide, epinephrine administration from a health professional to treat anaphylaxis almost doubled to reach 30.6% in 2015–2017.[63] While this study examines epinephrine use in healthcare professionals generally, rather than ED clinicians, it does suggest that epinephrine usage was very low 10 years ago and has improved over time, but may still remain suboptimal. This study does not examine epinephrine use by anaphylaxis etiology (e.g. food-induced anaphylaxis), so it is not possible to know if food-induced anaphylaxis also has an improvement over time.

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We found that for both food-induced and any cause anaphylaxis, any epinephrine use (pre-ED or ED) did appear to improve over time with rates as high as 80% in two different studies. Among the patients who did not receive epinephrine for their anaphylaxis pre-ED or in the ED, it is possible that non-guideline based care was given; however, there may be alternative explanations in many cases. For example, anaphylaxis may have resolved prior to ED presentation (e.g, Pouessel and colleagues found that among 116 children seen in an ED for grade 3 or 4 anaphylaxis, 52% had rapid improvement of anaphylaxis symptoms prior to ED arrival without epinephrine administration[64]), the anaphylaxis may have been mild (e.g., flushing and abdominal pain without other symptoms) and the patient may have preferred not to receive an intramuscular medication, or the provider may have felt that the risk outweighed the benefit (e.g., mild anaphylaxis in a patient with severe coronary artery disease). Indeed, a study by Baalmann et al found that although more than 60% of patients with anaphylaxis did not receive epinephrine in the ED, case review by two board certified allergy immunology physicians deemed ED management appropriate in 98% of total cases.[39] In sum, epinephrine should always be used as soon as anaphylaxis symptoms are recognized. However, ED clinicians may evaluate patients whose anaphylaxis has already been treated with epinephrine prior to ED arrival or whose anaphylaxis spontaneously resolved prior to evaluation, and therefore will likely not administer epinephrine to 100% of patients who are presenting for anaphylaxis.

4.2 Limitations of the evidence

Limitations of the evidence used in this systematic review include, most importantly, differences in the way anaphylaxis was defined. Some studies performed chart review of all potential allergic reaction cases applying the NIAID/FAAN criteria for anaphylaxis, which is the most widely accepted definition. Others used ICD-9 and/or ICD-10 codes for anaphylaxis to identify possible cases and then performed chart review using NIAID/FAAN criteria to verify the diagnosis, likely producing a higher severity group of patients with anaphylaxis as there may have been cases that presented to the ED who met the NIAID/FAAN criteria, but were not given an ICD-9 and/or ICD-10 code for anaphylaxis, but rather were labeled with a different code like adverse food reaction or allergic reaction not otherwise specified. Still others used only ICD-9 and/or ICD-10 codes for anaphylaxis without additional validation, which has been shown to both over and under-include true anaphylaxis cases in a sample.[65] There were also other methods in identified articles, which have not been validated or present possible concern for bias. We attempted to address this by performing sensitivity analyses using anaphylaxis definition (Figure 3).

An additional limitation is that several studies used in the food allergy analysis were focused on single foods and therefore may not be representative of food allergy generally. Further, several of the more recent food allergy studies are from the Cross-Canada Anaphylaxis Registry (C-CARE). We ensured that we did not use overlapping samples by excluding the study that covered a larger time period, if there were two timeframes that overlapped, but it does give large representation to data from the C-CARE cohort, especially for food-induced anaphylaxis data over the last 10 years. Reassuringly, C-CARE is the most robust Canadian data available on anaphylaxis which includes data from multiple centers across Canada. It has both retrospective and prospective data collection and therefore is less

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likely to be missing substantial numbers of observations. Finally, severity of anaphylaxis was not reported in the vast majority of studies and therefore we were not able to report whether treatment of anaphylaxis with epinephrine varied between mild, moderate and severe presentations.

4.3 Limitations of the review process

Limitations of the review process include that we based our inclusion and exclusion criteria on the primary outcome, rate of use of epinephrine for treatment of anaphylaxis in the ED, and therefore studies that only reported data for our secondary outcomes (pre-ED epinephrine use, any epinephrine use [pre-ED or ED], epinephrine autoinjector prescription and allergy clinical referral on discharge) were not included in the systematic review. This limits our ability to interpret the secondary outcomes, as we likely did not capture all extant relevant literature on these different topics.

5.0 Conclusion

Epinephrine treatment of food-induced anaphylaxis in the ED has improved over time to 45% in the last 10 years. There is no clear change over time for anaphylaxis of any cause, but there was the similar usage of epinephrine (45%) over the last 10 years as seen for food-induced anaphylaxis. These data show possible improvements in pre-ED epinephrine use and any epinephrine use (pre-ED or ED) for anaphylaxis, but our systematic search was focused on ED administration and therefore may not have completely captured literature related to these secondary outcomes. It is important to emphasize that pre-ED epinephrine use will affect the rate of ED epinephrine use. We encourage future studies (including systematic reviews) on epinephrine use in the treatment of food-induced and other cause anaphylaxis to focus on pre-ED epinephrine use and any epinephrine use (pre-ED or ED) for treatment of anaphylaxis. Similar studies (and systematic reviews) could be completed for epinephrine prescriptions and allergy referral.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Papers of special note have been highlighted as either of interest (*) or of considerable interest (**) to readers.

1. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med 2006;47:373–80. DOI: 10.1016/j.annemergmed.2006.01.018#1. [PubMed: 16546624] * This reference establishes the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network

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(NIAID/FAAN) definition of anaphylaxis which is the most widely accepted definiton of anaphylaxis at this time. It also states that anaphylaxis is probably under recognized and undertreated in both the prehospital setting and in the ED.

2. Lieberman P, Camargo CA Jr., Bohlke K, et al. Epidemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. Ann Allergy Asthma Immunol 2006;97:596–602. DOI: 10.1016/S1081-1206(10)61086-1 [PubMed: 17165265]
3. Wood RA, Camargo CA Jr., Lieberman P, et al. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol 2014;133:461–7. DOI: 10.1016/j.jaci.2013.08.016 [PubMed: 24144575]
4. Sampson HA. Anaphylaxis and emergency treatment. Pediatrics 2003;111:1601–8 [PubMed: 12777599]
5. Motosue MS, Bellolio MF, Van Houten HK, et al. Increasing Emergency Department Visits for Anaphylaxis, 2005–2014. J Allergy Clin Immunol Pract 2017;5:171–5. DOI: 10.1016/j.jaip.2016.08.013 [PubMed: 27818135]
6. Brown JC, Simons E, Rudders SA. Epinephrine in the Management of Anaphylaxis. J Allergy Clin Immunol Pract 2020;8:1186–95. DOI: 10.1016/j.jaip.2019.12.015 [PubMed: 32276687]
7. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. Clin Exp Allergy 2000;30:1144–50. DOI: 10.1046/j.1365-2222.2000.00864.x [PubMed: 10931122]
8. Sheikh A, Shehata YA, Brown SG et al. Adrenaline for the treatment of anaphylaxis: cochrane systematic review. Allergy 2009;64:204–12. DOI: 10.1111/j.1398-9995.2008.01926.x [PubMed: 19178399]
9. Clark S, Bock SA, Gaeta TJ, et al. Multicenter study of emergency department visits for food allergies. J Allergy Clin Immunol 2004;113:347–52. DOI: 10.1016/j.jaci.2003.10.053#2. [PubMed: 14767453] * This reference is one of the earliest multi-center studies to describe low rates of epinephrine use among EDs in the United States to treat food-induced anaphylaxis.
10. Clark S, Long AA, Gaeta TJ, et al. Multicenter study of emergency department visits for insect sting allergies. J Allergy Clin Immunol 2005;116:643–9. DOI: 10.1016/j.jaci.2005.06.026 [PubMed: 16159637]
11. Campbell RL, Li JT, Nicklas RA, et al. Emergency department diagnosis and treatment of anaphylaxis: a practice parameter. Ann Allergy Asthma Immunol 2014;113:599–608. DOI: 10.1016/j.anai.2014.10.007 [PubMed: 25466802]
12. Kemp SF, Lockey RF, Simons FE, et al. Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization. Allergy 2008;63:1061–70. DOI: 10.1111/j.1398-9995.2008.01733.x [PubMed: 18691308]
13. Lieberman P, Nicklas RA, Oppenheimer J, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. J Allergy Clin Immunol 2010;126:477–80 e1–42. DOI: 10.1016/j.jaci.2010.06.022 [PubMed: 20692689]
14. Joint Task Force on Practice Practice Parmeters. The diagnosis and management of anaphylaxis: an updated practice parameter. J Allergy Clin Immunol 2005;115:S483–523. DOI: 10.1016/j.jaci.2005.01.010 [PubMed: 15753926]
15. Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy 2014;69:1026–45. DOI: 10.1111/all.12437 [PubMed: 24909803]
16. Alrasbi M, Sheikh A. Comparison of international guidelines for the emergency medical management of anaphylaxis. Allergy 2007;62:838–41. DOI: 10.1111/j.1398-9995.2007.01434.x [PubMed: 17620061]
17. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372:n160. DOI: 10.1136/bmj.n160 [PubMed: 33781993]
18. Migliavaca CB, Stein C, Colpani V, et al. Quality assessment of prevalence studies: a systematic review. J Clin Epidemiol 2020;127:59–68. DOI: 10.1016/j.jclinepi.2020.06.039 [PubMed: 32679313]

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19. Munn Z, Moola S, Riitano D, et al. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Health Policy Manag 2014;3:123–8. DOI: 10.15171/ijhpm.2014.71 [PubMed: 25197676]
20. Munn Z, Moola S, Lisy K, et al. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. Int J Evid Based Healthc 2015;13:147–53. DOI: 10.1097/XEB.0000000000000054 [PubMed: 26317388]
21. Barker TH, Migliavaca CB, Stein C, et al. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. BMC Med Res Methodol 2021;21:189. DOI: 10.1186/s12874-021-01381-z [PubMed: 34544368]
22. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health 2014;72:39. DOI: 10.1186/2049-3258-72-39 [PubMed: 25810908]
23. Banerji A, Rudders SA, Corel B, et al. Repeat epinephrine treatments for food-related allergic reactions that present to the emergency department. Allergy Asthma Proc 2010;31:308–16. DOI: 10.2500/aap.2010.31.3375 [PubMed: 20819321]
24. Clark S, Boggs KM, Balekian DS, et al. Changes in Emergency Department Concordance with Guidelines for the Management of Food-Induced Anaphylaxis: 1999–2001 versus 2013–2015. J Allergy Clin Immunol Pract 2019;7:2262–9. DOI: 10.1016/j.jaip.2019.04.004 [PubMed: 30974210]
25. Ducharme L, Gabrielli S, Clarke AE, et al. Tree nut-induced anaphylaxis in Canadian emergency departments: Rate, clinical characteristics, and management. Ann Allergy Asthma Immunol 2022;129:335–341. DOI: 10.1016/j.anai.2022.06.008 [PubMed: 35718284]
26. Fleming JT, Clark S, Camargo CA, et al. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. J Allergy Clin Immunol Pract 2015;3:57–62. DOI: 10.1016/j.jaip.2014.07.004 [PubMed: 25577619]
27. Gabrielli S, Clarke AE, Morris J, et al. Fruit-Induced Anaphylaxis: Clinical Presentation and Management. J Allergy Clin Immunol Pract 2021;9:2825–2830.e2. DOI: 10.1016/j.jaip.2021.02.055 [PubMed: 33727108]
28. Kim SL, Suresh R, Mayampurath A, et al. Increase in Epinephrine Administration for Food-Induced Anaphylaxis in Pediatric Emergency Departments From 2007 to 2015. J Allergy Clin Immunol Pract 2022;10:200–5.e1. DOI: 10.1016/j.jaip.2021.09.024 [PubMed: 34563738]
29. Rehimini S, Gabrielli S, Langlois A, et al. Specific IgE antibody levels during and after food-induced anaphylaxis. Clin Exp Allergy 2021;51:364–368. DOI: 10.1111/cea.13796 [PubMed: 33252817]
30. Ross MP, Ferguson M, Street D, et al. Analysis of food-allergic and anaphylactic events in the National Electronic Injury Surveillance System. J Allergy Clin Immunol 2008;121:166–171. DOI: 10.1016/j.jaci.2007.10.012 [PubMed: 18206508]
31. Rudders SA, Banerji A, Vassallo MF, et al. Trends in pediatric emergency department visits for food-induced anaphylaxis. J Allergy Clin Immunol 2010;126:385–388. DOI: 10.1016/j.jaci.2010.05.018 [PubMed: 20621344]
32. Rudders SA, Banerji A, Corel B, et al. Multicenter study of repeat epinephrine treatments for food-related anaphylaxis. Pediatrics 2010;125:e711–8. DOI: 10.1542/peds.2009-2832 [PubMed: 20308215]
33. Sehayek D, Gold MS, Gabrielli S, et al. Seafood-induced anaphylaxis in children presenting to Canadian emergency departments: Rates, clinical presentation, and management. Ann Allergy Asthma Immunol 2022;128:583–588. DOI: 10.1016/j.anai.2022.02.003. [PubMed: 35172181]
34. Sillcox C, Gabrielli S, Clarke AE, et al. Sesame-induced anaphylaxis in pediatric patients from the cross-Canada anaphylaxis registry. Ann Allergy Asthma Immunol 2022;129:342–6. DOI: 10.1016/j.anai.2022.06.005 [PubMed: 35697193]
35. Clark S, Boggs KM, Balekian DS, et al. Changes in emergency department concordance with guidelines for the management of stinging insect-induced anaphylaxis: 1999–2001 vs 2013–2015. Ann Allergy Asthma Immunol 2018;120:419–23. DOI: 10.1016/j.anai.2018.01.029 [PubMed: 29407420]

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36. Rudders SA, Clark S, Wei W, et al. Longitudinal study of 954 patients with stinging insect anaphylaxis. Ann Allergy Asthma Immunol 2013;111:199–204. DOI: 10.1016/j.anai.2013.06.020 [PubMed: 23987196]
37. Arroyo AC, Robinson LB, Cash RE, et al. Trends in Emergency Department Visits and Hospitalizations for Acute Allergic Reactions and Anaphylaxis Among US Older Adults: 2006–2014. J Allergy Clin Immunol Pract 2021;9:2831–43. DOI: 10.1016/j.jaip.2021.03.032 [PubMed: 33798790]
38. Asai Y, Yanishevsky Y, Clarke A, et al. Rate, triggers, severity and management of anaphylaxis in adults treated in a Canadian emergency department. Int Arch Allergy Immunol 2014;164:246–52. DOI: 10.1159/000365631 [PubMed: 25170673]
39. Baalmann DV, Hagan JB, Li JT, et al. Appropriateness of epinephrine use in ED patients with anaphylaxis. Am J Emerg Med 2016;34:174–9. DOI: 10.1016/j.ajem.2015.10.003 [PubMed: 26542795]
40. Calderón E, Méndez J, Nazario S. Anaphylaxis diagnosis and treatment at an emergency department in Puerto Rico. P R Health Sci J 2013;32:170–4. [PubMed: 24397213]
41. Carrillo-Martin I, Gonzalez-Estrada A, Funni SA, et al. Increasing Allergy-Related Emergency Department Visits in the United States, 2007 to 2015. J Allergy Clin Immunol Pract 2020;8:2983–88. DOI: 10.1016/j.jaip.2020.05.056 [PubMed: 32553832]
42. Castilano A, Sternard B, Cummings ED, et al. Pitfalls in anaphylaxis diagnosis and management at a university emergency department. Allergy Asthma Proc 2018;39:316–321. DOI: 10.2500/aap.2018.39.4144 [PubMed: 30095397]
43. Chiang D, Ade JM, Liu XW, et al. Assessment of ED triage of anaphylaxis patients based on the Emergency Severity Index. Am J Emerg Med 2021;46:449–55. DOI: 10.1016/j.ajem.2020.10.057 [PubMed: 33176953]
44. Cohen N, Test G, Scolnik D. Predictors of epinephrine undertreatment in anaphylaxis—the experience of a busy North American tertiary care pediatric emergency department. J Allergy Clin Immunol Pract 2021;9:2090–2. DOI: 10.1016/j.jaip.2020.12.063 [PubMed: 33453451]
45. Gabrielli S, Clarke A, Morris J, et al. Evaluation of Prehospital Management in a Canadian Emergency Department Anaphylaxis Cohort. J Allergy Clin Immunol Pract 2019;7:2232–8. DOI: 10.1016/j.jaip.2019.04.018 [PubMed: 31035000]
46. Gaeta TJ, Clark S, Pelletier AJ, et al. National study of US emergency department visits for acute allergic reactions, 1993 to 2004. Ann Allergy Asthma Immunol 2007;98:360–5. DOI: 10.1016/S1081-1206(10)60883-6 [PubMed: 17458433]
47. Goetz VL, Kim K, Stang AS. Pediatric Anaphylaxis in the Emergency Department: Clinical Presentation, Quality of Care, and Reliability of Consensus Criteria. Pediatr Emerg Care 2019;35:28–31. DOI: 10.1097/PEC.0000000000001136 [PubMed: 28398938]
48. Hemler JA, Sharma HP. Management of children with anaphylaxis in an urban emergency department. Ann Allergy Asthma Immunol 2017;118:381–3. DOI: 10.1016/j.anai.2016.12.021. [PubMed: 28132736]
49. Hochstadter E, Clarke A, De Schryver S, et al. Increasing visits for anaphylaxis and the benefits of early epinephrine administration: A 4-year study at a pediatric emergency department in Montreal, Canada. J Allergy Clin Immunol 2016;137:1888–90. DOI: 10.1016/j.jaci.2016.02.016 [PubMed: 27106202]
50. Huang F, Chawla K, Järvinen KM, et al. Anaphylaxis in a New York City pediatric emergency department: Triggers, treatments, and outcomes. J Allergy Clin Immunol 2012;129:162–8. DOI: 10.1016/j.jaci.2011.09.018 [PubMed: 22018905]
51. Lee AYM, Enarson P, Clarke AE, et al. Anaphylaxis across two canadian pediatric centers: Evaluating management disparities. J Asthma and Allergy 2017;10:1–7. DOI: 10.2147/JAA.S123053 [PubMed: 28115856]
52. Liu X, Lee S, Lohse CM, et al. Biphasic Reactions in Emergency Department Anaphylaxis Patients: A Prospective Cohort Study. J Allergy Clin Immunol Prac 2020;8:1230–8. DOI: 10.1016/j.jaip.2019.10.027

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53. Manivannan V, Campbell RL, Bellolio AF, et al. Factors associated with repeated use of epinephrine for the treatment of anaphylaxis. Ann Allergy Asthma Immunol 2009;103:395–400. DOI: 10.1016/s1081-1206(10)60358-4 [PubMed: 19927537]
54. Meir LR, Habbsa S, Waqar O, et al. Anaphylaxis among elderly emergency department patients in a large health system in New York. Ann Allergy Asthma Immunol 2022;129:63–70. DOI: 10.1016/j.anai.2022.03.020 [PubMed: 35346881]
55. Owusu-Ansah S, Badaki O, Perin J, et al. Under Prescription of Epinephrine to Medicaid Patients in the Pediatric Emergency Department. Glob Pediatr Health 2019;6:2333794×19854960. DOI: 10.1177/2333794×19854960
56. Russell S, Monroe K, Losek JD. Anaphylaxis management in the pediatric emergency department: Opportunities for improvement. Pediatr Emerg Care 2010;26:71–6. DOI: 10.1097/PEC.0b013e3181ce2e1c [PubMed: 20094000]
57. Sidhu N, Jones S, Perry T, et al. Evaluation of Anaphylaxis Management in a Pediatric Emergency Department. Pediatr Emerg Care 2016;32:508–513. DOI: 10.1097/PEC.0000000000000864 [PubMed: 27490724]
58. Tiyyagura GK, Arnold L, Cone DC, et al. Pediatric anaphylaxis management in the prehospital setting. Prehosp Emerg Care 2014;18:46–51. DOI: 10.3109/10903127.2013.825352 [PubMed: 24028748]
59. Trainor JL, Pittsenbarger ZE, Joshi D, et al. Outcomes and Factors Associated with Prehospital Treatment of Pediatric Anaphylaxis. Pediatr Emerg Care 2022;38:E69–E74. DOI: 10.1097/PEC.0000000000002146 [PubMed: 32544141]
60. Wright CD, Longjohn M, Lieberman PL, et al. An analysis of anaphylaxis cases at a single pediatric emergency department during a 1-year period. Ann Allergy Asthma Immunol 2017;118:461–4. DOI: 10.1016/j.anai.2017.02.002 [PubMed: 28390586]
61. Patel N, Chong KW, Yip AYG, et al. Use of multiple epinephrine doses in anaphylaxis: A systematic review and meta-analysis. J Allergy Clin Immunol 2021;148:1307–15. DOI: 10.1016/j.jaci.2021.03.042 [PubMed: 33862009]
62. Hochstadter E, Clarke A, De Schryver S, et al. Increasing visits for anaphylaxis and the benefits of early epinephrine administration: A 4-year study at a pediatric emergency department in Montreal, Canada. J Allergy Clin Immunol 2016;137:1888–9. DOI: 10.1016/j.jaci.2016.02.016 [PubMed: 27106202]
63. Grabenhenrich LB, Dolle S, Rueff F, et al. Epinephrine in Severe Allergic Reactions: The European Anaphylaxis Register. J Allergy Clin Immunol Pract 2018;6:1898–1906. DOI: 10.1016/j.jaip.2018.02.026 [PubMed: 29606638]
64. Pouessel G, Antoine M, Lejeune S, et al. The time course of anaphylaxis manifestations in children is diverse and unpredictable. Clin Exp Allergy 2020;50:117–120. DOI: 10.1111/cea.13510 [PubMed: 31594029]
65. Castilano A, Sternard B, Cummings ED, et al. Pitfalls in anaphylaxis diagnosis and management at a university emergency department. Allergy Asthma Proc 2018;39:316–21. DOI: 10.2500/aap.2018.39.4144 [PubMed: 30095397]

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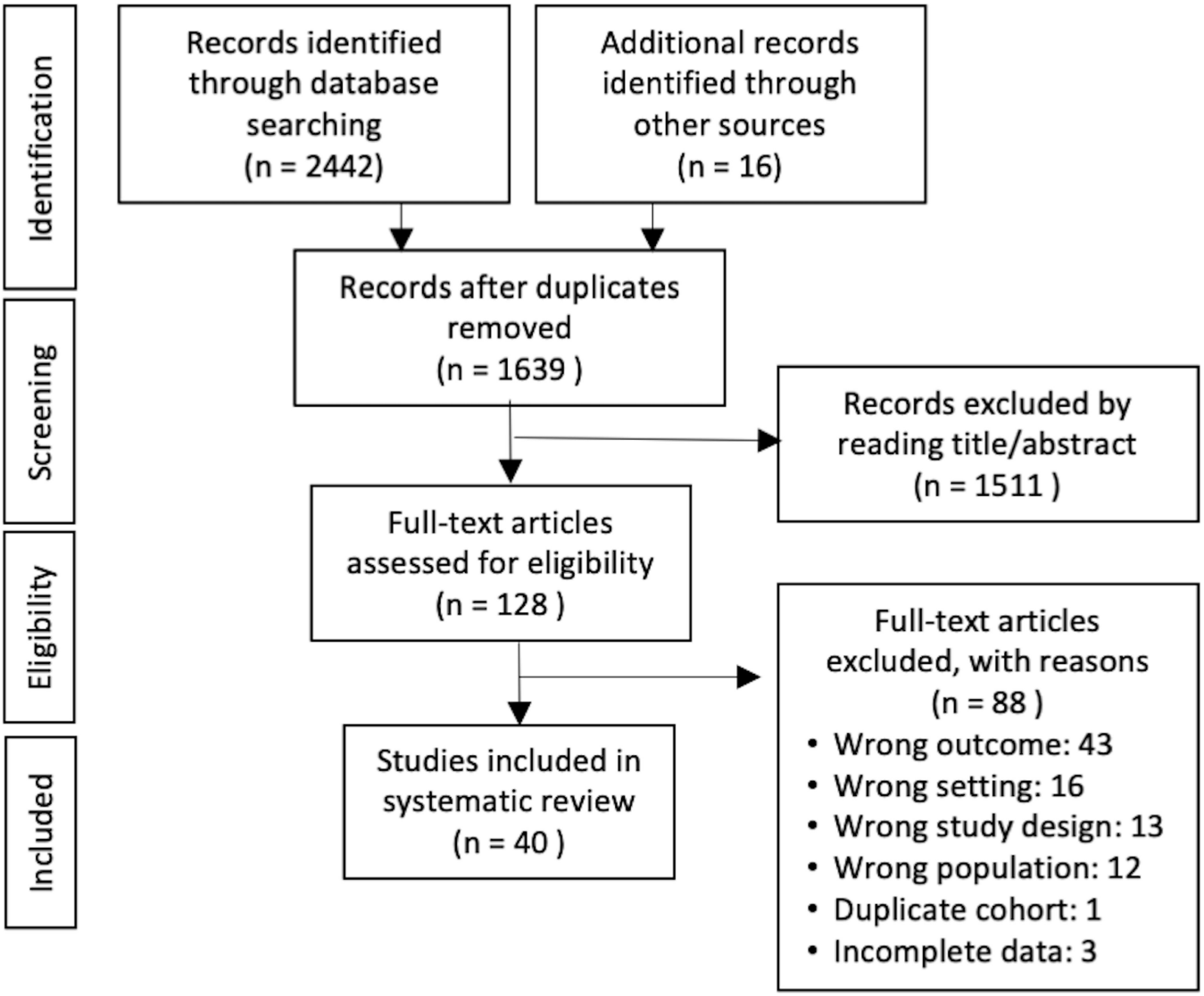

Figure 1.
PRISMA flowchart: selection process of the included articles

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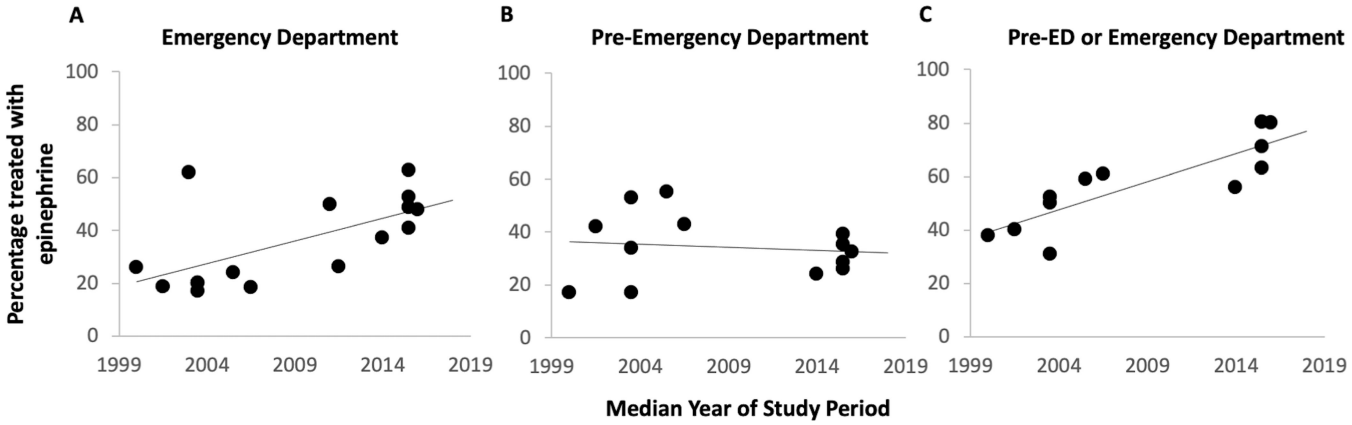

Figure 2.

Epinephrine use in the emergency department, pre-ED or either location for treatment of food-induced anaphylaxis. ED: Emergency Department

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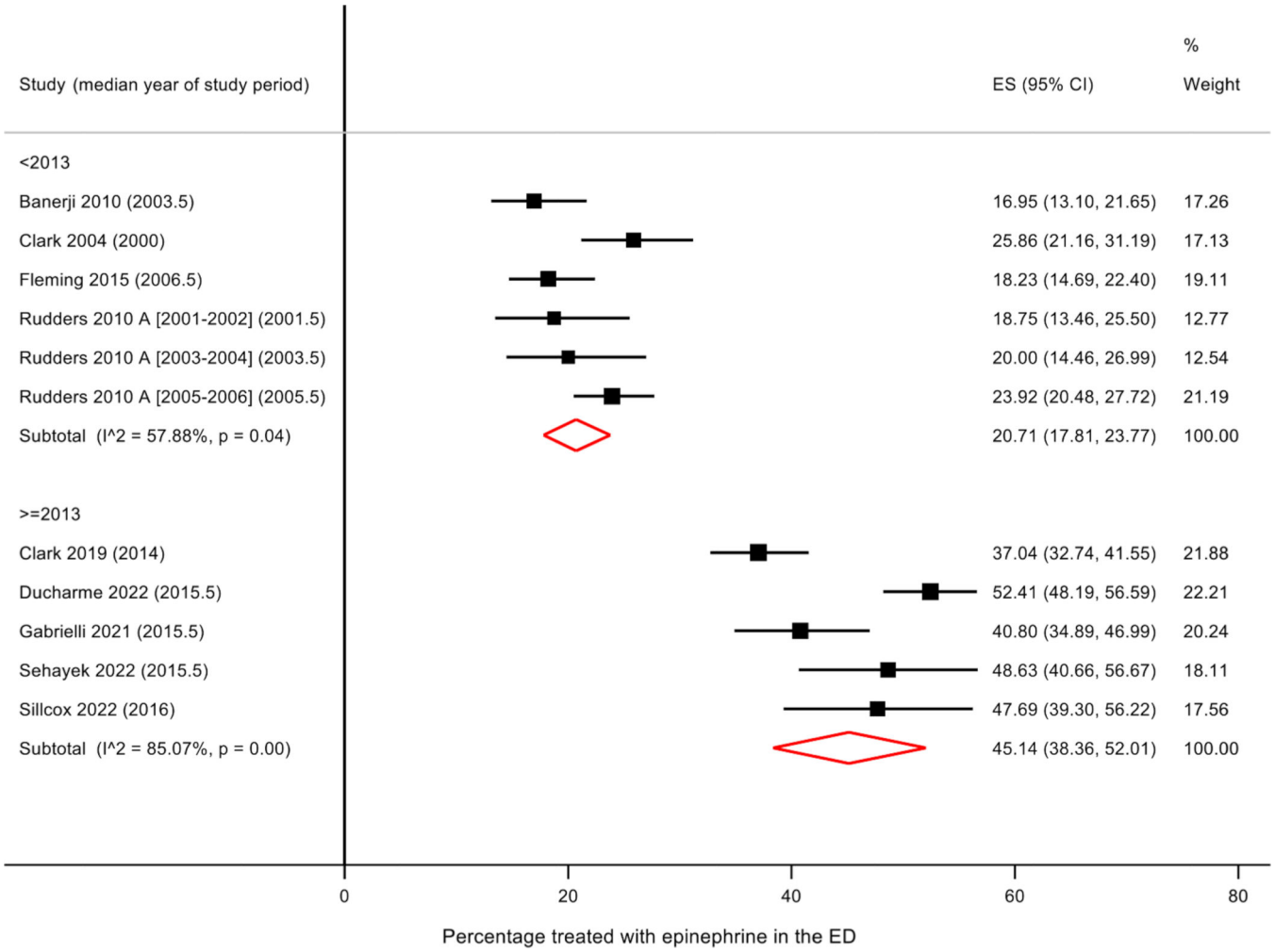

Figure 3.

Forest plot – Epinephrine use in the emergency department to treat food-induced anaphylaxis by time period, among studies using similar definition of anaphylaxis. All studies included in meta-analysis use National Institute of Allergy and Infectious Diseases/ Food Allergy and Anaphylaxis Network (NIAID/FAAN) definition of anaphylaxis

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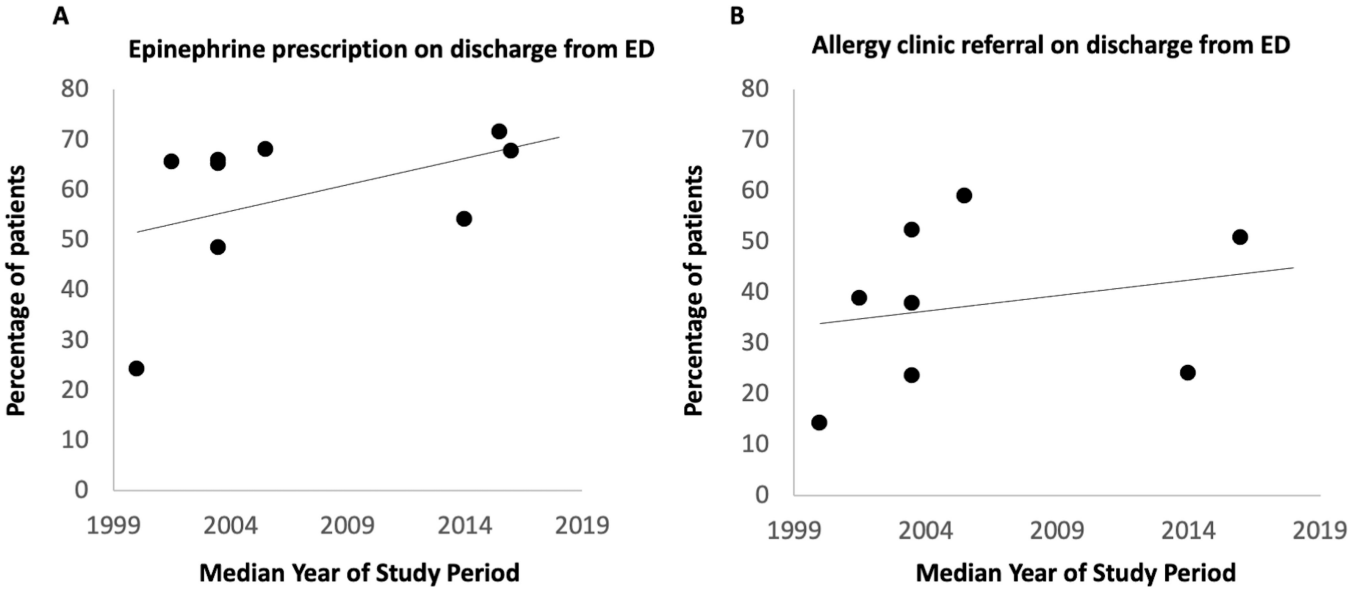

Figure 4.

Frequency of epinephrine prescription and allergy referral on emergency department discharge among patients presenting with food-induced anaphylaxis. ED: Emergency Department

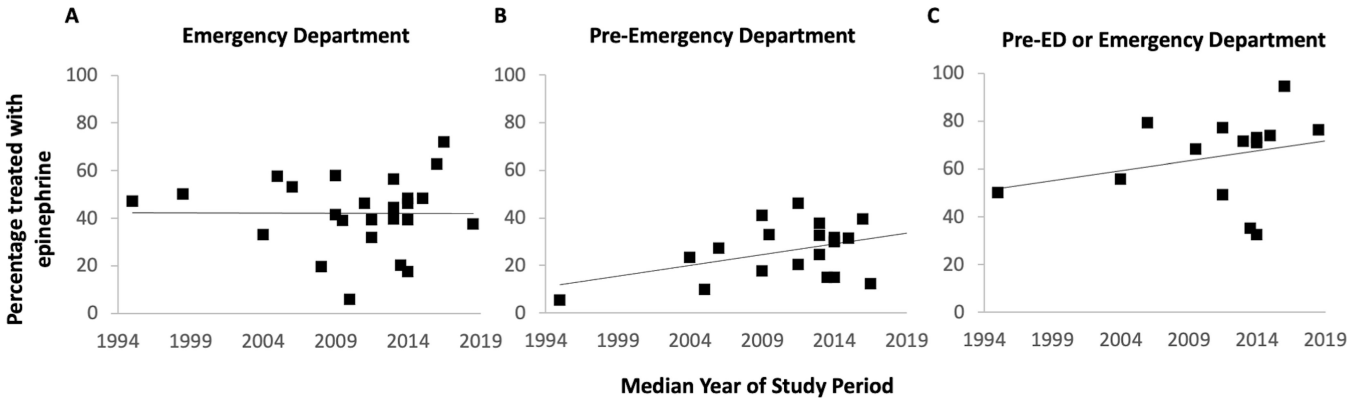

Figure 5.

Epinephrine use in the emergency department, pre-ED or either location for treatment of anaphylaxis of any cause. ED: Emergency Department.

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Table 1.

Summary of emergency department studies included in systematic review.

Study (Author, Year Published)	Reference Number	Study Period	Age Group	Study Setting	Study Design	Anaphylaxis Definition	Number of participants
Food-induced anaphylaxis							
Banerji 2010 *	23	2001–2006	Adult	Multi-center	Observational, retrospective	NIAID/FAAN	295
Clark 2004	9	1999–2001	Both	Multi-center	Observational, retrospective	NIAID/FAAN	290
Clark 2019	24	2013–2015	Both	Multi-center	Observational, retrospective	NIAID/FAAN	459
Ducharme 2022	25	2011–2020	Pediatric	Multi-center	Observational, retro-/prospective	NIAID/FAAN	540
Fleming 2015	26	2004–2009	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	384
Gabrielli 2021	27	2011–2020	Both	Multi-center	Observational, retro-/prospective	NIAID/FAAN	250
Kim 2022	28	2007–2015	Pediatric	Multi-center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes	15318
Rehimini 2021 †	29	2012–2019	Pediatric	Single center	Observational, prospective	NIAID/FAAN	51
Ross 2008	30	2003	Both	Multi-center	Observational, retrospective	Other	21
Rudders 2010 A	31	2001–2002 2003–2004 2005–2006	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	160 155 531
Rudders 2010 B ‡	32	2001–2006	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	658
Sehayek 2022	33	2011–2020	Pediatric	Multi-center	Observational, retro-/prospective	NIAID/FAAN	146
Sillcox 2022	34	2011–2021	Pediatric	Multi-center	Observational, retro-/prospective	NIAID/FAAN	130
Venom-induced anaphylaxis							
Clark 2005	10	1999–2001	Both	Multi-center	Observational, retrospective	NIAID/FAAN	182
Clark 2018	35	2013–2015	Both	Multi-center	Observational, retrospective	NIAID/FAAN	148
Rudders 2013	36	2002–2008	Both	Multi-center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes	807
Medication-induced anaphylaxis							
None							
Anaphylaxis of any cause							

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Study (Author, Year Published)	Reference Number	Study Period	Age Group	Study Setting	Study Design	Anaphylaxis Definition	Number of participants
Arroyo 2021	37	2006–2014	Adult	Multi-center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes	459304
Asai 2014	38	2011–2012	Adult	Single center	Observational, retrospective	NIAID/FAAN	98
Baalmann 2016[§]	39	2010–2013	Both	Single center	Observational, prospective	Other	61
Calderon 2013	40	2007–2009	Adult	Single center	Observational, retrospective	NIAID/FAAN	31
Carrillo-Martin 2020	41	2007–2015	Both	Multi-center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes	278000
Castilano 2018	42	2012–2015	Both	Single center	Observational, retrospective	NIAID/FAAN	60
Chiang 2021[‖]	43	2010–2018	Both	Single center	Observational, retro-/prospective	NIAID/FAAN	1090
Cohen 2021	44	2018–2019	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	368
Gabrielli 2019	45	2011–2017	Both	Multi-center	Observational, retro-/prospective	NIAID/FAAN	3498
Gaeta 2007	46	1993–2004	Both	Multi-center	Observational, prospective	Anaphylaxis ICD-9/−10 codes	143000
Goetz 2019	47	2009–2010	Pediatric	Single center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes, then NIAID/FAAN	211
Hemler 2017	48	2013	Pediatric	Single center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes, then NIAID/FAAN	64
Hochstadter 2016	49	2011–2015	Pediatric	Single center	Observational, retro-/prospective	NIAID/FAAN	965
Huang 2012	50	2004–2008	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	213
Lee 2017	51	2014–2016	Pediatric	Multi-center	Observational, retro-/prospective	NIAID/FAAN	977
Liu 2020	52	2010–2018	Both	Multi-center	Observational, prospective	NIAID/FAAN	430
Manivannan 2009	53	1990–2000	Both	Multi-center	Observational, retrospective	Other	208
Meir 2022	54	2016–2017	Adult	Multi-center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes, then NIAID/FAAN	82
Owusu-Ansah 2019	55	2012–2014	Pediatric	Multi-center	Observational, retrospective	NIAID/FAAN	86
Russell 2010	56	2002–2006	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	124
Sidhu 2016	57	2004–2006 2007–2011	Pediatric	Single center	Observational, retrospective	Anaphylaxis ICD-9/−10 codes, then NIAID/FAAN	61 126
Tiyyagura 2014	58	2008–2010	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	218
Trainor 2022	59	2015–2017	Pediatric	Single center	Observational, retrospective	Other	414
Wright 2017	60	2014	Pediatric	Single center	Observational, retrospective	NIAID/FAAN	40

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NIAID/FAAN National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network 2006 definition of anaphylaxis; ICD-9/ICD-10 International Classification of Disease, Ninth Revision/Tenth Revision.

[*] Study reports unweighted frequencies for epinephrine use and weighted frequencies for epinephrine prescription and allergy clinical referral.

[†] Overlapping cohort with Ducharme 2022, Gabrielli 2021, Sehayek 2022, Sillcox 2022.

[‡] Overlapping cohort with Rudders 2010 A.

[§] Study stratifies by food- and venom-induced anaphylaxis.

[‖] Overlapping study cohort with Baalmann 2016 and Liu 2022.

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Table 2.

Frequency of epinephrine use, epinephrine prescription, and allergy clinical referral among patients who present to the emergency department with anaphylaxis.

Study (Author, Year Published)	Median year of study periods	Total # with anaphylaxis	Treated with epinephrine in the ED		Treated with epinephrine pre-ED		Treated with epinephrine pre-ED or ED		Epinephrine prescription on discharge		Allergy referral on discharge	
Food-induced anaphylaxis		N	N	%	N	%	N	%	N	%	N	%
Baalmann 2016 (food) *	2011.5	19	5	26								
Banerji 2010	2003.5	295	50	17	50	17	91	31				
Banerji 2010 (weighted) †	2003.5	802							388	48	189	24
Clark 2004	2000	290	75	26	49	17	110	38	70	24	41	14
Clark 2019	2014	459	170	37	110	24	257	56	248	54	110	24
Ducharme 2022	2015.5	540	283	52	190	35	433	80				
Fleming 2015	2006.5	384	70	18	164	43	234	61				
Gabrielli 2021	2015.5	250	102	41	71	28	158	63	179	72		
Kim 2022	2011	15318	7600	50								
Rehimini 2021 ‡	2015.5	51	32	63	20	39						
Ross 2008	2003	21	13	62								
Rudders 2010 A‡	2003.5	658	132	20	222	34	329	50	434	66	249	38
Rudders 2010 B [2001–2002]	2001.5	160	30	19	67	42	64	40	105	66	62	39
Rudders 2010 B [2003–2004]	2003.5	155	31	20	82	53	81	52	101	65	81	52
Rudders 2010 B [2005–2006]	2005.5	531	127	24	292	55	313	59	361	68	313	59
Sehayek 2022	2015.5	146	71	49	38	26	104	71				
Sillcox 2022	2016	130	62	48	42	32	104	80	88	68	66	51
Venom-Induced anaphylaxis												
Baalman 2016 (venom) *	2011.5	10	5	50								
Clark 2005	2000	182	25	14	31	17	55	30	62	34	51	
Clark 2018	2014	148	37	25	41	28	73	49	84	57	18	12
Rudders 2013	2005	807	50	6								

Expert Rev Clin Immunol. Author manuscript; available in PMC 2024 July 01.

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Study (Author, Year Published)	Median year of study periods	Total # with anaphylaxis	Treated with epinephrine in the ED		Treated with epinephrine pre-ED		Treated with epinephrine pre-ED or ED		Epinephrine prescription on discharge		Allergy referral on discharge	
Food-induced anaphylaxis		**N**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Anaphylaxis of any cause												
Arroyo 2021	2010	459304	26033	6								
Asai 2014	2011.5	98	31	32	20	20	48	49				
Baalmann 2016	2011.5	61	24	39	28	46	47	77				
Calderon 2013	2008	31	6	19							7	23
Carrillo-Martin 2020	2011	278000	127880	46					41700	15		
Castilano 2018	2013.5	60	12	20	9	15	21	35	28	47	9	15
Chiang 2021 ‡	2014	1090	503	46	324	30	780	72				
Cohen 2021	2018.5	368	138	38			281	76	262	71		
Gabrielli 2019	2014	3498	1686	48	1070	31	2549	73				
Gaeta 2007 §	1998.5	143000		50								
Goetz 2019	2009.5	211	82	39	69	33	144	68	180	85	119	56
Hemler 2017	2013	64	36	56	24	38			53	83	31	48
Hochstadter 2016	2013	965	427	44	313	32	690	72				
Huang 2012	2006	213	113	53	58	27	169	79	116	54		
Lee 2017	2015	977	471	48	305	31	722	74				
Liu 2020	2014	430	169	39	136	32	305	71				
Manivannan 2009	1995	208	98	47	11	5	104	50	79	38	87	42
Meir 2022	2016.5	82	59	72	10	12			28	34	14	17
Owusu-Ansah 2019	2013	86	34	40	21	24			55	64	15	17
Russell 2010	2004	124	41	33	29	23	69	56				
Sidhu 2016 [2004–2006]	2005	61	35	57	6	10			34	56	25	41
Sidhu 2016 [2007–2011]	2009	126	52	41	22	17			81	64	60	48
Tiyyagura 2014	2009	218	126	58	89	41						
Trainor 2022	2016	414	259	63	163	39	391	94				
Wright 2017	2014	40	7	18	6	15	13	33	26	65	12	30

ED: Emergency Department.

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[*] Sub-analysis of Baalmann 2016

[†] Study reports both weighted and unweighted counts

[‡] Excluded from Spearman correlation and meta-analysis due to cohort overlap.

[§] Excluded from Spearman correlation and meta-analysis due to no reported frequency of epinephrine use.