

REVIEW ARTICLE

Gaps in anaphylaxis management at the level of physicians, patients, and the community: a systematic review of the literature

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Abstract

Diagnosis and management of anaphylaxis can be a challenge because reactions are often unexpected and progress quickly. The focus of anaphylaxis management has mostly been on the acute episode, with little attention given to the long-term management of patients at risk. This is compounded by conflicting information in current guidelines and a general lack of agreement among clinicians about which management strategies are the most appropriate. We systematically reviewed the literature to identify and summarize studies that investigated gaps in anaphylaxis management. Our search included MEDLINE, EMBASE, CINAHL, and Evidence-Based Medicine Reviews. Studies were included if they addressed an outcome describing gaps in anaphylaxis knowledge, education, anaphylaxis management, and quality of life (QOL). Populations of interest were health care professionals involved in the care of patients at risk for anaphylaxis, and patients of any age, their parents, caregivers, and teachers in primary care, hospital or community settings. Of 5014 citations that were identified, the final 59 studies (selected from 75 full-text articles) met the inclusion criteria. Two hundred and two gaps were identified and classified according to major themes: gaps in knowledge and anaphylaxis management (physicians and patients); gaps in follow-up care (physicians); and QOL of patients and caregivers. Findings from this systematic review revealed gaps in anaphylaxis management at the level of physicians, patients, and the community. Findings will be used to provide a basis for developing interventional strategies to help address these deficiencies.

Management of anaphylaxis can be a challenge for several reasons. Allergic reactions can be severe, are often unexpected, and can progress quickly (1). Although definitions of anaphylaxis exist: 'a serious allergic reaction that is rapid in onset and may cause death' (United States) (2), and 'a severe, life-threatening, generalized or systemic hypersensitivity reaction' (Europe) (3), they may not be universally accepted or have poor uptake by practitioners because anaphylaxis symptoms are nonspecific and its presentation can be variable (3). Additionally, the lack of a clear definition of anaphylaxis can also hamper studies investigating the epidemiology and pathophysiology of this disorder (2). Another challenge is that there is no single diagnostic test that can be used routinely to identify anaphylaxis in clinical practice (4, 5). The focus of management has mostly been on the acute episode, with little attention given by physicians to the long-term management of patients

at risk for anaphylaxis (4, 5). However, evidence shows that both immediate and long-term anaphylaxis management are inadequate in all settings (1, 6). Factors contributing to this care gap are poor training of primary care physicians (7), lack of access to epinephrine auto-injectors and specialist advice (7, 8), problems in school-based management (9), and a lack of anaphylaxis preventative strategies for patients and caregivers (10). This is compounded by conflicting information in guidelines about management, which are often anecdotal and nonevidence-based (1). There is also a general lack of agreement among clinicians on the appropriate dose and route of epinephrine administration, and which anaphylaxis management strategies are the most appropriate (11).

The first step toward closing these gaps is to investigate the current state of anaphylaxis management across different populations and settings. The objective of this study was to

systematically review the literature to identify and summarize relevant studies that examined gaps in anaphylaxis management.

Methods

Search strategy

Studies were identified by searching MEDLINE (1966–August 2008), EMBASE (1980–2008), CINAHL (1982–August 2008), and Ovid Evidence-Based Medicine Reviews (Cochrane Database of Systematic Reviews and Clinical Trials Register, ACP Journal Club, Database of Abstracts of Reviews of Effects). We also searched the gray literature: websites of Anaphylaxis Canada, the Canadian Society of Allergy and Clinical Immunology (CSACI), American Academy of Allergy, Asthma, and Immunology (AAAAI), the Food Allergy and Anaphylaxis Network (FAAN), and digital dissertations. We hand searched relevant journals (e.g., *Allergy*, *Journal of Allergy and Clinical Immunology*, *Annals of Allergy Asthma and Immunology*), reviewed the reference lists of relevant articles, and contacted experts in the field. Search terms were generated using known terms and synonyms suggested by librarians and allergy specialists to capture all text words and Medical Subject Heading (MeSH) terms that describe gaps in anaphylaxis management. MeSH terms and text words were then combined with the Boolean 'OR' and then 'AND-ed' with 'anaphylaxis' in each database using Ovid interface.

Study selection

Studies were included if they were prospective or retrospective quantitative studies (including epidemiologic and intervention studies) or qualitative studies as long as they investigated gaps in anaphylaxis management, and could be addressed in the context of quality of life (QOL) of patients at risk for anaphylaxis or their caregivers. We excluded basic science or animal studies, case reports, and narrative reviews. Gaps in anaphylaxis management were defined according to different settings, populations, and outcomes. Outcomes of interest were gaps in knowledge and education, anaphylaxis management behaviors (e.g., prescribing by physicians, allergy avoidance by patients), QOL, and morbidity and mortality. Studies investigating these outcomes in different settings (primary care, hospital, and community) were categorized according to two broad populations: (1) physicians and other health care professionals involved in the care of patients at risk for anaphylaxis and (2) patients of any age, and their parents, caregivers, and teachers. From the physician/health care professional perspective, we defined knowledge or education gaps as an insufficient or conflicting understanding related to any aspect of anaphylaxis diagnosis, treatment, or management (e.g., symptoms, treatment options, dose, or route of epinephrine administration). Gaps in anaphylaxis management were defined as incorrect practice behaviors resulting from these knowledge gaps (e.g., diagnosis, prescribing, acute treatment administration, and management). For patients, we defined gaps in knowledge or

education as a lack of understanding or insufficient knowledge about self-management (e.g., recognition and awareness of signs and symptoms, consequences of allergic reactions), and anaphylaxis behaviors as incorrect or insufficient actions on allergen avoidance, compliance with therapy, or preparedness for potential reactions.

Three authors were initially calibrated for applying the inclusion/exclusion criteria on a random sample of ten abstracts. Once agreement was at least 80% between the three authors, the titles and abstracts of potentially relevant citations were independently reviewed in duplicate by dividing the yield among the three reviewers. The final list of included studies was selected independently by two authors (MK, SW), who screened full-text articles by applying the inclusion/exclusion criteria. Agreement between reviewers for full-text review was over 90% beyond chance ($k = 0.92$, confidence interval 0.86–0.97). Any disagreements were resolved through consensus.

Study quality assessment

It was decided not to use a study quality assessment scale because there is evidence that they lack empirically supported components (12), and authors of scales can be influenced by their own perception of study quality (13). Studies were assessed according to each type of study design that was considered for inclusion in the systematic review. Study quality for randomized controlled trials (RCTs) was assessed according to specific methodological criteria that are the most relevant to the control of bias (randomization, allocation concealment, blinding, and follow-up) (14). Epidemiological studies (cohort, case-control, and cross-sectional) were assessed using critical appraisal factors according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (15), because there is no current reliable tool available to assess the quality of observational studies (16). Qualitative studies were assessed using a guide developed by the Evidence-Based Medicine Working Group consisting of appropriateness of study design, sampling, data collection methods, and analysis (17).

Data extraction and synthesis

Using a standardized form, two authors extracted data on the setting, study design and elements of study quality or critical appraisal factors, population characteristics, interventions (if applicable), outcomes, results, analysis, and follow-up. We anticipated that a meta-analysis would not be possible because studies were too heterogeneous to pool. However, potential sources of heterogeneity were explored according to differences in study design, participants, interventions (if applicable), settings, and outcomes. Findings were qualitatively assessed using grounded theory methodology to identify themes from the content analysis of data (18).

Results

Of 5014 potentially relevant articles identified by our search, 4605 did not meet the inclusion/exclusion criteria or were

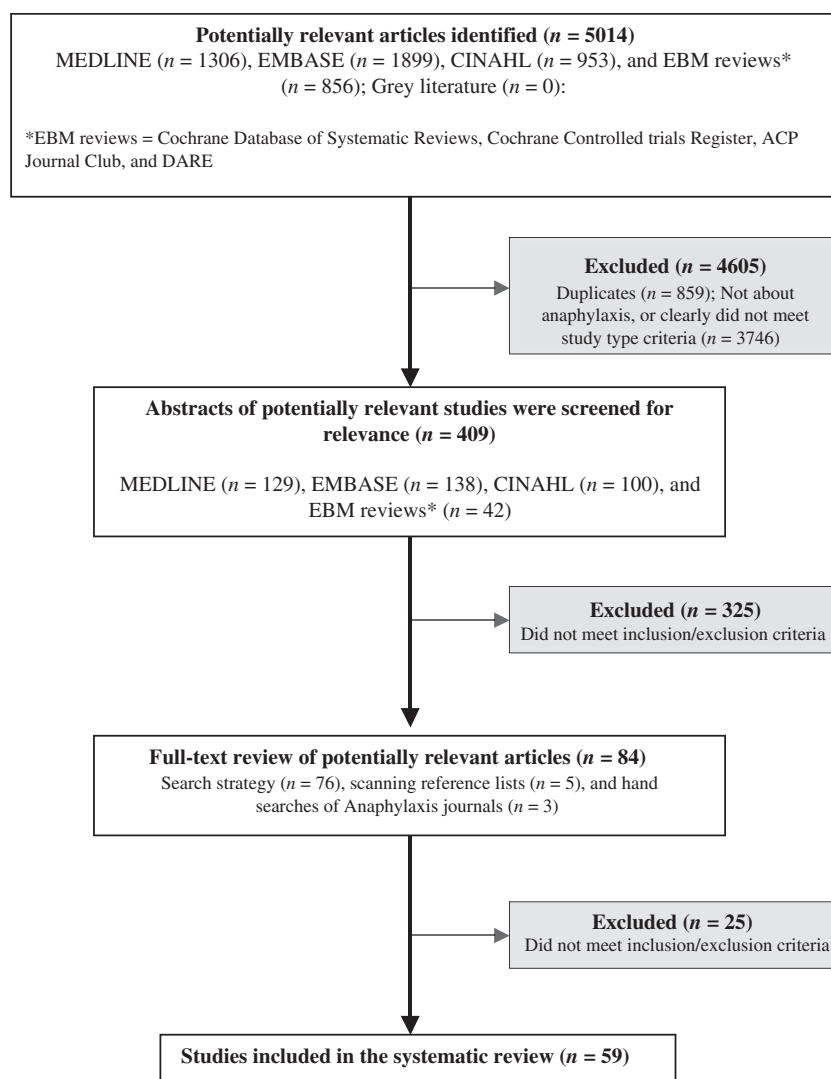


Figure 1 Study identification flowchart.

duplicates and thus were excluded from the systematic review. Of 409 citations that were screened for relevance, 76 articles were selected for full-text review. We identified a further eight articles from the reference lists of relevant articles (n = 5) and hand searches of allergy journals (n = 3), but none were found from searching the gray literature. Of the total of 84 articles that were considered for review in full text, 59 met the inclusion/exclusion criteria and were included in the systematic review (1, 4, 9, 11, 19–73) (see Fig. 1).

Analysis of the differences between studies confirmed our hypothesis that a meta-analysis was not possible. We found considerable differences between studies for objectives, populations, study design, settings, outcomes, and study quality or appraisal (see study characteristics of included studies in the Appendix). The majority of studies were epidemiological

consisting of cross-sectional surveys, case-based surveys, and prospective cohort studies (n = 36). Other studies were chart reviews (n = 11), qualitative studies (n = 7), systematic reviews (n = 4), and one RCT (n = 1). Eighty percent of the studies were spread across hospital or clinic (n = 24) and community (n = 23) settings, and populations varied across studies for age, and whether the objective of the study was to investigate patients with anaphylaxis or caregivers involved in the care of these patients.

We identified 202 gaps in anaphylaxis management across the 59 studies (1, 4, 9, 11, 19–73). Using grounded theory methodology (17), two authors independently categorized these gaps according to major themes and classified the frequency of these themes from the perspective of two broad populations: physicians (primary care, pediatricians, and allergy specialists) and patients or the community (schools,

Table 1 Summary of anaphylaxis management gaps at the level of physicians

Theme	Gap (<i>number of gaps</i>)	Setting
Lack of knowledge	Anaphylaxis	
	The signs and symptoms or to correctly diagnose (3)	Army hospital database, US (43); Pediatric allergy hospital, UK (49); AAP organization, US (51)
	Auto-injectors	
	How to use (8)	Community hospitals, UK (11); Pediatric medical convention, Canada (41); Tertiary pediatric hospital, Australia (59); Pediatric hospital allergy clinic, US (68); Hospital, New Zealand (72)
	Correct dose (6)	Schools, UK (28); ED, UK (40); Pediatric convention, Canada (41); General hospitals, UK (47); Hospital, New Zealand (72)
	Appropriate route of administration (6)	AAAAI members, US (27); ED, UK (40); Army hospital database, US (43); General hospitals, UK (47); Pediatric and general practice, Germany (58); Hospital, New Zealand (72)
Anaphylaxis management	Inadequate or no training provided to patients on how to use (12)	Communities, UK (1); Community hospitals, UK (11); Specialist pediatric allergy clinic, UK (21); FAAN organization, US (25); Schools, UK (32); Army hospital database, US (43); Pediatric allergy clinic, UK (49); Support group and pediatric allergy clinic, US (50); Tertiary pediatric hospital, Australia (59); Children's hospital, France (63)
	Treatment with epinephrine	
	Infrequent (8)	Independent childcare centers, US (24); EDs, US (31, 37); ED, UK (40); Army hospital database, US (43); Support group and pediatric allergy clinic, US (50); AAP members, US (51); Allergy clinic, France (60)
	Delayed administration (5)	Communities, UK (1); AAAAI members, US (27); Data from communities of a national registry, US (29); ED, Australia (33); Children's hospital, US (52)
Follow-up care	Diagnostic coding of anaphylaxis	
	Infrequent or not determined (3)	Systematic review (4); EDs, US (37); Military medical center, US (46)
	Prescribing auto-injectors or epinephrine	
	Infrequent (6)	EDs, US (31); Army hospital database, US (43); Multidisciplinary pediatric allergy clinic, UK (49); Tertiary pediatric hospital, Australia (59); Pediatric and general practices, Germany (58); Communities, US (67)
	Not the most commonly prescribed treatment for anaphylaxis (5)	EDs, US (31, 37); Army hospital database, US (43); AAP members, US (51); Pediatric and general practices, Germany (58)
	Referral to an allergy specialist	
	Infrequently or not done after acute reaction (6)	University hospital ED, France (26); Schools, UK (28); EDs, US (31); Community pediatric service, UK (35); Army hospital database, US (43); The quintile of the most deprived local authority area, UK (71)

US, United States; UK, United Kingdom; AAAAI, American Academy of Allergy, Asthma and Immunology; ED, emergency department; FAAN, Food Allergy and Anaphylaxis Network; AAP, American Association of Pediatrics.

childcare centers, and allergy organizations). Major themes that included at least three gaps in anaphylaxis management are summarized in Table 1 (physician level) and in Table 2 (patient or community level).

Gaps in anaphylaxis management – physician level

Gap analysis revealed three main themes concerning the physician population: (1) lack of knowledge (anaphylaxis and auto-injectors); (2) anaphylaxis management (treatment with epinephrine and diagnostic coding of anaphylaxis); and (3) follow-up care (prescribing auto-injectors or epinephrine, and referral to an allergy specialist) (Table 1).

Theme 1: Lack of knowledge

Anaphylaxis knowledge

Three studies indicated that primary care physicians and pediatricians have insufficient knowledge to identify the signs and symptoms of anaphylaxis or to correctly diagnose anaphylaxis (43, 49, 51).

Auto-injectors

Gaps in epinephrine auto-injector use revealed that physicians not only lacked the knowledge on how to use auto-injectors (11, 41, 59, 68, 72), but they also did not provide adequate instructional training to patients (1, 11, 22, 25,

Table 2 Summary anaphylaxis management gaps at the level of patients or the community

Theme	Gap (<i>number of gaps</i>)	Setting
Lack of knowledge	Anaphylaxis	
	Signs and symptoms, and which foods to avoid (8)	Community GP practice, UK (19); Independent childcare centers, US (24); PAC, CO, Australia (44); PAC, UK (49); University, UK (53); Childcare setting, US (62); Children's hospital, France (63); Communities, US (67)
	General management (5)	Schools, UK (32); Pediatric allergy service, Australia (39); Pediatric allergy clinics, CO, Australia (44); PAC, UK (49)
	Provision of educational materials	
	Lacking or inaccurate (6)	Community-based GP practice, UK (19); North American EDs (31); Pediatric allergy clinics, CO, Australia (44); Multidisciplinary PAC, UK (49); Military hospital, medical school or HMO, US (56); Hospital PAC, US (68)
	Auto-injectors	
Anaphylaxis management	How to use or incorrectly use (7)	Community hospitals, UK (11); Allergy and clinical immunology clinic, Canada (20); PAC, UK (22); Schools, UK (28); Pediatric allergy service, Australia (39); Childcare setting, US (62); Hospital PAC, US (68)
	Receive inadequate, infrequent or no instruction on its use (10)	Community-based GP practice, UK (19); The FAAN organization, US (25); Schools, UK (28, 32); Schools, Canada (35); Pediatric allergy service, Australia (39); Multidisciplinary PAC, UK (49); Children's hospital, France (63)
	Auto-injectors	
	Do not carry one, or unavailable at the time of reaction (8)	Community-based GP practice, UK (19); Data from a national registry, US (29); Children's hospital, US (34); Food allergy support group, PAC, US (50); University, UK (53); School districts, US (57); Communities, US (67); Hospital PAC, US (68)
	Carry it but do not use it (4)	Pediatric allergy service, Australia (39); Local support group and PAC, US (50); Pediatric and general practices, Germany (58); University-based allergy clinic, US (73)
	Anaphylaxis management plans	
Quality of life	Do not have one (5), or missing information (4)	Schools, UK (28, 32); Pediatric allergy service, Australia (39); School districts, US (57); Children's hospital, France (63); Schools, US (64)
	Restrictions and disruptions of social activities and interactions (7)	Specialty clinic, University Allergy practice, US (30); Community pediatric service, UK (35); PACs, CO, Australia (44); Anaphylaxis educational seminar, children's hospital, community support group, Canada (54); Schools, Sweden (55); The FAAN organization, US (69)
	Fear and anxiety of severe reactions (4)	Prairie city communities, Canada (38); Anaphylaxis educational seminar, a children's hospital, and a community support group, Canada (54); Schools, Sweden (55)
	Lack of understanding by others (3)	Anaphylaxis educational seminar, children's hospital, community support group, Canada (54); Schools, Sweden (55)
	Feeling of being a bother or an outsider (3)	Prairie city communities, Canada (38); Schools, Sweden (55)

UK, United Kingdom; PAC, pediatric allergy clinic; US, United States; CO, consumer organization; GP, general practitioner; ED, emergency department; HMO, health maintenance organization; FAAN, Food Allergy and Anaphylaxis Network.

32, 43, 49, 50, 59, 63). One study found that patients who were prescribed auto-injectors by their primary care physicians either never carried the device or were less aware of how to activate it compared to those who received their prescription from allergists (22). Other gaps were lack of familiarity with the device (68), or the inability to correctly demonstrate all the steps in its use (62, 68, 72). Injecting the device into a thumb (59) or forgetting to hold the auto-injector at the site for > 5 s (41, 59) were also major errors. Other gaps were related to physicians' lack of knowledge of

the correct dose of auto-injector administration. Few physicians knew the two available doses of epinephrine auto-injectors (40, 41, 47). Furthermore, one study indicated that some children were incorrectly prescribed a low-dose auto-injector even though they reached a weight of 30 kg, which would require a full dose (28). Lack of knowledge of the correct route of epinephrine administration was also an identified gap. First-line use by physicians of subcutaneous (s.c.) or intravenous epinephrine instead of the recommended intramuscular (i.m.) route (across all levels of

severity) was demonstrated in a number of studies (27, 40, 43, 47, 58, 72).

Theme 2: Anaphylaxis management

Treatment with epinephrine

Eight studies identified that epinephrine use in acute allergic reactions is infrequent (24, 31, 37, 40, 43, 50, 51, 60). Furthermore, significant delay in epinephrine administration (i.e., ≥ 5 min) was also found to be an important gap in clinical practice (1, 27, 29, 33, 52).

Diagnostic coding

Accurate diagnosis is also hindered by the lack of diagnostic coding – two studies indicated that anaphylaxis coding by physicians was not done in all cases of anaphylaxis in the emergency department (ED) (37, 46). There are also an insufficient number of codes available to document episodes of diagnosed anaphylaxis (4).

Theme 3: Follow-up care

Prescribing auto-injectors or epinephrine

Many studies indicated that the rate of auto-injector prescription is low across different settings: pediatric and military hospitals (43, 49, 59), general community practices (hospital or office-based) (58, 67), and ED (31). One study found that residents were significantly less likely to prescribe an auto-injector than more senior staff (59). Studies also indicated that antihistamines and steroids were prescribed more often than adrenaline (31, 37, 43, 51, 58).

Referral to an allergy specialist

Lack of referral for an allergy consultation was also identified. Five studies found that few patients were referred to an allergist after being seen for an acute reaction in community or hospital clinics (35, 43, 71) or the ED (26, 31). However, one study found that allergy testing and follow-up were more frequent in children attending hospital clinics (28).

Gaps in anaphylaxis management – patient and community level

Analysis of gaps in the patient and community population revealed three major themes: (1) lack of knowledge (anaphylaxis and auto-injectors); (2) anaphylaxis management [auto-injectors and anaphylaxis management plans (AMPs)]; and (3) QOL (see Table 2).

Theme 1: Lack of knowledge

Anaphylaxis

Patients and parents of children at risk for anaphylaxis lacked the knowledge to recognize the signs and symptoms of anaphylaxis (19, 24, 53, 62, 63) and were unaware of which foods to avoid (49, 67). Other barriers to care were the lack of knowledge in the general management of anaphylaxis (39, 49), the extent to which allergens should be

excluded from a child's diet and environment (32, 44), and how to react in an anaphylactic emergency (32). One study reported that teachers and staff had not received formal training on how to manage acute allergic reactions in a school setting (32).

Provision of information

Provision of anaphylaxis educational materials to patients was also lacking. Studies showed that most patients were not given accurate information by their primary care physicians on anaphylaxis management (19), were not given discharge instructions from the ED on avoidance of the offending allergen (31, 56), or written information on indications for auto-injectors (68). One study found that children who were referred by general pediatricians to allergy specialist care were given more advice and had better knowledge than those who were referred to allergy specialists from primary care (49).

Auto-injectors

Knowledge gaps in auto-injector use included lack of awareness and inadequate training on how to use auto-injectors. Patients in most community settings (schools, childcare centers), hospitals, or allergy clinics were either not able to recall all the steps for correct auto-injector use (11, 39, 62) or were unable to correctly activate the device (20, 22, 28, 68). Lack of instruction and training on how to use auto-injectors was a major gap identified in eight studies. These included patients or families who were not shown how to use the device (19, 25, 32, 49, 63) and school teachers who were not provided training on the device (28, 32, 36, 39).

Theme 2: Anaphylaxis management

Auto-injectors

Seven studies identified that many patients did not carry an auto-injector or did not have one available at the time of a reaction (29, 34, 50, 53, 57, 67, 68). One study suggested that hesitation in using or forgetting to carry the device may in part explain these behaviors (19). Furthermore, even when patients or parents of children with anaphylaxis carried auto-injectors, many did not use it (39, 50, 58, 73). The most common reasons for not using auto-injectors were: 'I recognized the symptoms but gave *Benadryl* first' and 'I did not think the reaction was serious' (50).

Anaphylaxis management plans

Lack of AMPs in schools was also identified as a problem in five studies (28, 32, 39, 57, 63). Furthermore, many AMPs did not provide epinephrine auto-injector administration instructions and were missing essential components such as critical emergency contact and health history information (64).

Theme 3: Quality of life

Studies indicated that the main factors that negatively affected the QOL for patients at risk for anaphylaxis and their caregivers were restrictions and disruptions of social

activities and interactions. Findings from six studies indicated that restrictions affected patients and their caregivers differently (30, 35, 44, 54, 55, 69). Patients expressed their restrictions in terms of limitations on social activities such as birthday parties, sleepovers, and field trips (30, 54), and the feeling of sadness from having to abstain from certain foods (55). Family members were affected by restrictions designed to ensure the allergic child's safety, which often affected the entire family (35, 54). In one study, parents felt challenged by the need to keep their child safe from accidental allergen exposures yet not overly restrict their child's life and social opportunities (44).

Fear and anxiety in parents were related to insufficient information about how to manage anaphylaxis (54), and living with the fear of their child's new experiences in social situations (38). Key events such as a new accidental exposure, information about new potential risks, and child developmental changes (e.g., increased independence) were also triggers of anxiety (54, 55). Other studies showed that QOL may also be impaired by obstacles to coping, such as lack of understanding by others and the feeling of being a bother or an outsider. In one study, adolescents perceived that other people did not understand the seriousness of their condition, showed indifference to their requests for special meal orders, or felt subject to teasing and harassment (54). Lack of public understanding, unwillingness to accommodate, and hostility were also identified as major obstacles to coping (54). In one study, children in schools perceived themselves as being a bother, an outsider, and causing trouble for others because of special food requests which involved extra work for their friends (55). From the caregiver perspective, mothers saw the auto-injector as a visual reminder that their child was 'different' and the worry that they would be treated differently or excluded (38).

Discussion

Our systematic review identified over 200 gaps in anaphylaxis management. Themes that were common to physicians, patients, and caregivers in all settings were insufficient knowledge of anaphylaxis and its management, and how to use epinephrine auto-injectors. Consideration of these gaps is particularly important given the increasing prevalence of anaphylaxis, especially in young children (74). Although this apparent rise in the prevalence of anaphylaxis may be explained by the recently broadened definition of anaphylaxis (2, 75), the findings of our review highlight the current landscape of anaphylaxis management across different settings and populations. However, the extent of deficits reported in the included studies is surprising and troubling, as children at risk for anaphylaxis depend on others to help treat them (i.e., family, schools, and community), yet at every level, deficiencies have been identified.

Our findings indicated that lack of information is an important barrier to coping, and patients' QOL is severely affected. Anaphylaxis is a lifelong medical condition for most, requiring strict avoidance of the offending allergen, as there is currently no other available therapy. There is clearly

a need for improved patient education to better support those at risk and their caregivers. The provisions of appropriate educational materials about emergency self-care and avoidance and for specific immunotherapy (e.g., management of Hymenoptera venom allergy) have the potential to assist patients and caregivers of children at risk because it helps to develop successful coping strategies, which can positively impact QOL. For children at risk, coping strategies can be especially helpful as they mature and assume more responsibility for their condition.

Regarding health care professionals, our review confirmed that there is still a lack of clarity among physicians and in existing guidelines on how to appropriately manage patients at risk for anaphylaxis, even though clinical practice guidelines for anaphylaxis management exist (2, 5, 76, 77). A lack of a universally accepted definition of anaphylaxis may also in part explain these identified knowledge gaps. For example, some practitioners still think that 'shock' needs to be present for an anaphylaxis diagnosis even though this has been eliminated from new definitions. The majority of studies that were included in the systematic review were published prior to 2006, for which the most recent definition of anaphylaxis published by Sampson et al. (2) do not apply. The new definition may also not be universally accepted because the need to consider several clinical criteria in its definition can be complicated or may not be relevant to all physicians (including allergists) or countries. More robust evidence is needed to guide practice at all levels. However, this is a challenge for several reasons. First, the first-line use of epinephrine for anaphylactic emergencies is largely based on expert opinion and suboptimal evidence (78). Second, there needs to be universal agreement on the optimal route and dose of epinephrine administration. Although studies advocate the i.m. over the s.c. route of epinephrine administration for treatment of anaphylaxis (2, 79, 80), this conclusion is largely based on studies investigating the differences in the plasma levels of epinephrine concentrations achieved through both routes (81). Third, the recommended dose of i.m. administration for adults for the emergency medical treatment of anaphylaxis varies from a maximum initial dose of 0.3–0.5 mg in Canada, the United States, Australia, and the United Kingdom (21, 80) to 0.5–1.0 mg in other European countries (76, 80). Another challenge is epinephrine dosing in children, which is problematic because there are only two fixed doses of epinephrine auto-injectors available: a 0.15 mg dose for children weighing between 10 and 25 kg (22–55 lb) and a 0.3 mg dose for children weighing ≥ 25 kg (≥ 55 lb) (82). However, as Sicherer et al. (79) point out, providing the appropriate dose for children who fall below the lowest weight parameter (15 kg) can be difficult and can lead to overdosing (with the 0.15 mg dose in infants who weigh < 15 kg).

Strengths and limitations

To our knowledge, no systematic review has previously attempted to synthesize available evidence on the gaps in anaphylaxis management across different populations and settings. To reduce the effects of bias, we ensured that our

literature search was comprehensive with well-defined terms and inclusion/exclusion criteria, screening articles independently at each level of article selection using standardized data extraction forms, and measuring inter-rater reliability using kappa statistics. A potential limitation to our study is that it was not possible to combine the results in a meta-analysis because the studies were too heterogeneous to pool. However, we addressed potential sources of variability between relevant studies (in addition to random error) by the rigorous study quality assessment and critical appraisal of studies, as well as the differences between studies for populations, settings, and outcomes.

Another possible limitation of our study is that we did not limit our search to study designs with the best quality of evidence such as RCTs. However, our objective was to identify gaps in anaphylaxis management, which can be addressed in prospective, retrospective, or qualitative studies, but most appropriately in epidemiologic evaluations that assess risk factors and long-term rare outcomes such as in cross-sectional and cohort studies. In fact, prospective, placebo-controlled trials in anaphylaxis research are largely lacking because they are difficult to conduct and unethical in most cases. This is evidenced by a recent systematic review that attempted to assess the benefits and harms of adrenaline in the emergency treatment of anaphylaxis, but failed to retrieve any randomized or quasi-randomized trials (78). Controlled studies are also difficult to conduct because anaphylactic reactions are relatively uncommon or under recognized, are unpredictable, and can occur in health care settings even if preventive efforts are established (82). Furthermore, there is great variability among patients for the clinical presentation of anaphylaxis. Patients vary in the onset of symptoms after exposure (from minutes to hours), the number and severity of symptoms (from mild to fatal within minutes) (83), and the exposure may be fatal even if optimal treatment is provided immediately (1).

Lastly, the included studies that were captured by our systematic review are most representative of anaphylaxis from food allergy in mostly pediatric patients. However, the

authors recognize that adequate management of anaphylaxis should also include other important causes of anaphylaxis such as drug allergy, which can particularly affect elderly patients with comorbidities such as cardiovascular disease requiring treatment with β -blockers or angiotensin-converting enzyme (ACE)-inhibitors.

Conclusions

The classification of the specific domains of anaphylaxis management gaps that were identified in this systematic review will provide an enhanced understanding of the learning and practice needs of physicians, patients, and their caregivers in different settings. Our future work will target the development of interventional strategies and practice tools to address these knowledge and practice gaps, which are needed to improve anaphylaxis management at all levels.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Characteristics of included studies.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

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Appendix: Characteristics of included studies

Study	Study objective	Study Population	Setting	Design	Quality assessment or critical appraisal
Akeson N (2007) ¹⁹	To explore the psychosocial impact of anaphylaxis on adolescents and their parents	Adolescents (13-16 years of age) with a history of clinician-diagnosed anaphylaxis (N = 7) and their parents (N = 8)	GP practice: A Scottish community-based GP practice in the UK	Qualitative	Study design (structured interviews) addressed research question; Ethics review described; Sampling justified and discussed; Data collection methods described; The duration of observation was described; Analysis appropriate to methodology; Limitations described but potential biases not addressed; Findings consistent with similar studies
Al-Matar H (2001) ²⁰	To assess the technical use of an epinephrine self-injection device (EpiPen®)	55 anaphylactic patients (mean age 34 years) who were prescribed an EpiPen® were asked to demonstrate injection techniques using a training device	Allergy hospital or clinic: An allergy and clinical immunology clinic in Canada	Prospective cohort	Demonstrations of correct use of EpiPen® with placebo device over a 1 year period; Selection criteria of participants not described; Lacks details in methodology and analysis; Study Limitations not described
Alrasbi M (2007) ²¹	To identify and compare national guidelines for the emergency medication management of anaphylaxis	Number of included studies = 6	Not applicable	Systematic review	Database sources and search strategy identified; Study selection criteria not described; Study abstraction done in duplicate; Study quality assessment not done; Tests of heterogeneity not done; Results don't describe data synthesis; Limitations discussed
Arkwright PD (2006) ²²	To examine the major factors which determine a carer's ability to use an auto-injectable adrenaline device	The caregivers of 122 children with food allergies (age range 6-13) who were previously prescribed EpiPen® were asked to demonstrate its use	Pediatric allergy hospital or clinic: Single specialist pediatric allergy clinic in the UK	Prospective cohort	Demonstrations with correct use of EpiPen trainer device assessed with main caregiver; Statistical analysis not described in detail; Possible bias not described; Limitations not described
Avery NJ (2003) ²³	To ask children directly how they perceive their peanut allergy affects their quality of life	20 children with peanut allergy (mean age 9 years) and 20 IDDM (mean age 10 years) completed a survey at the child's clinic or home	Allergy hospital or clinic: Allergy and diabetic clinic in the UK	Cross-sectional survey	Participant eligibility criteria described; Data sources and outcome measurement details described; Described comparability of assessment methods of both groups; Described statistical methods used; 100 % response rate; Described characteristics of study participants, and summarized outcome results; Study limitations described
Bansal PJ (2005) ²⁴	To evaluate the ability of child care centers to recognize, evaluate and treat anaphylactic episodes	85 child care centers were randomly selected; 44 centers agreed to participate; 42 completed survey; 39 completed post-tests (95%) at 4 weeks	Community (child care center): Independent child care centers in the US	Cross-sectional survey	49% response rate, no reasons provided for non-participation; Participant eligibility criteria described; Statistical methods not described in detail; Potential bias not described; Demographic information of participants who completed questionnaire not described; Summary measures described in results
Barnett CW (2005) ²⁵	To determine if community pharmacist provided food-allergy education and auto-injector training is needed	Questionnaires sent to FAAN members: 1887 respondents (93 food allergic patients; 1791 parents or caregivers of food-allergic patient)	Community (allergy organization): FAAN in the US	Cross-sectional survey	Eligibility criteria and sources and methods for selection of participants described; Questionnaire pilot tested; Statistical methods described; 36.5% response rate; Demographic info of respondents described; Results reported numbers of outcome events and summary measures; Summary of key results referenced to study objectives; Study limitations described
Bellou A (2003) ²⁶	To establish the incidence of suspected allergic reaction of patients admitted to the ED	324 patients admitted for an allergic event (mean age 55 years)	ED: A university hospital ED in France	Chart review	Ethics approval described; Defined study variables; Statistical methods described; Data abstraction protocol not described; More than one data abstractor and inter-rater reliability not described; Did not address missing data; Calculation of sample size not described; Pilot study not described; Data from abstracted from charts supplemented with data from other sources described; Study limitations described

Bernstein DI (2004) ²⁷	To estimate the incidence of fatal and near-fatal reactions to immunotherapy injections, if the fatal reactions were related to allergen skin testing	646 physician members of the Academy of Allergy, Asthma and Immunology who responded to a survey	Community (allergy organization): Members of the AAAAI in the US	Cross-sectional survey	Relevant dates of when survey was conducted unclear; Sources and selection, eligibility of participants unclear; Unclear selection methods on how study participants were selected to complete short survey versus long survey; Statistical methods described; Study participant demographics not described; 25% response rate to short survey; Error in reporting near fatal group size in results; Study limitations described
Blyth (2002) ²⁸	To obtain information about all schoolchildren using adrenaline auto-injectors	Of 86 schools sent a questionnaire, 56 were returned; 30 families were contacted by telephone, of which 25 children were interviewed (age 4-17 yrs)	Community - Schools: Schools in the UK	Cross-sectional survey	Study design unclear (questionnaire and interview); Relevant dates of when data was collected not described; Statistical analysis not described; Study participant selection criteria unclear; Study participant characteristics unclear; Questionnaire results not described; Only 25 of 60 families consented to interview; No information provided about non-responders
Bock SA (2001) ²⁹	To report fatal cases of anaphylaxis that continue to be reported by a national registry	Family members of 32 fatal cases of anaphylaxis, selected from national registry	Community: Data from communities of a national registry in the US	Qualitative	Study design unclear – structured questionnaire was used to interview participants; Although sampling is justified, a qualitative data collection and analysis techniques are not described; Study limitations not described
Bollinger (2006) ³⁰	To determine the impact of food allergy on the daily activities of food allergic children and their families	Of 101 caregivers of food allergic children (8 months to 17 years of age) who completed the informed consent, 87 completed the questionnaire (86%)	Allergy hospital or clinic: A specialty clinic at the University of Maryland Allergy practice in the US	Cross-sectional survey	Study design addressed research question and objectives; Sampling strategy /study participant selection described; Participant eligibility criteria described; Data sources and outcome measures described; Data collection and analysis blinded; Questionnaire not validated; Described statistical methods used; 86% response rate; Described characteristics of study participants, and summarized outcome results; Study limitations described
Clark S (2004) ³¹	To describe the management of food-related acute allergic reactions	In 21 EDs, a random sample of 648 charts were reviewed of patients diagnosed with acute allergic reactions to food	ED: North American EDs	Chart review	Random sampling and criteria for selection clear; Ethics approval described; Defined study variables; Data abstraction protocol clear; Data abstraction forms underwent review by trained personnel and then double data entry to avoid data entry errors; Did not provide strategy to address missing data; Statistical method described; Data from abstracted from charts supplemented with data from other sources described; Study limitations described
Clegg SK (2001) ³²	To identify school aged children with an EpiPen® and to assess the quality of training received by their parents and teachers	44 of 76 charts identified of school aged children with a previous allergic reaction requiring an EpiPen®.	Community - Schools: Schools in Scotland, UK	Cross-sectional survey	Setting unclear, study period, duration of data collection not described; Method of participant selection described; Statistical methods not described; Results reported summary of outcome events; Summarized key results and referenced to study objective; Study results compared to previous studies
de Silva IL (2008) ³³	To describe the characteristics, clinical features, causative agents, and therapy in children with anaphylaxis	123 cases of anaphylaxis in 117 children who received therapy at initial anaphylaxis over a 5-year period were identified	ED: ED at a hospital in Melbourne, Australia	Chart review (case-note review)	Defined study variables; Data abstraction protocol not described; Data abstractors and inter-rater reliability not described; Did not provide strategies to address missing data; No calculation of sample size; Ethics approval described; Data from abstracted from charts supplemented with data from other sources described; Study limitations described
Dibs SD (1997) ³⁴	To identify the causative agents, presenting signs and symptoms, and course of disease in children with anaphylaxis	50 children (19 years of age and younger), of whom 55 episodes of nonfatal anaphylaxis were identified	Pediatric hospital or clinic: Children's hospital in Philadelphia, PA, in the US	Chart review	Defined study variables; Study participant selection described; Data abstractor and inter-rater reliability not described; Did not strategies for addressing missing data; Statistical methods described; Calculation of sample size not described; Data from abstracted from charts supplemented with data from other sources described; Study limitations not described
Dobbie A (1998) ³⁵	To investigate the prevalence of carrying adrenaline for children to treat anaphylaxis	84 children (mean age 9 years) who were prescribed self-injectable adrenaline were identified, and their carers sent a survey	Pediatric hospital or clinic: A community pediatric service in the UK	Cross-sectional survey	Setting described; Method of recruitment of study participants clear; Statistical methods not described; No follow-up with non-responders; Characteristics of study participants described; Results report summary of outcome events; Study limitations not described

Frost DW (2005) ³⁶	To examine the relationship between the low-income households and the adequacy of anaphylaxis management plans in primary schools	Principal in 100 of 168 elementary schools were randomly chosen to fill out a survey; 50% responded representing 287 children with serious allergies reported to the school	Community - Schools: Schools in Canada	Cross-sectional survey	Presented key elements of study design; Setting described clearly, participants selection described; Described efforts to address bias in income by compiling data for both responders and non-responders; Statistical methods described clearly; The number of observations described, lacked description of duration of study period; Study findings not generalizable due to poor response rate, and data were collected indirectly from the principals and not the children or caregivers; Study limitations described
Gaeta TJ (2006) ³⁷	To characterize ED visits for acute allergic reactions and to evaluate national trends in ED management	Patients (mean age 35 years); ED visits for acute allergic reactions for 12 years (1993-2004)	ED: EDs in the US	Chart review	Ethics review not described; Defined study variables; Data abstraction protocol clear; Trained hospital staff performed sampling and data collection and addressed missing data/non-response; Calculation of sample size not described; Data from abstracted from charts supplemented with data from other sources described; Study limitations described
Gillespie CA (2007) ³⁸	To develop a narrative description of the meaning of mothers' lived experience of parenting a child with food-induced anaphylaxis	6 mothers of children with food-induced anaphylaxis (age 6-12 years) were interviewed	Community: Families living in prairie city communities in Canada	Qualitative	Study design addressed research question and objectives (phenomenology); Ethics review described; Study sample selection criteria described (typical cases of FIA); Data collection described; Comprehensive data collection technique; Data analysis concurrent with data collection; Investigators were extensively involved in data collection but degree of agreement not described; Findings corroborated with similar studies
Gold MS (2000) ³⁹	To determine parental knowledge and practice in the first aid management of anaphylaxis, and the frequency of recurrent allergic reactions	Of 94 children who were prescribed EpiPen®, the parents of 68 children with anaphylaxis were interviewed over the telephone	Pediatric hospital or clinic: A pediatric allergy service Hospital in Australia	Cross-sectional survey	Study participant selection described; Extensive data collection methods by investigators; Described efforts to contact non-responders; Provided corresponding proportion of children with insect venom and food anaphylaxis of non-responders and participants at every stage being studied; Results reported numbers of outcomes events and summarized with reference to the study objectives; Study limitations not clearly stated
Gompels LL (2002) ⁴⁰	To investigate what treatment recommendations senior house staff would prescribe for 5 patient cases	78 physicians at the start of their emergency post were given a questionnaire on 5 patient cases	ED: An ED in the UK	Case-based survey	Study objective not clearly stated; Setting poorly described, selection of participants not described; Duration of observation and study period not described; Statistical methods not described; Results reported responses, no statistical significance measures; Study limitations not described
Grouhi M (1999) ⁴¹	To assess community-based professionals' knowledge of epinephrine auto-injector use and their ability to educate patients	122 (79%) health care professionals filled out a survey: physicians, medical students, pharmacists, nurses	Community – Convention: A general pediatric medical convention in Canada	Cross-sectional survey	Study setting described, including location, period of recruitment and data collection; Participant eligibility criteria provided and described efforts to decrease bias; Statistical methods described clearly; Characteristics of study participants described clearly; No data provided about non-responders; Results summarized findings of main outcomes of the study; Study limitations described
Hannaway PJ (2005) ⁴²	To analyze school children dispensed injectable epinephrine with widely diverse socioeconomic status	School nurses of 44 schools filled out a survey; 181 children in the 3 school systems were dispensed injectable epinephrine	Community – Schools: 3 Massachusetts school districts in the US	Cross-sectional survey	Setting described location and data collection methods; Participant selection described; Duration of observation not clear; Duration of study period not clear; Described data collection technique and statistical methods; Results provided demographic information about study participants; Interpretation not consistent with results; Study limitations not described
25 Hayman GR (2003) ¹¹	GPs' evaluations of patients referred after anaphylaxis; interview about when and how injectable adrenaline should be used	60 patient cases were reviewed; 50 GPs were interviewed and asked to demonstrate use of auto-injector training device	Hospital or clinic: 3 community hospitals in southwest London in the UK.	Case note review and Qualitative interviews	Brief article; Study case selection criteria described briefly; Efforts to address bias not described; Data collection methods (questionnaire development or interview methodology) and statistical analysis not described; Reported summary measures; Study limitations not described
Haymore BR (2005) ⁴³	To determine epinephrine prescribing patterns in a large hospital setting	A review of 220 medical records of adults and children; 24 cases met the criteria for anaphylaxis	Hospital or clinic: A large military hospital database in the US	Chart review	Defined study variables; Ethics review described; Statistical methods described briefly; Data abstraction protocol not described; Data abstractor and inter-rater reliability not described; Did not address missing data; Calculation of sample size not described; Pilot study not described; Study limitations described

Hu W (2007) ⁴⁴	To examine the information needs and preferences of parents regarding food allergy	84 parents of children with food allergies recruited from 3 clinics (N = 44) and one CO (N = 25)	Pediatric hospital or clinic: 3 pediatric allergy clinics and a CO in Australia	Qualitative	Study design addressed research question and objectives; Ethics review described; Study sample selection criteria described; Comprehensive data collection technique; Procedures for data analysis described; Duration of observation and study period not described; Characteristics of study participants described; Findings corroborated with similar studies; Study limitations not described
Hu W (2008) ⁴⁵	To report on the families' views of the differences between an allergy clinic and a CO for the provision of information	84 parents of children with food allergies recruited from 3 clinics (N = 44) and one CO (N = 25) participated	Allergy hospital or clinic: 3 pediatric allergy clinics and a CO in Australia	Qualitative	Study design addressed research question and objectives; Ethics review described; Study sample selection criteria described; Comprehensive data collection technique; Procedures for data analysis described; Duration of observation and study period not described; Demographic characteristics of study participants described for 2 groups; Results summarized events and referenced similar studies; Study limitations described
Johnson TL (2006) ⁴⁶	To determine prescription fill rates of auto-injectors and if an association between demographic factors and lack of filling the prescription	Of 769 patients whose records were reviewed for one year; 881 SIE prescriptions were entered	Hospital or clinic: A large military medical center in the US	Chart review	Defined study variables; Ethics review not described; Data abstraction protocol and strategies to address potential bias not described; Did not address missing data; No calculation of sample size; Data from abstracted from charts supplemented with data from other similar studies; Study limitations described
Jose R (2007) ⁴⁷	To investigate how junior physicians administer epinephrine using an adult case of anaphylactic shock	95 junior physicians were asked to complete a short case-based questionnaire in the presence of the investigator	Hospital or clinic: 2 district general hospitals in the UK	Case-based questionnaire	Objectives of study not clearly stated in introduction; Selection criteria of study population not described; Sampling bias not addressed; Statistical methods not described, although provided a sample questionnaire; Results summarized observations, no test of significance conducted; Discussion summarizes key results, does not relate to other similar studies; Study limitations not described
Kane KE (2004) ⁴⁸	To examine EMS case definitions of allergy, the incidence of anaphylaxis and epinephrine administration, and anaphylaxis deaths	Data were collected from a national EMS association	Community: EMSs in 10 US states, and one large city (Toronto) in Canada	Database review	Data collection sources described; Study variables described, but unclear inclusion/exclusion criteria; Ethical review described; Strategies to reduce bias not addressed; Statistical methods not described; Data abstraction protocol not described; Results summarized events and referenced similar studies; Study limitations described
Kapoor S (2004) ⁴⁹	To examine the effectiveness of a consultation intervention on parental knowledge of food allergy and the rate of allergic reactions	62 children (age <17 years) with food allergy were enrolled (53 followed up), and parents were provided education in the hospital	Pediatric allergy hospital or clinic: Multidisciplinary pediatric allergy clinic in the UK	Prospective cohort (pre-/post-test)	Objectives and setting clearly stated; Eligibility criteria described; Statistical methods appropriate Clearly defined all outcomes; Tested the validity of questionnaire and was piloted, degree of agreement described; Reported the numbers of individuals at each stage of the study; 85.5% subjects were followed-up at 3 months; Provided characteristics of study participants; Reported summary of measures over time; Provided key results and linked them to study objectives
Kim JS (2005) ⁵⁰	To explore if underuse of EpiPen® might be attributed to parental discomfort with administration	360 surveys were sent to parents of children age 1-19 years with food allergy; 170 surveys completed; 165 were analyzed	Community: An allergy support group and a pediatric allergy clinic in the US	Case-based survey	Study objective clearly described; Statistical analysis described; Inclusion criteria described and duration of data collection clear; Poor response rate of 46% and characteristics of non-responders not described; Results provided demographic information about study participants and reported summary measures; Study results are not generalizable; Study limitations described
Krugman SD (2006) ⁵¹	To assess pediatricians' knowledge of the diagnosis and management of food-induced anaphylaxis	Of 1130 surveys mailed to pediatricians that were recruited from the AAP, 468 responded (41%), 49 were excluded.	Community – Allergy organization: The AAP in the US	Case-based survey	Did not provide degree of agreement after pilot tests; Described data collection methodology and statistical analysis described; Sampling from AAP database was random; Study population inclusion / exclusion criteria described; Response rate was 41%; Characteristics of respondents described, but non-responders not described; Results reported summaries of observation; Key results of study were referenced to study objectives; Study limitations described

Lee JM (2000) ⁵²	To determine the incidence of biphasic reactions in children with anaphylaxis, and the risk factors that predict progression to a biphasic reaction,	106 children (age 6 months to 21 years) admitted to a hospital with acute anaphylaxis between ; 108 anaphylaxis episodes were identified	Pediatric hospital or clinic: A children's hospital inpatient unit in the US	Chart review	Defined study variables; Ethics review not described; Data abstraction protocol clear, coding uncertainties were resolved by discussion among the authors; Data abstractor inter-rater reliability not described; abstractor not blinded; No sample size calculation; Data abstracted from charts supplemented with data from similar studies; Study limitations described
Lieberman P (2008) ⁴	To review the epidemiology of anaphylaxis, and the underlying predisposing factors	Number of included studies – Not indicated	Not applicable	Systematic review	Database sources and search strategy identified; Study selection criteria not described; Study abstraction not described; Study quality assessment not done; Tests of heterogeneity not done; Results don't describe data synthesis; Limitations not discussed
Lyons AC (2004) ⁵³	To explore young adults awareness of food allergy, and their perceptions of people with food allergy	162 young adults attending a seminar responded to a survey; 24 had an allergy to at least one food	Community – University: A University in the UK	Cross-sectional survey	Convenient sample and did not address bias; Statistical methods not described; Results provided descriptive data on study participant demographics; The main results provided summary of measures; Provides cautious interpretation of the results and similar to other studies but due to the sampling strategy, results may not be generalizable; Study limitations described
Mandell D (2005) ⁵⁴	To investigate how parents and children experience coping with anaphylaxis, how they adapt, and what they need as supports to positive adaptation	Parents in 17 families were recruited and were interviewed about their experiences adjusting to a diagnosis of anaphylaxis in a child	Community / Pediatric hospital: An anaphylaxis seminar, a children's hospital, and a support group in Canada	Qualitative	Study design addressed research question and objectives; Ethics review described; Study sample selection criteria and sources described; Comprehensive data collection technique; Data collection partially blinded; Procedures for data analysis described; Duration of observation described; Demographic characteristics of study participants described; Findings were corroborated (triangulation of data and analysis); Study limitations described
Marklund B (2007) ⁵⁵	To illuminate adolescents' experiences of being food-hypersensitive	3 focus group interviews and 6 interviews with 17 adolescents (age 14-18 years) who had food hypersensitivity	Community – Schools: Schools in a municipality in Sweden	Qualitative	Study design addressed research question and objectives; Ethics review described; Study sample selection criteria and sources described; Comprehensive data collection technique; Data collection conducted by 3 investigators; Duration of observation described; Procedures for data analysis described; Findings were referenced to other published studies; Study limitations described
McDougle L (1994) ⁵⁶	To evaluate what physicians base their aftercare instructions for patients with hymenoptera sting anaphylaxis	Of 174 physicians who were mailed a questionnaire, 124 completed questionnaire (71% response rate)	ED: Physicians from 37 states in a military hospital ED, medical school, or HMO in the US	Cross-sectional survey	Demographic information about the participants of study not described; Non responders not described; Sampling strategy unclear and did not address potential for bias; Statistical methods not described; Duration of data collection or study period not provided; Results provided summary of data collected, tests for significance between groups not described; Study limitations not discussed
McIntyre CL (2005) ⁵⁷	To determine the frequency of epinephrine administration in schools, circumstances around anaphylactic events and identify clinical features of reactions	School nurse leaders in 109 school districts completed an epinephrine form; 48 school districts reported a total of 115 forms in 2 years	Community – Schools: 109 school districts in the US	Prospective cohort	Provided the eligibility criteria and sources of and methods of selection of participants; Did not describe strategy to address potential recall bias; Data collection form validated by experts in the field, however degree of agreement not described; Duration of observation and study period described; Statistical methods described; Study participant characteristics described; Non responder reasons or characteristics not described; Results did not summarize data with follow-up time; Key results referenced to study objectives and results from similar studies
Mehl A (2005) ⁵⁸	To describe the most important triggers, pattern of clinical reaction, site of occurrence and treatment of anaphylactic in children	93 pediatricians, clinicians and GPs were asked to fill out a questionnaire about 103 of their pediatric anaphylaxis cases (age range 3 months to 12 years)	Pediatric clinic or general practice: Pediatric and general practices in Germany	Cross-sectional survey	Provided the eligibility criteria and sources of and methods of selection of participants; Did not describe strategy to address potential selection and recall bias; Data collection by 2 investigators conducted extensively, but degree of agreement not described; Duration of observation, frequency of data collection and study period described; Statistical methods described; Study participant characteristics described but excluded subjects not described; Results reported numbers of outcome events and related to study objectives in the discussion; Study limitations not described

Mehr S (2006) ⁵⁹	To determine the rate of correct EpiPen® trainer demonstration by junior and senior medical staff	100 physicians with median 5 years clinical experience were asked to demonstrate how to use an EpiPen® trainer	Hospital or clinic: A tertiary pediatric hospital in Australia	Prospective cohort	Inclusion/exclusion criteria described; Data collection described; Statistical methods described; Efforts to address selection bias not described; Study participant characteristics described; Results reported unadjusted estimates; Study limitations not described
Moneret-Vautrin DA (2001) ⁶⁰	To evaluate the efficiency of a personalized care project (PCP) plan and the training in the use of the emergency kit	45 families of children (age range 4-20 years) with food anaphylaxis attending an allergy clinic were asked to complete a phone survey	Hospital or clinic: An allergy clinic in France	Cross-sectional survey	Sources and methods of selection of participants not described; Duration of observation and study period not described; Efforts to address interviewer bias not described; Data collection techniques not clear; Characteristics of non-responders not described; Characteristics of study participants described; Results reported unadjusted estimates; Follow-up data included 86.6% of study participants; Study limitations not described
Oude-Elberink JNG (2006) ⁶¹	To examine the possible negative aspects of EpiPen® compared with VIT as perceived by patients	94 patients with yellow jacket anaphylaxis were randomized to VIT (N = 47) or EpiPen® (N = 47)	Hospital or clinic: Allergy outpatient department in the Netherlands	Part-randomized controlled trial	Randomization methods, allocation concealment or blinding not indicated; Data was analyzed according to intention to treat analysis; Follow-up was at least 80%; Limitations not discussed
Patel BM (2006) ⁶²	To determine whether child care centers can recognize, evaluate, and treat anaphylactic episodes in children 1-6 years of age after attending an allergy seminar	Child care directors of 39 child care centers completed survey and completed follow-up at 6 months (N = 37) and 1 year (N = 29)	Child care center: Child-care setting in the US	Prospective cohort (before/after)	Setting described clearly providing locations, periods of recruitment, duration of study, exposure, follow-up and data collection; Eligibility criteria of subjects described; Statistical methods appropriate to the study; Reported the numbers of individuals at each stage of the study; Reported summary of measures over time; Provided key results and linked them to study objectives and provided results from similar studies; Study limitations described
Pouessel G (2006) ⁶³	To determine the use of Anapen® for food allergic children, to assess parental knowledge of Anapen®	Of 152 families contacted, 109 parents (73% response) of 111 children (age 17 months and 18 years) with food allergy previously prescribed Anapen®	Pediatric hospital or clinic: A children's hospital in France	Cross-sectional survey	Study participant selection described; Duration of observation and study period described; Efforts to address bias described – blinding of data abstraction; Data collection techniques clear; Characteristics of non-responders not described; Characteristics of study participants described; Results reported unadjusted estimates; Study limitations not described
Powers J (2007) ⁶⁴	To compare and evaluate food allergy emergency plans used by schools to the FAAN plan	Of 250 attendees of a regional school health issues conference, 94 school nurses (38%) responded to the survey	Community – School health conference: Schools in the US	Cross-sectional survey	Study duration and study period described; Efforts to address bias not described; Characteristics of non-responders not described; Statistical methods described; Results reported numbers of outcome events; Provided cautious interpretation of findings and limit generalizability beyond the sample; Study limitations not described
Primeau MN (2000) ⁶⁵	To compare the QOL and family relations of children and adults with a peanut allergy (PA) or rheumatological disease (RD)	Of 648 questionnaires sent out, 343 were returned (53%) and 301 were analyzed: 153 children with PA, 69 children with RD, 37 adults with PA, and 42 adults with RD	Pediatric hospital or clinic and community: A children's hospital in Canada	Prospective cohort	Provided extensive eligibility criteria and sources of and methods of selection of participants; Did not describe strategy to address potential volunteer bias; Validated questionnaires described; Duration of observation and study period not described; Statistical methods described; Poor response rate; Study participant characteristics described; Key results referenced to study objectives and results from similar studies; Study limitations described
Pumphrey RSH (2000) ¹	To investigate the circumstances leading to fatal anaphylaxis	A register of 164 fatal anaphylactic reactions from 1992 to 1998 were reviewed	Community: Communities in the UK	Chart review	Retrospective review of coroner's registry; Ethical review described; Defined study variables; Statistical methods not described; Data abstraction protocol not described; Did not address bias; Results summarized events and referenced similar studies; Study limitations not described
Rankin KE (2006) ⁹	To investigate the number of children considered to be at risk of anaphylaxis, and the school's approach to minimizing food-induced allergic risk,	Of 250 schools in the sample, 248 were sent a survey about approaches to managing children at risk for anaphylaxis (age 4-17 years)	Community – Schools: Scottish schools in the UK.	Cross-sectional survey	Study participant selection described; Duration of observation and study period described; Efforts to address bias described; Follow-up with non-responders described; Data collection techniques and statistical methods described; Characteristics of non-responders compared to responders; Results reported unadjusted estimates with CIs; Key results summarized with reference to study objectives; Provides caution to interpretation of results; Study limitations done

Safdar B (2000) ⁶⁶	To systematically review the literature for studies evaluating pre-hospital use of SC epinephrine	Number of included studies = 5	Pre-hospital setting	Systematic review	Database sources and search strategy identified; Study selection criteria not described; Study abstraction done in duplicate; Study quality assessment not done; Tests of heterogeneity not done; Results don't describe data synthesis; Limitations discussed
Sampson HA (1992) ⁶⁷	To report severe food-induced anaphylactic reactions in children and adolescents	13 children and adolescents (6 fatal, age 2-16 years; and 7 non-fatal cases, age 9-17 years) with food-induced anaphylaxis identified	Community: Communities in the US	Chart review	Convenience sample; Study participant selection described clearly; Duration of observation and study period described; Efforts to address bias not described; Data collection techniques described; Characteristics of study participants described; Key results summarized with reference to study objectives; Study limitations not described
Sicherer SH (2000) ⁶⁸	To assess patient and physician use of self-administered epinephrine	101 families of newly referred food allergic children (mean age 6.4 years); 46 physicians and residents were surveyed and asked to demonstrate auto-injector use	Pediatric hospital or clinic: An allergic pediatric clinic at a hospital in the US	Prospective cohort	Study participant selection described; Convenient sampling of physicians; Efforts to address potential bias not described; Statistical methods described briefly; Study participant characteristics described Results reported outcome event Key results summarized with reference to study objectives; Study limitations not described
Sicherer SH (2001) ⁶⁹	To determine the impact of food allergy on parental perceptions of physical and psychosocial functioning	253 of 400 surveys (63%) were completed by parents of food allergic children from a random sample of members of FAAN	Community – Allergy organization: the FAAN in the US	Cross-sectional survey	Study participant selection described clearly; Duration of observation and study period unclear; Efforts to address bias described clearly; Follow-up with non-responders described; Statistical methods described clearly; Characteristics of study participants described; Results reported unadjusted estimates with confidence intervals; Key results summarized with reference to study objectives; Provides caution to generalize results; Study limitations described
Simons FER (2005) ⁷⁰	To determine the availability of epinephrine for use in the first-aid, out-of-hospital treatment of anaphylaxis in different countries	From a sample of allergists from 39 countries worldwide, 75 WAO members were surveyed from 2003-2005 (100% responded)	Community: Communities worldwide	Cross-sectional survey	Convenient sample; Investigators were involved in development of survey (pilot tested), but degree of agreement not described; Statistical methods not described; Characteristics of study participants described; Results reported unadjusted estimates with confidence intervals; Key results summarized with reference to study objectives; Study limitations not described
Singh J (2003) ⁷¹	To assess the quality of training provided to parents of children prescribed auto-injectors, adherence to specialist referral, and QOL	Of 154 parents with children who were prescribed an auto-injector, 107 parents responded (76%) to a questionnaire	Community: The quintile of the most deprived local authority areas in the UK	Cross-sectional survey	Study participant selection described clearly; Duration of observation and study period unclear; Investigators were involved in development of survey, but degree of agreement not described; Statistical methods not described; Characteristics of study participants described, non-responders not described; Results provided summaries of measures; Study limitations not described
Thain S (2007) ⁷²	To identify which medications physicians would prescribe for anaphylaxis, and how administered	91 physicians were randomly selected within a 24-hour period to anonymously complete a questionnaire	Hospital or clinic: A public hospital in New Zealand	Case-based survey	Study participant selection described clearly; Duration of observation and study period described; Efforts to address bias described—random sampling of physicians; Statistical methods not described; Characteristics of non-responders not described; Characteristics of study participants described; Key results summarized with reference to study objectives; Study limitations not described
Webb LM (2006) ⁷³	To examine the natural history, clinical manifestations, and factors that affect the patients' adherence to treatment of anaphylaxis	601 charts were reviewed for patients with a diagnosis of anaphylaxis over a 25 year period (mean age 37 years)	Allergy clinic: A private university-affiliated allergy clinic in the US	Chart review and questionnaire	Defined study variables; Exclusion of cases described; Data abstraction protocol for chart review not described; Duration of observation and study period unclear; Poor response rate to follow-up survey (34%); Characteristics of participants described but non-responders not described; Statistical methods not described; Results reported summary measures; Data supplemented with data from other sources; Study limitations described

FAAN = Food Allergy & Anaphylaxis Network; ED = emergency department; CO = consumer organization; EMS = emergency medical services; AAP = American Association of Pediatrics; HMO = health maintenance organization; WAO = world allergy organization; VIT = venom immunotherapy;