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RECOVER Guidelines: First Aid. Evidence, Treatment Recommendations, Knowledge Gap Analysis, and Clinical Guidelines for Acute Allergy and Anaphylaxis in Dogs and Cats

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ABSTRACT

Objective: To systematically evaluate relevant evidence, devise and present treatment recommendations, and identify and present critical knowledge gaps regarding treatment of uncomplicated allergic reaction and anaphylaxis in dogs and cats.

Design: Standardized, systematic evaluation of literature pertinent to uncomplicated allergic reaction and anaphylaxis following Grading of Recommendations, Assessment, Development, and Evaluation methodology, modified for two clinical questions. Identified literature regarding prioritized questions in the Population–Intervention–Comparator–Outcome (PICO) format was reviewed independently by Evidence Evaluators, and findings were reconciled by Domain Chairs and Reassessment Campaign on Veterinary Resuscitation (RECOVER) Co-Chairs to arrive at treatment recommendations. This process used an evidence profile worksheet for each PICO question including an introduction, consensus on science, treatment recommendations, justification of recommendations, and knowledge gaps. Treatment recommendations underwent a 4-week comment period among international

Abbreviations: aOR, adjusted odds ratio; BAR, biphasic anaphylactic reaction; CI, confidence interval; CoSTR, consensus on science and treatment recommendation(s); CPA, cardiopulmonary arrest; CRI, continuous rate infusion; CT, controlled trial; ED, emergency department (for people); EE, Evidence Evaluator; ES, experimental study; FA, First Aid (Domain); GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; H1R, histamine-1 receptor; IM, intramuscular; LOS, length of stay; OR, odds ratio; OS, observational study; PICO, Population–Intervention–Comparator–Outcome; RECOVER, Reassessment Campaign on Veterinary Resuscitation.

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veterinary stakeholders prior to finalization. These 2026 RECOVER First Aid Guidelines: Acute Allergy and Anaphylaxis summarize treatment recommendations for dogs and cats.

Setting: Transdisciplinary, international collaboration in university, specialty, emergency, and general practice.

Results: Six PICO questions pertaining to uncomplicated allergic reaction and anaphylaxis were addressed in this subproject of the RECOVER First Aid Domain. These six PICO questions resulted in 12 treatment recommendations. All recommendations are supported by low or very low quality of evidence (7) or based on expert opinion (5). The RECOVER First Aid Acute Hypersensitivity Reaction Algorithm displays the flow of assessments and treatments for dogs and cats with uncomplicated allergic reaction and anaphylaxis.

Conclusions: These 2026 RECOVER First Aid Guidelines: Acute Allergy and Anaphylaxis present a concise and comprehensive framework for recognizing and treating acute hypersensitivity in dogs and cats. However, meaningful uncertainty remains regarding optimal diagnosis and treatment of these conditions in dogs and cats, and high-priority knowledge gaps are presented to guide collaborative clinical research in this area.

1 | Introduction

Acute hypersensitivity reactions are relatively common in dogs and occur less commonly in cats; such reactions are treated relatively frequently in small animal general and emergency practice. Acute hypersensitivity in dogs and cats is most often reported to be caused by vaccines, other medications, and *Hymenoptera* and other insect venoms, though in many cases the inciting antigen is unknown [1–5]. While acute hypersensitivity can manifest as mild, uncomplicated allergic reactions, it can also manifest as anaphylaxis, which can be life-threatening [2, 6, 7].

The Reassessment Campaign on Veterinary Resuscitation (RECOVER) initiative first published evidence- and consensus-based consensus guidelines for CPR in dogs and cats in 2012, with an update in 2024 [8, 9]. While many resources exist regarding the management of uncomplicated allergic reaction and anaphylaxis in small animals, no evidence- and consensus-based treatment recommendations and guidelines have been previously available [10–13]. Such guidelines could allow for standardization and optimization of preclinical and emergency treatment recommendations for acute hypersensitivity reactions in small animals to strengthen the chain of survival and more clearly describe critical knowledge gaps surrounding diagnosis and management in these species. Thus, evidence-based consensus guidelines for management of acute hypersensitivity reactions in dogs and cats were developed as part of the RECOVER 2026 First Aid Guidelines project.

The goal of the acute hypersensitivity subdomain of the RECOVER 2026 First Aid Guidelines project was to provide evidence-based consensus guidelines to enable veterinary professionals to improve outcomes for dogs and cats experiencing acute hypersensitivity reactions, and to identify specific knowledge gaps for future study. To this end, the objective of the project was to generate evidence- and consensus-based treatment recommendations for management of canine and feline acute hypersensitivity reactions. The purpose of this paper is to present the 2026 RECOVER First Aid: Acute Allergy and Anaphylaxis evidence, treatment recommendations, knowledge gaps, and clinical guidelines for dogs and cats.

2 | Methods

2.1 | Definitions

Historically, veterinary authors have proposed a variety of definitions for acute allergic reactions and anaphylaxis in dogs [7, 14, 15]. Nomenclature such as “localized” versus “systemic,” or “simple” versus “complicated” to distinguish uncomplicated allergic reactions from anaphylaxis may create confusion; for example, cutaneous signs such as urticaria and angioedema occur distant from the inciting cause and are thus systemic even though they are non-life-threatening signs of uncomplicated allergic reaction, while cardiovascular collapse could be considered “simple” (i.e., single-system) but denotes anaphylaxis and is life-threatening. In human medicine, there has been a move toward defining clinical syndromes, for instance sepsis, in a treatment-focused way that helps clinicians distinguish patients at greatest risk and thus institute early and appropriate therapy to improve outcomes [16]. Thus, more recent human guidelines regarding the identification and management of anaphylaxis have emphasized the use of specific clinical criteria to identify (clinically define) anaphylaxis to facilitate timely institution of appropriate therapy [17–19].

2.1.1 | Key Definitions for Acute Hypersensitivity Reactions in Dogs and Cats

The RECOVER First Aid writing group has adopted the following definitions, based on a combination of the system proposed by Rostaher et al. [15], reports of clinical findings in dogs and cats [2–5, 7], evidence derived from experimental studies in canine anaphylaxis [20–22], and current human definitions [17–19].

Uncomplicated allergic reaction in dogs and cats is a systemic hypersensitivity reaction involving peracute onset (i.e., within minutes to hours) of cutaneous signs and may include self-limiting gastrointestinal signs such as mild vomiting or diarrhea. An uncomplicated allergic reaction is not immediately life-threatening.

Anaphylaxis in dogs and cats is a severe, systemic hypersensitivity reaction involving peracute onset (i.e., within minutes to hours) of clinical signs that may be immediately life-threatening and

TABLE 1 | Acute hypersensitivity reactions in dogs and cats: A treatment-based grading system.

Peracute onset (minutes to hours) of clinical signs, and possible or known allergen exposure				
	Uncomplicated allergic reactions		Anaphylaxis	
Grade →	**0**	**1**	**2**	**3**
Reaction subtype →	**Cutaneous**	**Cutaneous and self-limiting GI**	**Moderate anaphylaxis**	**Severe anaphylaxis**
Organ system	This single system only	These two systems only	Two or more systems: Anaphylaxis is the most likely diagnosis if cutaneous signs present	Cardiovascular collapse Other signs variably present
Skin, mucosa, subcutis—Sign(s) in any combination	• Urticaria such as wheals and angioedema • Flushing • Pruritus	• Urticaria such as wheals and angioedema • Flushing • Pruritus	Variably present.If present: • Urticaria such as wheals and angioedema • Flushing • Pruritus De-emphasize cutaneous signs for patients with likely sensitive allergen exposure	
Gastrointestinal system	None	Mild, self-limiting vomiting or diarrhea (e.g., isolated episode)	Persistent vomiting or diarrhea or abdominal pain	
Respiratory	None	None	Increased effort Stridor Wheezing Severe respiratory distress	
Cardiovascular	None	None	Bradycardia Tachycardia Pallor	Collapse or hypotension
Treatment	H1R antagonist	H1R antagonist	Epinephrine IM	Epinephrine CRI

Abbreviations: CRI, continuous rate infusion; GI, gastrointestinal; H1R, histamine-1 receptor.

generally include cardiovascular, respiratory, or gastrointestinal signs, with or without cutaneous signs. A dog or cat with anaphylaxis that has clinical signs in two or more body systems without collapse or hypotension is considered to have *moderate anaphylaxis*, while a dog or cat with anaphylaxis and cardiovascular collapse or hypotension is considered to have *severe anaphylaxis* regardless of how many other body systems are affected (Table 1).

2.1.2 | Pertinent RECOVER First Aid Definitions

The *prehospital* setting is any setting outside the veterinary clinic or hospital, including homes, community locations, businesses, campsites, wilderness, or any other space not equipped to provide clinic-level veterinary care. The prehospital setting also includes civilian, public service/safety, or professional (e.g., pet ambulance) vehicles used to transport the animal to a veterinary facility. As implied by the term "prehospital," animals requiring first aid should be presented to a veterinary facility as soon as possible after first aid is administered.

Provider in these guidelines is defined as a person who provides first aid for a specific urgent medical condition in the prehospital setting. The provider may be an owner, handler, paraprofessional, or other bystander. In some circumstances, a trained veterinary professional such as a veterinarian or veterinary technician/veterinary nurse may act as a first aid provider in the prehospital setting due to time sensitivity of the aid, as in the case of administering an intramuscular (IM) injection of epinephrine in the prehospital setting.

A *veterinary professional* is a person working in a clinical setting who is a licensed veterinarian, licensed veterinary technician or registered veterinary nurse, or unlicensed person working in the capacity of, for instance, an assistant veterinary technician or veterinary nurse.

2.2 | Intended Audience

Unlike the main first aid clinical guidelines for dogs and cats [23], all parts of this paper, including the RECOVER First Aid Acute Hypersensitivity Reaction Algorithm (Figure 1), are written for a veterinary professional readership and intended for use by veterinary professionals.

2.3 | General Methodological Approach

This project followed the 2024 RECOVER Guidelines methodology, published in detail elsewhere (Figure 2) [24]. Where

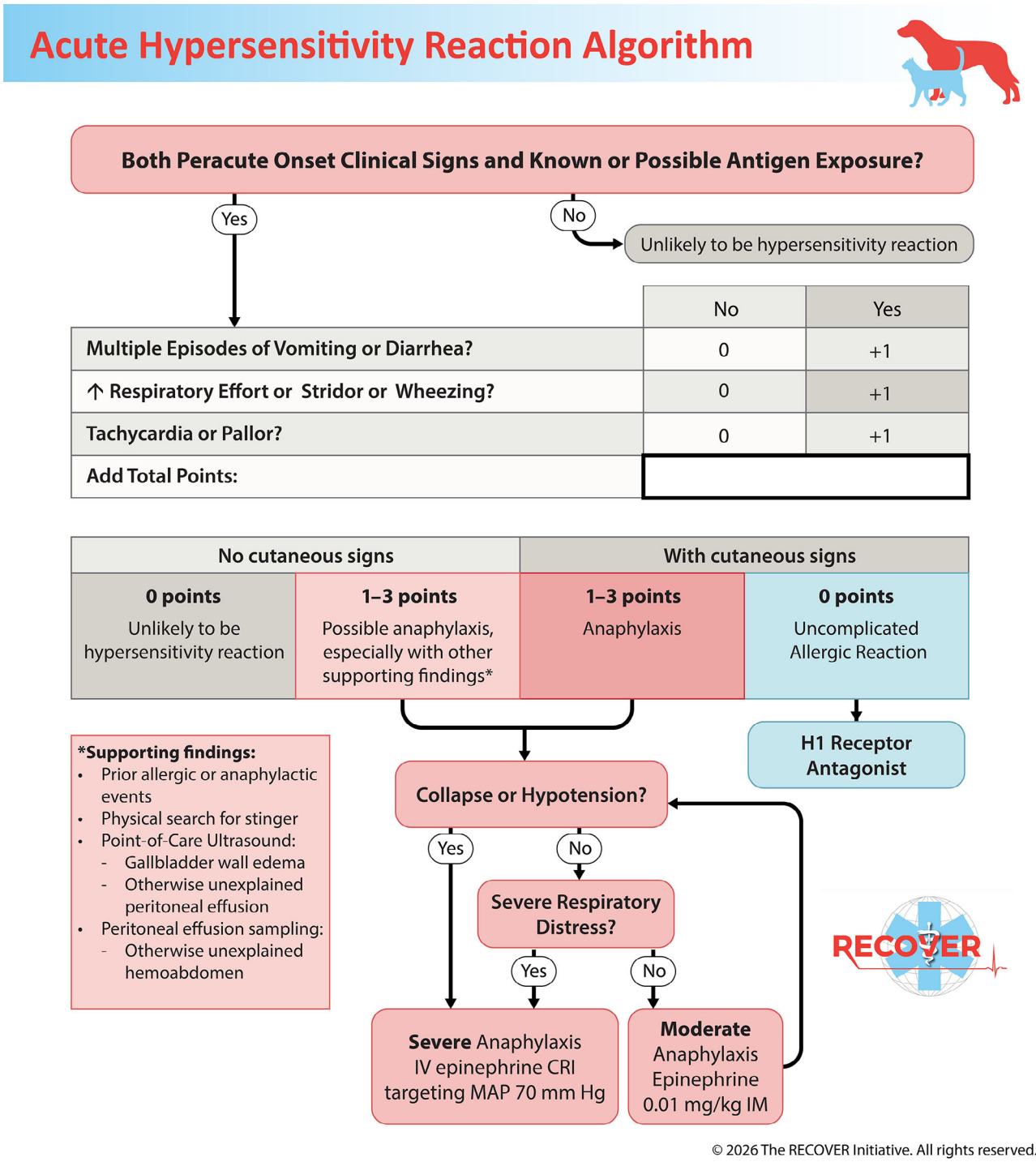

FIGURE 1 | RECOVER First Aid Acute Hypersensitivity Reaction Algorithm for clinical recognition and decision-making in dogs and cats suspected to have an acute hypersensitivity reaction. Abbreviations: CRI, continuous rate infusion; H1, histamine-1

methodology was modified, for instance to perform more recent literature searches to bridge time gaps between the original literature search and evidence analysis, such deviation is noted below in Sections 2.5 and 2.6 or in the individual Population–Intervention–Comparator–Outcome (PICO) subsection of the current paper, generally in the PICO's Consensus on Science section. In short, these RECOVER Guidelines on First Aid: Acute Allergy and Anaphylaxis were generated using a modified version of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system for guideline generation in health care [25]. The First Aid (FA) Domain project work started in 2018 with the generation of a list of prioritized questions pertaining to first aid, many of which were extrapolated from topics covered in contemporaneous human first aid guidelines [26, 27] and finished with a consensus period and manuscript writing in 2026. A concise summary of the iterative evidence evaluation and consensus process is provided below.

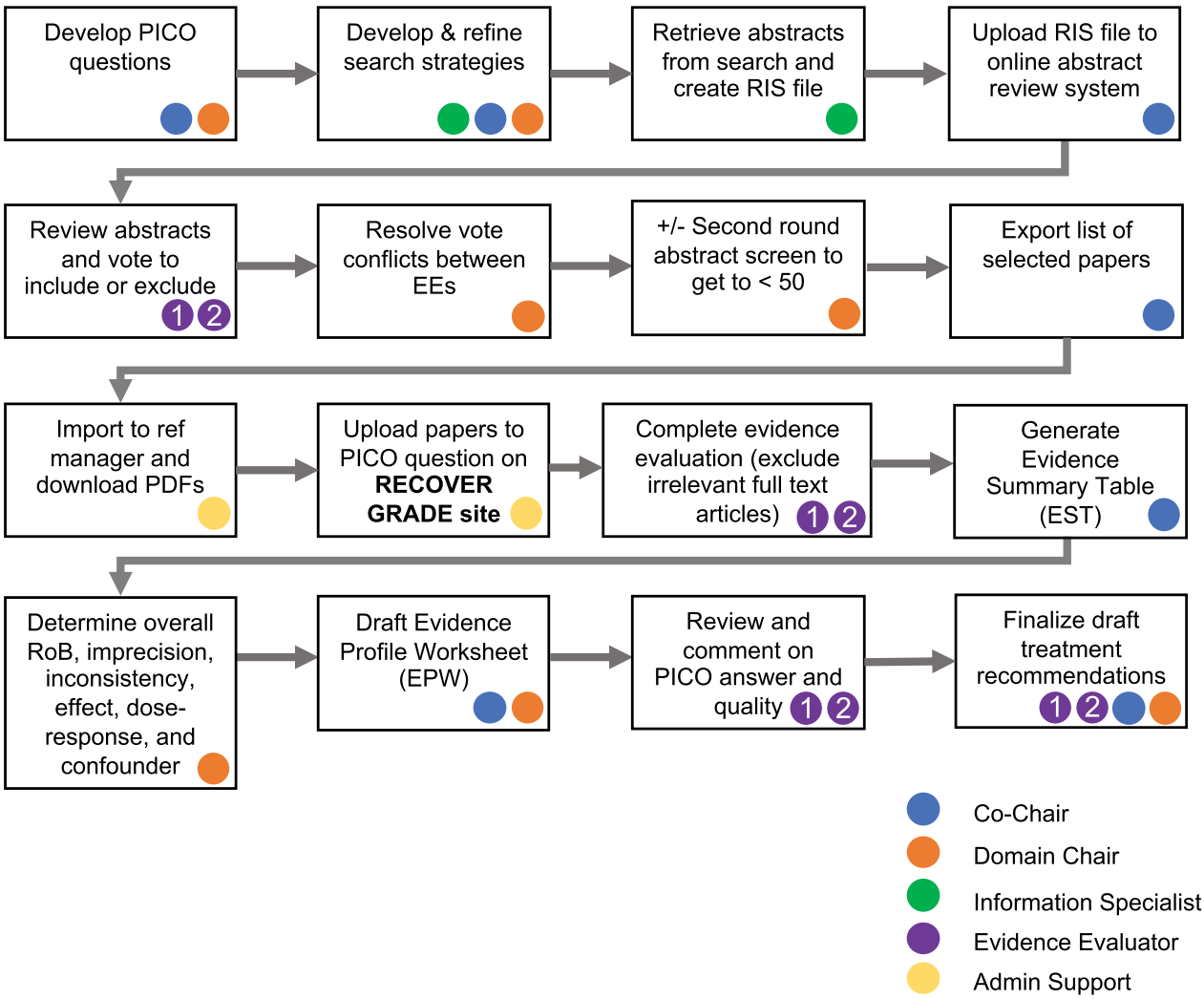

FIGURE 2 | Evidence evaluation process overview for the RECOVER First Aid: Acute Allergy and Anaphylaxis subdomain. GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PICO, Population–Intervention–Comparator–Outcome; RECOVER, Reassessment Campaign on Veterinary Resuscitation; RIS, Research Information System.

2.4 | Defining PICO Questions

The RECOVER Co-Chair originally overseeing the FA Domain (D.F.) appointed content experts to serve as Domain Chairs for the FA Domain (D.M., V.T.). These Domain Chairs, together with the Co-Chair, generated research questions in the PICO format and identified three to five clinically relevant outcomes for each PICO question. PICO questions were rated as high, moderate, or lower priority. Fourteen of 28 initially proposed PICO questions were included in the evidence evaluation. During evidence synthesis, two additional PICO questions were added in late 2025. Thus, a total of 16 FA Domain PICO questions were addressed; six are presented in this paper and 10 in a companion paper on general first aid in dogs and cats [23].

For each PICO question, Domain Chairs ranked the outcomes according to their clinical importance, so that treatment recommendations could be made based on the evidence pertaining to the highest priority outcome for which clinically relevant evidence was available. The most commonly included outcomes were survival to discharge, severity of clinical signs, and length of hospital stay (LOS), generally in this order of priority. Additional or different outcomes were investigated depending on the PICO question.

2.5 | Literature Search, Screening, and Evidence Evaluation for PICOs FA-01, FA-02, FA-12, and FA-13

Specialist librarians (Information Specialists) worked with RECOVER Co-Chairs to develop the search strategy for the project [28]. Literature search strings were developed for each PICO question using an iterative process among Information Specialists and Domain Chairs to optimize the number and type of articles returned in each search. Peer review of search strategies occurred using modified Peer Review of Electronic Search Strategy Guidelines and informal meetings [29]. Databases searched included PubMed, CAB Abstracts using the CAB Direct platform, and Scopus, and date coverage included the years 1966–2020. Articles written in non-English languages, letters,

and other nonanalytical publications were excluded at the level of search strategies.

For each PICO question, two Evidence Evaluators (EEs) (e.g., specialist veterinarians, general veterinarians in emergency or specialty practice, or veterinary technician specialists in emergency and critical care) independently reviewed titles and abstracts of initially identified articles to eliminate irrelevant publications and to arrive at potentially relevant primary literature for further review[1]. Reviews, meta-analyses, case reports and case series, and non-peer-reviewed publications (e.g., proceedings) were excluded either during this title and abstract screening process or later at the full-text review stage. Domain Chairs or Co-Chairs resolved any conflicts between EEs by casting the tie-breaking vote on pertinent articles. Full texts of these potentially relevant publications were then reviewed for each PICO by the same EEs; first, they established the relevance of each publication for the PICO question, and if confirmed, they extracted relevant information from these publications for each predefined outcome.

EEs used a purpose-developed, web-based evaluation platform to proceed through a predetermined, standardized set of questions to evaluate key aspects of evidence quality (e.g., risk of bias; indirectness of population, intervention, and outcomes). Based on EE responses, the evaluation platform generated a Summary of Findings Table for each outcome for every PICO question. EEs also provided succinct overview evidence summaries for their PICO question.

Prior to completing the Evidence Profile Worksheets for these PICOs in late 2025, the RECOVER Guidelines Co-Chair (J.B.) executed bridge literature searches to identify new or missed relevant research for each PICO, as the formal literature searches were approximately 5 years old at that time. Details of these bridge literature searches and notes on relevant identified publications are included in each PICO's Evidence Profile Worksheet along with their consensus on science and treatment recommendation (CoSTR); these full Evidence Profile Worksheets are available elsewhere[2]. If additional pertinent publications were identified on the bridge search, the Co-Chair conducted an evidence quality evaluation (i.e., risk of bias, indirectness, imprecision, inconsistency) and reported the studies' qualities and findings separately from the 2-EE GRADE-evaluated literature in the CoSTRs.

2.6 | Literature Search, Screening, and Evidence Evaluation for PICOs FA-29 and FA-30

PICO questions FA-29 and FA-30 were developed after the CoSTR generation process for PICOs FA-01, FA-02, FA-12, and FA-13 was complete. Thus, the literature identification and evaluation methods for these two PICO questions differ from those of the other FA Domain PICO questions.

The literature search, evidence quality evaluation, and results recording for FA-29 were performed from December 2025 to January 2026. The literature search was performed by first identifying the most recent, high-quality meta-analyses on the topic through PubMed search with the help of an Information Specialist [30–32]. Backward and forward citation searching was performed using each meta-analysis and cited article to capture relevant primary studies. Finally, a PubMed literature search was performed using a search string developed with an Information Specialist. Results of this search were then date-limited to include studies published from the year of the final literature search of the most inclusive meta-analysis (2023) to January 24, 2026. Prospective controlled trials (CTs) were included. Finally, PubMed was searched with simple search strings for veterinary studies regarding acute or uncomplicated allergic reaction and various glucocorticoid terms; all relevant, primary studies including five or more individuals and available in English identified with this method were included, as were any additional relevant references known by the writing group.

The literature search, evidence quality evaluation, and results recording for FA-30 were performed from December 2025 to February 2026. The literature search was performed by first identifying the most recent, comprehensive meta-analysis on the topic through PubMed search with the help of an Information Specialist [33]. A further search was performed using the "Cited by" tool in Scopus to identify relevant primary studies published after this meta-analysis. Also, a PubMed literature search was performed using a search string developed with an Information Specialist. Results of this search were then date-limited to include studies published from the year of the final literature search of the most inclusive meta-analysis (2018) to February 1, 2026. Finally, PubMed was searched with simple search strings for veterinary studies regarding anaphylaxis and various glucocorticoid terms. All relevant, primary studies including five or more individuals and available in English identified with this method were included, as were any additional relevant references known by the writing group.

Further details regarding the search strategies and article selection process for FA-29 and FA-30 are available[2]. Evidence was evaluated for quality using GRADE-based metrics (i.e., risk of bias, indirectness, imprecision, inconsistency). All literature identified by these methods is assigned an additional level of uncertainty since it did not undergo evidence quality evaluation by two independent EEs through the full GRADE process. Study findings were recorded in the Evidence Profile Worksheet, and outcome-pertinent information was recorded in the consensus on science section for that PICO. Any additional methods that varied from the 2024 RECOVER methodology [24] or these modified methods are noted in this publication within the consensus on science for the individual PICO.

2.7 | Generation of Treatment Recommendations

From the EEs' Summary of Findings Table and Evidence Summaries for FA-01, FA-02, FA-12, and FA-13, the FA Domain Chairs or a RECOVER Co-Chair (J.B.) drafted Evidence Profile Worksheets for each PICO question. From the Co-Chair's (J.B.) evidence quality evaluation and the identified studies' qualities and findings for FA-29 and FA-30, that Co-Chair drafted Evidence Profile Worksheets for those two PICO questions. The Evidence Profile Worksheets included a structured summary (introduction, CoSTR, justification for the treatment recommendation(s), and knowledge gaps for future study), and additional notes were

made during the evaluation of individual studies. The resulting Evidence Profile Worksheets for the six PICOs in this subdomain were then reviewed and edited by two Co-Chairs (J.B., D.F.), and then collectively reviewed and edited by the two FA Domain Chairs (D.M., V.T.) and two Co-Chairs (J.B, D.F.).

In accordance with the GRADE system, each treatment recommendation is written either as a *recommendation* where the RECOVER writing group found stronger evidence (or perceived risk/benefit relationship, where evidence was poor or not available) or as a *suggestion* where the writing group found weaker evidence (or perception of risk/benefit relationship, where evidence was not available) for or against the intervention. From the six PICO questions, the writing group proposed a total of 11 treatment recommendations.

2.8 | Consensus Process

Drafted versions of 11 First Aid: Acute Allergy and Anaphylaxis treatment recommendations and the RECOVER First Aid Acute Hypersensitivity Reaction Algorithm were made accessible[3] to the EEs, subject matter experts, and the international veterinary community at large for a 4-week commenting period from March to April 2026. The RECOVER Initiative directly contacted emergency and critical care specialty groups and general veterinary societies worldwide to invite comments. After the 4-week comment period closed, comments were considered by the Co-Chairs and Domain Chairs, and relevant treatment recommendations were refined to create 12 finalized treatment recommendations for uncomplicated allergic reactions and anaphylaxis in dogs and cats. These finalized treatment recommendations appear in this publication along with background information, consensus on science, justifications of the treatment recommendations, and key knowledge gaps for each PICO. Clinical guidelines based on these treatment recommendations are also included in this publication.

3 | Results—Consensus on Science and Treatment Recommendations

Table 2 contains a concise summary of the 12 treatment recommendations derived from the GRADE evidence evaluation of RECOVER's six PICO questions on acute hypersensitivity reactions in dogs and cats.

3.1 | Prehospital Antihistamines for Uncomplicated Allergic Reaction (FA-12)

In cats and dogs in the prehospital setting with acute allergic reactions not affecting breathing (P), does oral antihistamine administration (I), compared to no oral antihistamine administration (C), result in improved outcome (O)?

3.1.1 | Introduction

Allergic reactions resulting in urticaria and facial edema (uncomplicated allergic reactions) are a common emergency and presenting complaint in dogs and are rarely seen in cats. Uncomplicated allergic reactions may progress to multisystemic reactions (anaphylaxis), which can include moderate signs such as repeated vomiting and diarrhea, or life-threatening conditions such as bronchoconstriction with respiratory distress or cardiovascular collapse. Histamine-1 receptor (H1R) antagonists such as diphenhydramine and cetirizine are commonly recommended in people and small animals to treat uncomplicated allergic reactions [3, 5, 34, 35]; however, it is unclear whether H1R antagonists are effective in uncomplicated allergic reactions in dogs and cats, or if their administration can help prevent progression to anaphylaxis in these species. This PICO question was designed to investigate whether the prehospital treatment of cats and dogs experiencing uncomplicated allergic reactions with oral antihistamine leads to improved outcomes.

3.1.2 | Consensus on Science

3.1.2.1 | Outcome 1: Survival to Discharge. For the most critical outcome of survival to discharge, we identified one observational study (OS) (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) and two experimental studies (ESs) (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question; all studies were identified in the search for FA-13 [7, 36, 37]. Smith et al. performed a retrospective OS of 67 dogs with severe anaphylaxis seen at a single university veterinary hospital between 2016 and 2018. This study found that the in-hospital use of diphenhydramine in dogs with severe anaphylaxis did not affect survival, though mortality was low (10/67; 15%), nonsurvival cases included euthanized dogs, and the study was small [7]. An ES by Campbell et al. found that diphenhydramine pretreatment did not improve survival in rabbit or guinea pig models of anaphylaxis [36]. Using a guinea pig model of anaphylaxis, Felix et al. similarly found that while pretreatment with an H1R antagonist delayed death from anaphylaxis in antigen-exposed guinea pigs, it did not improve survival in this setting and species [37].

3.1.2.2 | Outcome 2: Severity of Clinical Signs. For the critical outcome of severity of clinical signs, we identified one CT (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision), two OSs (low quality of evidence, downgraded for serious indirectness and upgraded for large effect), and four ESs (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, imprecision, and inconsistency) that addressed the PICO question [37–43]. Runge et al. performed a small randomized, double-blinded clinical trial in 39 people comparing the impact of IV diphenhydramine (14 people), IV cimetidine (12), or IV diphenhydramine plus IV cimetidine (13) on acute allergic severity using a standardized visual analog scale [38]. This trial found that diphenhydramine with placebo led to more improvement in pruritus (35 patients) than cimetidine with placebo ($p = 0.03$); combination therapy did not differ from either single therapy for treatment of pruritus. Of the 33 people with urticaria, 5 of 11 (46%) receiving diphenhydramine plus placebo had clinically significant relief compared with 8 of 10 (80%) receiving cimetidine plus placebo ($p = 0.18$). Eleven of 12 patients (92%) receiving diphenhydramine plus cimetidine

TABLE 2 | RECOVER 2026 First Aid treatment recommendations for uncomplicated allergic reaction and anaphylaxis in dogs and cats.

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
Uncomplicated allergic reaction: Prehospital administration of antihistamines			
We recommend administering an oral H1 receptor antagonist in the prehospital setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing).	Strong	Low	FA-12
We recommend against administering an oral H1 receptor antagonist in the prehospital setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing) when risk to the rescuer is high.	Strong	Expert opinion	FA-12
Uncomplicated allergic reaction: In-hospital administration of antihistamines			
We recommend administering an H1 receptor antagonist in the practice setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing).	Strong	Low	FA-12
Uncomplicated allergic reaction: Administration of glucocorticoids			
In cats and dogs in the prehospital setting with uncomplicated allergic reaction, we suggest against the routine use of glucocorticoids.	Weak	Very low	FA-29
In cats and dogs with uncomplicated allergic reactions that fail to respond to H1 receptor antagonists, we suggest adding a short course of low-dose glucocorticoids (i.e., ≤0.5 mg/kg/day of prednisolone equivalent for ≤5 days) while continuing H1 receptor treatment.	Weak	Expert opinion	FA-29
Anaphylaxis: Prehospital administration of IM epinephrine			
We suggest prehospital administration of IM epinephrine for dogs and cats experiencing anaphylaxis, provided it does not delay transport to a veterinary clinic for definitive care.	Weak	Very low	FA-01
We suggest the dispensation of epinephrine prefilled syringes dosed to patient body weight with instructions for home use to the owners of dogs and cats that have experienced a prior anaphylactic event.	Weak	Expert opinion	FA-01
We recommend against prehospital administration of IM epinephrine to dogs and cats if risk to the rescuer is perceived to be high (strong recommendation, expert opinion).	Strong	Expert opinion	FA-01
Anaphylaxis: In-hospital administration of epinephrine			
In dogs and cats experiencing anaphylaxis without hypotension (moderate anaphylaxis) in the hospital setting, we suggest that epinephrine be administered as early as possible by the IM route.	Weak	Very low	FA-02
In dogs and cats in the hospital experiencing anaphylaxis with hypotension (severe anaphylaxis), we suggest epinephrine given by continuous IV infusion targeting a MAP of 70 mm Hg rather than by IV bolus dosing.	Weak	Very low	FA-02
Anaphylaxis: Prehospital administration of antihistamines			
In dogs and cats in the prehospital setting with acute allergic reactions affecting breathing, we suggest against oral administration of antihistamines.	Weak	Expert opinion	FA-13
Anaphylaxis: In-hospital administration of glucocorticoids			
In cats and dogs experiencing anaphylaxis in the hospital, we recommend against routine administration of systemic glucocorticoids.	Strong	Very low	FA-30

Abbreviations: FA, First Aid [domain]; H1, histamine-1; PICO, population-intervention-comparator-outcome.

had relief, which performed better than diphenhydramine plus placebo ($p = 0.027$) [38].

Two large, retrospective OSs in people were identified in the search. Kawano et al. compared emergency medical services or emergency department (ED) practitioner-administered H1R antagonist influence on the incidence of anaphylaxis in 2376 adults presenting to the ED for simple allergic reactions (i.e., not experiencing anaphylaxis at ED presentation). This study found that of the 1880 people managed with an H1R antagonist, 36 of 1880 (1.9%) developed anaphylaxis, compared with 17 of 496 (3.4%) in the non-H1R antagonist-treated group (adjusted odds ratio [aOR] 0.34, 95% confidence interval [CI] 0.17–0.70); thus, adult people experiencing simple allergic reactions were less likely to progress to anaphylaxis if treated with an H1R antagonist. Gabrielli et al. performed a retrospective observational, registry-based study including 3498 adult and pediatric (80.3%) cases of anaphylaxis presenting to the ED [40]. Among other analyses, this study evaluated associations between prehospital treatment with antihistamine and "uncontrolled reaction," defined as the need for two or more doses of epinephrine in the ED, and found that prehospital treatment with antihistamine decreased the likelihood of receiving multiple doses of epinephrine in the ED (aOR 0.61, 95% CI 0.44–0.85). However, prehospital treatment with antihistamine was not associated with IV fluid administration in the ED, suggesting no decrease in need for fluid support [40].

An additional, large, combined retrospective and prospective OS relevant to this outcome was identified in the bridge search and thus is included here, though the study did not undergo full GRADE evaluation [44]. This study of 5364 allergic reactions in 11 EDs across Canada and Israel found that, when adjusting for antigen, pre-existing asthma, and other treatments, patients were less likely to require two or more doses of epinephrine in the ED (i.e., to have an "uncontrolled reaction") if treated prehospital with antihistamines (aOR 0.9786, 95% CI 0.9675–0.9898) [44].

The four experimental studies investigating the PICO question were identified in the literature search for FA-13; the one identified study that included a species of interest (dogs) and H1R antagonist administration is described here [41]. Silverman et al. divided 24 anesthetized dogs into three equal groups and pretreated them with placebo, chlorpheniramine, or chlorpheniramine plus cimetidine before administering histamine. Antihistamine pre-administration prevented the cardiopulmonary signs associated with histamine administration. However, when the same pretreatments were given and followed by pre-sensitized antigen, antihistamine pretreatment did not prevent cardiopulmonary changes of anaphylaxis, and dogs still experienced hypotension, decreased cardiac output, decreased lung compliance, increased pulmonary vascular resistance, and markedly increased airway resistance [41].

3.1.2.3 | Outcome 3: Need for Intervention From a Medical Professional. For the important outcome of need for intervention from a medical professional, we identified no studies that addressed the PICO question.

3.1.2.4 | Outcome 4: Length of Stay. For the important outcome of LOS, we identified one OS (very low quality of evidence, downgraded for serious indirectness) that addressed the PICO question [40]. As detailed above, Gabrielli et al. performed a retrospective observational, registry-based study including 3498 adult and pediatric (80.3%) cases of anaphylaxis presenting to the ED. This study found that prehospital treatment with antihistamine was not associated with admission to the hospital/the ICU [40].

Additionally, the Delli Colli study identified in the bridge search addressed this outcome [44]. This study of 5364 allergic reactions in 11 EDs across Canada and Israel found that, when adjusting for antigen, pre-existing asthma, and other treatments, patients were less likely to require hospital admission for their allergic reaction if they were pretreated with antihistamine (aOR 0.963, 95% CI 0.949–0.977) [44].

3.1.3 | Treatment Recommendations

We recommend administering an oral H1R antagonist in the prehospital setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing) (strong recommendation, low quality of evidence).

We recommend administering an H1R antagonist in the practice setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing) (strong recommendation, low quality of evidence).

We recommend against administering an oral H1R antagonist in the prehospital setting to dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing) when risk to the rescuer is high (strong recommendation, expert opinion).

3.1.4 | Justification of Treatment Recommendations

Although no studies were found directly addressing the PICO in the target species, three large observational studies of acute allergic reactions in people found that H1R antagonist antihistamine decreases the likelihood of progression to anaphylaxis, and one study suggested shorter LOS with prehospital antihistamine [39, 40, 44]. The primary indirectness of these three large studies was a difference in species. The single clinical study in dogs included only 67 animals, appeared to evaluate only diphenhydramine administered in the hospital (rather than prehospital), and included only dogs experiencing severe anaphylaxis [7]; the primary benefit of prehospital/early antihistamine demonstrated by the three large human observational studies was the prevention of acute allergic reaction progressing to anaphylaxis, and such a population would have been excluded from the Smith study.

The single ES investigating the effect of H1R antagonists on dogs with acute allergic reactions included the pretreatment of anesthetized dogs with chlorpheniramine. Chlorpheniramine pretreatment prevented cardiopulmonary collapse when histamine was administered IV but did not prevent severe cardiopulmonary effects of anaphylaxis when antigen was given IV [41]. While the directness of species makes this study attractive, this study was

weighted less heavily than the three large human observational studies based on the latter studies' sizes and the natural and thus clinically relevant antigen exposures. Also, Delli Colli, Kawano, and Gabrielli focus on the ability of early antihistamine during an allergic reaction to prevent "uncontrolled reaction" or severe anaphylaxis [39, 40, 44]. The goal of early antihistamine treatment is not to treat anaphylaxis, as was induced in the experimental models, and which these data suggest antihistamine cannot treat, but rather the goal of early antihistamine is to prevent progression to anaphylaxis.

Given the low risk of harm and potential for benefit, the committee recommends oral H1R antagonist administration in dogs and cats with uncomplicated allergic reactions (acute allergic reactions not affecting breathing) in the prehospital setting. However, these decisions should be made on an individual basis, and people should not risk being bitten while administering an H1R antagonist to animals not amenable to accepting the medication.

The impact of histamine-2 receptor (H2R) antagonists (e.g., cimetidine) on allergic reactions was not well described or evaluated in the studies found here, and so no treatment recommendations were created regarding these medications.

3.1.5 | Knowledge Gaps

There are no clinical studies comparing no treatment to administration of diphenhydramine (or other H1R antagonists) in dogs and cats with uncomplicated allergic reaction. Randomized, placebo-controlled, clinical trials of H1R antagonists in dogs and cats experiencing uncomplicated allergic reactions would be helpful but may be considered unethical; thus, such evidence is likely to come from observational studies. Evaluation of the effectiveness of H1R versus H2R antagonist use or the use of newer generation H1R antagonists (e.g., cetirizine) for treatment of allergic reaction may provide further clinically useful information. There is no information in the veterinary literature as to whether early H1R antagonist administration prevents uncomplicated allergic reaction from progressing to anaphylaxis in dogs and cats. The ideal route for H1R antagonist administration in dogs and cats is likewise unknown.

3.2 | Prehospital Glucocorticoids for Uncomplicated Allergic Reaction (FA-29)

In cats and dogs in the prehospital setting with uncomplicated allergic reaction (P), does routine glucocorticoid administration (I), compared to no glucocorticoid administration (C), affect outcome (O)?

3.2.1 | Introduction

Uncomplicated allergic reactions in dogs (and, when they rarely occur, in cats) generally manifest as acute urticaria, which is a condition characterized by wheals (hives) or angioedema [15, 45]. H1R antagonists such as diphenhydramine and cetirizine are the mainstay of treatment for such reactions (see FA-12); however, glucocorticoids are also commonly given to small animals in cases of uncomplicated allergic reaction [10, 13]. Evidence supporting the use of glucocorticoids in uncomplicated allergic reaction is sparse, and it is unclear whether glucocorticoids have a place in the routine management of uncomplicated allergic reaction in dogs and cats. Of particular concern are common contraindications (e.g., NSAID use, diabetes mellitus) and possible adverse events (e.g., immune compromise, poor wound healing, prothrombotic tendency) associated with even short courses of glucocorticoids such as dexamethasone and prednisolone [46–48]. This PICO question was designed to investigate whether routine administration of glucocorticoids to small animals experiencing an acute allergic reaction affects occurrence of adverse events or improves outcome.

3.2.2 | Consensus on Science

3.2.2.1 | Outcome 1: Harm/Adverse Events. For the most critical outcome of harm/adverse events, we identified five CTs (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and inconsistency), all in people, that addressed the PICO question [49–53]. This literature did not undergo official GRADE evaluation by two independent EEs and so is assigned an extra degree of uncertainty. One of these articles is a letter to the editor, so was not likely peer reviewed [50]. Details of these studies are explained below with Outcome 2, because all were designed to assess the impact of glucocorticoids on improvement in urticaria when administered with various H1R antagonists; in all studies, adverse events were mentioned only briefly and were not outcomes of interest for statistical analysis. The minimal descriptions of adverse events are thus described here; all were considered minor by the respective study authors.

Pollack found no adverse events in any of the 43 adults treated with prednisone or placebo in addition to H1R antagonist [52]. In their study of 109 people with acute urticaria, Zuberbier et al. reported that no patients developed chronic urticaria or adverse effects, whether treated with H1R antagonist alone or in combination with prednisolone [53]. However, Godse et al. reported gastrointestinal side effects in three patients and sedation in two that received glucocorticoid in combination with levocetirizine, and sedation in two patients in the group that received levocetirizine alone [50]. Barniol et al. reported mild adverse events in 6 of 50 (12%) patients in their prednisone group and 7 of 50 (14%) in the placebo group [49]. Finally, Palungwachira et al. reported no adverse effects in the group that received only chlorpheniramine ($n = 24$), while five total patients from the two glucocorticoid groups ($n = 47$ together) had minor adverse events, including transient blurred vision, dry mouth, dyspepsia, dizziness, headache, palpitations, perineal itching, and urinary retention [51].

3.2.2.2 | Outcome 2: Time to Resolution of Urticaria. For the important outcome of time to resolution of urticaria, the literature search identified six CTs (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and inconsistency), all in people and one OS (very low quality of evidence, downgraded for imprecision) that addressed the PICO question [3, 49–54]. This literature did not undergo official GRADE evaluation by two independent EEs and so is assigned

an extra degree of uncertainty. One of these articles is a letter to the editor, so was not likely peer reviewed [50].

All six CTs evaluated an H1R antagonist in combination with glucocorticoid versus an H1R antagonist either alone or in combination with placebo [49–53]. The first study, published in 1995, is a double-blind, randomized, placebo-controlled clinical trial including 43 adults that compared the efficacy of a 4-day course of prednisone versus placebo added to oral hydroxyzine for the management of acute urticaria (wheals) in the ED; patients with angioedema were excluded [52]. Patients graded their pruritus score from 0 (no itch) to 10 (maximal itch) on a visual analog scale; pruritus scores on Days 2 and 5 were the main outcomes, and baseline pruritus scores were equivalent in those receiving prednisone ($n = 24$) and those receiving placebo ($n = 19$). In this study, the prednisone group had better pruritus scores (1.3 ± 1.3 [Day 2] and 0 ± 0 [Day 5] vs. 4.4 ± 2.2 [Day 2] and 1.6 ± 1.0 [Day 5], respectively; each $p < 0.0001$) when controlled for age, sex, and inciting allergen [52].

In a nonblinded, before-and-after clinical trial including 109 people seen by either a hospital's dermatology department or a rural dermatology clinic, Zuberbier et al. compared the effect of oral loratadine alone ($n = 44$) or in combination with oral prednisolone ($n = 65$) on time to remission in acute urticaria [53]. No placebo was used in the loratadine only group. This study found that more people in the prednisolone group (93.8%) achieved remission by 3 days than in the loratadine group (65.9%, $p < 0.001$). However, by 7 days, the loratadine group had achieved >80% remission, and all cases were resolved by 21 days in both groups [53].

In a single-blind, parallel trial, Godse et al. randomized 49 adults with acute urticaria to either oral levocetirizine and oral prednisolone for 5 days or only oral levocetirizine [50]. Urticaria activity score (UAS) was assessed at 0, 2, and 5 days; UAS for both groups was similar at baseline and on Day 2 of treatment ($p = 0.85$). However, on Day 5, UAS was better in the group receiving prednisolone plus levocetirizine than in the group receiving levocetirizine alone ($p = 0.03$) [50].

A randomized CT in 140 adults with acute urticaria compared seven treatment combinations in groups of 20 people each: H1R antagonist (Group A); H2R antagonist (Group B); H1R antagonist + H2R antagonist (Group C); H1R antagonist + H2R antagonist + dexamethasone (Group D); H1R antagonist + dexamethasone (Group E); H2R antagonist + dexamethasone (Group F); or Dexamethasone (Group G) alone [54]. Specific H1-antagonist and H2R antagonist were not named. This study did not report baseline severity or a standardized method to grade urticaria severity, nor did it report results of statistical analyses. Patients were monitored for at least 3 h after administration of allocated drug(s). Descriptively, H1-antagonist + H2R antagonist + dexamethasone were "effective" in 95% of patients in resolution of signs and symptoms of acute urticaria; H1R antagonist + dexamethasone "effective" in 90%; and H1-antagonist + H2R antagonist "effective" in 85% [54].

Barniol et al. conducted a double-blind, randomized, placebo-controlled clinical trial of 100 adults to evaluate the efficacy of a 4-day course of levocetirizine plus prednisone versus placebo for the management of acute urticaria in the ED [49]. Pruritus score at Day 2 was the primary outcome. Placebo or prednisone added to levocetirizine was equally effective, with resolution of symptoms within 2 days in most patients. By Day 2, 62% of patients in the prednisone group had a pruritus score of 0 versus 76% of those in the placebo group (difference 14%; 95% CI −31% to 4%). Thirty percent of patients in the prednisone group and 24% in the placebo group reported relapses (difference 6%; 95% CI −23% to 11%) [49].

Palungwachira et al. studied 71 adults presenting to the ED with acute urticaria (wheals only) and a pruritus score of ≥5/10 on a visual analog scale; patients with angioedema were excluded [51]. Patients were randomized into three groups: IV chlorpheniramine plus IV dexamethasone once followed by cetirizine for 7 days; IV chlorpheniramine plus IV dexamethasone once followed by oral cetirizine for 7 days and oral prednisolone for 5 days; or IV chlorpheniramine plus IV placebo once followed by oral cetirizine for 7 days. No oral placebo was provided for patients not randomized to receive oral prednisolone, so the study was not fully placebo controlled or fully blinded. Pruritus scores within 60 min of initial ED treatment were not different among groups ($p = 0.454$). UAS at 1 week was worse in the group receiving oral prednisolone than in the group treated with chlorpheniramine plus dexamethasone followed by oral cetirizine (7/24, 29.2% [95% CI 10.8%–51.3%]). Interestingly, UAS at 1 month was still worse in the group receiving oral prednisolone than in the group treated with chlorpheniramine plus dexamethasone followed by oral cetirizine (6/24, 25% [95% CI 7.4%–47%]). This study's authors concluded that oral prednisolone may prolong the course of acute urticaria [51].

One OS was identified during the literature search for this PICO and another was added based on comments received during the consensus period [3, 35]. A retrospective study of 880 dogs seen for uncomplicated allergic reactions by a referral emergency/critical care service compared outcomes for dogs treated either with IM diphenhydramine alone ($n = 299$) or IM diphenhydramine plus IV dexamethasone sodium phosphate ($n = 581$) [35]. An uncomplicated allergic reaction was defined as acute onset of muzzle or periocular angioedema, urticaria, or generalized erythema with pruritus; dogs with systemic signs were excluded. The study documented immediate response to treatment (i.e., improvement vs. no change/worsening prior to discharge from the visit) and found no difference between the treatment groups ($p = 0.93$). Telephone follow-up reports in 336 dogs at a median of 3 days after the visit revealed no difference between groups in persistence of clinical signs when follow-up contact was made ($p = 0.785$), full resolution of signs at follow-up contact ($p = 0.761$), or having required additional veterinary intervention after discharge ($p = 0.586$) [35]. Finally, a retrospective study included 73 cats with uncomplicated allergic reactions evaluated by the same referral emergency/critical care service and treated either with diphenhydramine alone ($n = 44$) or diphenhydramine plus dexamethasone ($n = 29$) [3]. Uncomplicated allergic reactions were defined in this study as acute onset of muzzle or periocular angioedema, urticaria, generalized erythema with pruritus, or paw swelling without trauma. Cats presenting for anaphylaxis, defined as an acute allergic reaction requiring epinephrine, oxygen supplementation

or IV fluid resuscitation as a part of treatment at initial presentation to treat life-threatening oxygenation, ventilation, or perfusion abnormalities, were excluded. There was no difference in baseline patient demographics (age, sex, weight, breed), the underlying cause of the reaction (when known), or the frequency of specific clinical signs between treatment groups ($p > 0.05$). Diphenhydramine was administered in all 73 cats by the IM route with a median dose of 2.0 mg/kg (range, 0.2–2.8 mg/kg). All 29 cats given adjunct glucocorticoids (i.e., all in addition to diphenhydramine) were given dexamethasone sodium phosphate either IM or IV at a median dose of 0.23 mg/kg (range, 0.06–0.43 mg/kg); none received oral glucocorticoids. During the visit, improvement was noted in 68 of 73 (93%) cats: 41 of 44 (93%) in the diphenhydramine-only group and 27 of 29 (93%) in the diphenhydramine–glucocorticoid group ($p > 0.05$), and no cases progressed to anaphylaxis. There was no difference in additional treatments given ($p = 0.63$) or discharge medications ($p = 0.11$) between the two groups. Follow-up information collected 2–3 days after the visit was available for 40 cats, 21 in the diphenhydramine group and 19 in the diphenhydramine–glucocorticoid group; all 40 cats were alive at follow-up. Signs persisted in 8 of 40 (20%) cats—3 of 21 (14%) in the diphenhydramine group and 5 of 19 (26%) in the diphenhydramine–glucocorticoid group ($p = 0.331$). Five cats required additional treatment after the initial visit, two from the diphenhydramine group and three from the diphenhydramine–glucocorticoid group ($p = 0.272$). This small veterinary study found no difference in clinical course between cats treated with dexamethasone versus those treated only with diphenhydramine for uncomplicated allergic reaction [3].

3.2.3 | Treatment Recommendations

In cats and dogs in the prehospital setting with uncomplicated allergic reaction, we suggest against the routine use of glucocorticoids (weak recommendation, very low quality of evidence).

In cats and dogs with uncomplicated allergic reaction that fail to respond to H1R antagonists, we suggest adding a short course of low-dose glucocorticoids (i.e., ≤0.5 mg/kg/day of prednisolone equivalent for ≤5 days) while continuing H1R treatment (weak recommendation, expert opinion).

3.2.4 | Justification of Treatment Recommendations

There is little human, and nearly no veterinary, evidence regarding the use of glucocorticoids to treat uncomplicated allergic reaction, and what evidence exists is inconsistent. While some studies show more rapid resolution of urticaria when glucocorticoid is used in conjunction with an H1R antagonist [50, 52, 53], other studies (including the two veterinary studies) found no difference with addition of a glucocorticoid [3, 35, 49], and one study reported a worse clinical response with glucocorticoid than with H1R antagonist alone [51]. While adverse event occurrence associated with glucocorticoid use in acute urticaria was not the primary objective of any identified study, no clear increased risk was found with short-course, low-dose glucocorticoids in these investigations. Finally, no analytical studies evaluated the effect of glucocorticoid as the sole treatment for acute urticaria, and histamine receptor antagonists (particularly H1R antagonists) remain the mainstay of therapy (see FA-12).

Considering the inconsistent findings from the limited available literature, the potential for adverse effects with each added medication, and the relatively low morbidity associated with acute urticaria, the committee chose to suggest against the routine use of glucocorticoids in the prehospital setting in dogs and cats with uncomplicated allergic reaction. However, in cases that fail to respond to treatment with H1R antagonist alone, it is reasonable to add a short course of low-dose glucocorticoid to the treatment regimen, while continuing the H1R antagonist; this suggestion is aligned with the human guidelines on treatment of H1R antagonist-nonresponsive, acute urticaria [45].

Interestingly, human guidelines recommend increasing the dose of H1R antagonist up to fourfold (e.g., up to 40 mg daily of cetirizine for an adult) before adding a glucocorticoid, which likely reflects the combination of equipoise regarding the efficacy of glucocorticoids in acute urticaria and their potential for adverse effects. At time of writing, a clinical trial including 240 people with acute urticaria comparing the use of prednisone versus placebo in addition to H1R antagonist (levocetirizine) recently concluded recruitment; the results of this larger study may lead to changes in human treatment recommendations [55].

3.2.5 | Knowledge Gaps

There is relatively little information in dogs and cats regarding the effect of adding a short-course of low-dose glucocorticoid to H1R antagonist for the prehospital or hospital treatment of acute urticaria, particularly as pertains to treatment of persistent urticaria following initial management with an H1R antagonist alone.

3.3 | Prehospital IM Epinephrine for Anaphylaxis (FA-01)

In cats and dogs in the prehospital setting experiencing anaphylaxis (P), does administration of IM epinephrine (I), compared to no epinephrine (C), result in improved outcome (O)?

3.3.1 | Introduction

Anaphylaxis is a severe and potentially life-threatening hypersensitivity reaction that may include collapse, circulatory shock, respiratory distress, gastrointestinal distress, and cutaneous signs like urticaria and flushing. Early IM epinephrine is considered a first-line treatment for people with anaphylaxis [18, 56–59]; however, evidence-based guidelines for the treatment of anaphylaxis in dogs and cats are lacking. We therefore investigated whether administration of IM epinephrine in the prehospital setting for dogs and cats experiencing anaphylaxis may be associated with improved outcomes.

3.3.2 | Consensus on Science

3.3.2.1 | Outcome 1: Survival to Discharge. For the most critical outcome of survival to discharge, we identified four OSs (very low quality of evidence, downgraded for serious risk of

bias and very serious indirectness) that reported the impact of earlier (pre-arrest) epinephrine administration on the likelihood of survival [60–63]. Xu et al. retrospectively reviewed coroners' reports from Ontario, Canada, from 1986 to 2011 and found that of the 92 human deaths attributed to anaphylaxis during that period, only 21 (23%) received epinephrine prior to cardiopulmonary arrest (CPA). Investigators determined that lack of pre-CPA epinephrine administration was associated with worse survival using grounded theory methodology [60]. Three other retrospective studies were found, all similar to one another. Ko et al. studied 340 adults with anaphylaxis who presented to the ED hemodynamically stable, 106 (31%) of whom were treated with epinephrine; Kondo et al. studied 68 adults, 48 (71%) of whom received prehospital epinephrine on scene or during helicopter transport; and finally, Russell et al. studied 124 children, 29 (23%) of whom received prehospital epinephrine and 69 (56%) of whom received it either prehospital or in the ED [61–63]. In all three of these studies, every patient survived whether treated with epinephrine or not. These three studies are all plagued by confounding by indication due to their observational nature. Epinephrine was likely correctly administered to patients who needed it—epinephrine recipients were likely sicker at baseline, though this was not specified in the studies. Despite this likelihood, all people survived, whether they did or did not receive epinephrine. The results of the Xu paper suggest that many of them may have died were they not given epinephrine [60]. The bridge search identified no additional observational studies, and neither the initial nor the bridge search found any CTs or ESs that addressed the PICO question. Nearly all identified studies for this PICO (for all outcomes) reported nearly or exactly 100% survival, which compromises the ability to assess the impact of any treatment on this outcome.

3.3.2.2 | Outcome 2: Incidence of CPA. For the critical outcome of incidence of CPA, we identified four OSs (very low quality of evidence, downgraded for serious indirectness and imprecision) that addressed the PICO question [60–62, 64]. As noted for Outcome 1, Xu et al. found that of 92 human deaths attributed to anaphylaxis, lack of epinephrine administration prior to CPA was associated with worse survival [60]. In the Kondo et al. study, also detailed for Outcome 1, one person experienced CPA prior to helicopter arrival, and no epinephrine had been administered prior to the CPA; all 68 people who were alive when the helicopter arrived survived, whether treated with epinephrine (48; 71%) or not (20; 29%) [61]. Similarly, a study of 27 people of all ages by Søreide et al. found that the only two people who died had experienced CPA in the field before arrival of first responders, and neither had received epinephrine [64]. Finally, as mentioned in Outcome 1, Russell et al. described 124 pediatric patients with anaphylaxis, of whom only 29 (23%) received IM epinephrine in the prehospital setting; all 124 children survived [62].

As for Outcome 1, this outcome was difficult to study because so few people died, whether they received epinephrine or not; however, the fact that the majority of people experiencing CPA due to anaphylaxis did not receive pre-CPA epinephrine while most reported patients who received epinephrine survived is consistent with a survival benefit of earlier use of epinephrine in anaphylaxis. The bridge search identified no additional observational studies, and neither the initial nor the bridge search found any clinical trials or experimental studies that addressed the PICO question.

3.3.2.3 | Outcome 3: Length of Stay. For the important outcome LOS, in the initial search we identified four OSs, all retrospective studies of human anaphylaxis (very low quality of evidence, downgraded for very serious indirectness and inconsistency, and upgraded for effect found despite confounding) that addressed the PICO question [40, 63, 65, 66]. Fleming et al. studied 384 children presenting to the ED for anaphylaxis associated with food allergy, 234 of whom had received epinephrine. Investigators found that prehospital epinephrine administration (prehospital in 164/234 [70%] epinephrine recipients) was associated with a shorter stay in the ED ($p = 0.003$) and reduced risk of hospital admission (aOR 0.25, 95% CI 0.10–0.62, $p = 0.003$), compared to children who received their first dose of epinephrine after arrival to the ED [66]. A study by Huang et al. of 213 pediatric visits in the ED for anaphylaxis found that epinephrine was administered in 169 of 213 (79%) cases [65]. In 58 (27%) cases, epinephrine was given in the prehospital setting, while 111 (52%) children received epinephrine only once presented to the ED. In this study, only 25% of children who required two doses of epinephrine and who received both doses before presentation required hospitalization, whereas 89% of kids who received their second or both epinephrine doses in the ED required hospitalization ($p = 0.05$) [65]. Ko et al. studied 340 adults with anaphylaxis who presented to the ED hemodynamically stable and found that epinephrine administration in these patients was associated with decreased risk for developing hypotension (odds ratio [OR] 0.254, 95% CI 0.091–0.706, $p = 0.009$); however, the timing of epinephrine administration (prehospital vs. in ED) was not discussed [63]. In this study, patients who developed hypotension (i.e., were less likely to have received epinephrine) had both a longer ED stay ($p < 0.001$) and an increased chance of admission to the hospital ($p = 0.001$) [63]. Gabrielli et al. studied 3498 cases of anaphylaxis (80% in children), 1070 (31%) of whom received prehospital epinephrine [40]. This study found no difference in hospitalization when epinephrine was administered in the prehospital setting, although prehospital epinephrine was associated with a reduced need for multiple doses of epinephrine in the ED (aOR 0.22, 95% CI 0.13–0.387, $p < 0.05$). Degree of severity of anaphylaxis varied in this study from mild to severe. Indeed, confounding by severity of illness was a frequent limitation among these studies, and the fact that some studies found an association between earlier epinephrine administration and shorter LOS may strengthen the case for prehospital epinephrine, given such confounding by illness severity would have made it less likely to find a treatment effect.

In the bridge search (July 27, 2025, detailed above), five additional, larger OSs of human anaphylaxis were identified [44, 67–70]. In aggregate, these studies included over 11,000 people, many of whom were children. Three of these studies found decreased LOS in cases that received epinephrine prior to ED presentation [44, 68, 69]. Perlman et al. studied 1127 children with food-associated anaphylaxis who were all treated with epinephrine prior to ED presentation and found that 209 of 1127 (18.5%) required an additional dose of epinephrine in the ED and ultimately only 30 of 1127 (2.7%) required hospitalization [70]. The study's authors attributed the low hospitalization to prehospital epinephrine administration. One investigation did not find a treatment effect

of receiving prehospital epinephrine [67]. This study of 3423 children in Japan showed no difference in hospital admission when epinephrine was used prior to ED presentation. However, prehospital epi use was uncommon in this group (225/3423 [6.6%] cases), which may have limited the ability to demonstrate a difference (Type II error) despite the relatively large total population studied [67].

3.3.2.4 | Outcome 4: Harm to Rescuer. For the important outcome of harm to rescuer, no studies were identified that addressed the PICO question. However, in the July 2025 bridge search, a meta-analysis was identified that included information regarding injury from prehospital epinephrine injection [71]. The study's focus was a user's ability to use a newer epinephrine autoinjector compared to their ability to use an older model. Report of adverse events was limited to accidental digital injection. Seven trials consisting of 1359 patients were analyzed. The only adverse event investigated was digital injection, which was significantly worse with the older model epinephrine autoinjector. Generally, people were able to successfully administer epinephrine with older and newer autoinjector types [71]. Two additional articles were found in the reference list of this meta-analysis, and those studies were also reviewed [72, 73]. Simons et al. investigated unintentional injection with epinephrine autoinjectors and found 69 reported cases of accidental epinephrine autoinjection over the prior 20 years. Most unintentional injections were to a finger or thumb; ~65% of injured people sought treatment at an ED, and treatments included warming, nitroglycerin paste, local injections of phentolamine or lidocaine, other treatments, or benign neglect. No permanent sequelae were reported [73]. The same group investigated United States Poison Control Center reports of unintentional epinephrine autoinjection from 1994 to 2007 and found a total of 15,190 reports of unintentional epinephrine injection [72]. When the situation was known, the person was attempting to inject themselves or another individual in 40% of unintentional injections. Injury severity was classified as none, minor, or "minimal"/not followed in 11,437 of 15,190 (75%) cases, while injury severity was considered "Major" in 27 of 15,190 (0.2%) cases. Management of these unintentional injections was reported in 4101 cases and included observation with no treatment in 53% of cases, treatment in 29%, and no observation or treatment in the remainder. Permanent sequelae were considered "rare" [72]. No studies were identified that investigated the risk to clients of administering injections to their pets outside the veterinary setting.

3.3.3 | Treatment Recommendations

We suggest prehospital administration of IM epinephrine for dogs and cats experiencing anaphylaxis, provided it does not delay transport to a veterinary clinic for definitive care (weak recommendation, very low quality of evidence).

We recommend against prehospital administration of IM epinephrine to dogs and cats if risk to the rescuer is perceived to be high (strong recommendation, expert opinion).

We suggest the dispensation of epinephrine prefilled syringes dosed to patient body weight with instructions for home use to the owners of dogs and cats that have experienced a prior anaphylactic event (weak recommendation, expert opinion).

3.3.4 | Justification of Treatment Recommendations

All studies identified for this PICO question were observational and all were in people. Most evidence surrounded the impact of earlier epinephrine administration on the important outcome of LOS in anaphylaxis. The majority of studies found that earlier epinephrine administration, particularly in the prehospital setting, reduced LOS or need for hospitalization; this finding is considered particularly persuasive in support of prehospital epinephrine, considering the sickest cases are probably more likely to receive prehospital epinephrine, which means a positive treatment effect was often found despite the population likely being sicker. Due to the prehospital nature of such cases, true baseline comparisons were not available in most studies, but common sense suggests that sicker patients would be more likely to receive this more aggressive prehospital treatment. Few studies found no effect of prehospital epinephrine on LOS, and it is possible that such neutral findings were attributable to this very effect: that the patients that received prehospital epinephrine were sicker at baseline and thus more likely to require hospitalization in the first place. Thus, the committee finds that the evidence supports prehospital administration of epinephrine to dogs and cats experiencing anaphylactic reactions prior to presentation to a veterinary hospital.

Very few studies were available regarding the impact of prehospital epinephrine on the most critical outcomes of survival or evolution of CPA during anaphylaxis, likely because the importance of early epinephrine to prevent death from anaphylaxis is well established in people. However, the single study that analyzed the impact of epinephrine on death found that lack of prehospital epinephrine was associated with mortality in people [60]. This finding also supports the prehospital administration of epinephrine to dogs and cats experiencing anaphylaxis. None of the studies evaluated called for a reconsideration of epinephrine in the treatment of anaphylaxis.

Limited evidence was found regarding the important outcome of harm to the rescuer as they attempt to administer epinephrine in the prehospital setting. The only adverse events reported involved unintentional injection of epinephrine either during an attempt to self-inject or during an attempt to inject another person, and the vast majority of these unintentional injections were into people's digits. Serious adverse events were rare (~0.2%) [72]. All three papers found in the bridge search regarding harm associated with epinephrine autoinjectors mentioned that many autoinjector models are challenging to use, though the most recent study mentions that newer models are easier to use and that fewer unintentional injections occur with the modern design [71]. No evidence was found regarding potential harm to people attempting to administer injections to their dogs or cats in the prehospital setting, and the real risk of serious bite and scratch injury to people must be considered in veterinary cases.

During the consensus process, concern was raised about the potential for patient harm associated with IM epinephrine

injection in the prehospital setting. There is a large body of literature that supports the safety and efficacy of IM epinephrine in people in the prehospital setting [40, 60, 63, 65, 66], but the writing group acknowledges the difference in species may be meaningful; treatment recommendations here are "weak" or conditional recommendations, and veterinarians should tailor advice to the individual patient. Additionally, harm from IM epinephrine injection in people has largely been attributed to autoinjector errors as mentioned above [72] or has been found in people who are significantly older, had comorbidities such as chronic systemic hypertension, received multiple doses of IM epinephrine, or received IV epinephrine in addition to IM [74]. We therefore suggest prehospital IM epinephrine for anaphylaxis in dogs and cats, provided it does not delay transport to a veterinary clinic for definitive care.

It seems reasonable to suggest the use of prehospital epinephrine to clients who own a dog or cat with established anaphylactic reactions, if the client receives adequate instruction and feels comfortable attempting to inject their pet if it experiences an allergen exposure and develops clinical signs consistent with early anaphylaxis outside the hospital. Options for prehospital epinephrine preparations include autoinjector, prefilled syringe, or rubber-stopper vial with accompanying small-volume syringe; any of these preparations would be adequate. Studies have shown that in-date epinephrine at clinically relevant concentrations (0.1–1 mg/mL) that is drawn aseptically into plastic syringes that are recapped, kept at room temperature, and protected from light is likely to remain stable and sterile for up to 90 days [75]. Since common pediatric autoinjectors contain 0.15 mg epinephrine, the appropriate dose for a 15-kg animal (0.01 mg/kg), prefilled syringes may be desirable for smaller pets. On the other hand, giant breed dogs may require multiple doses from standard autoinjectors (0.3 mg epinephrine) to reach therapeutic dose, which may be cost prohibitive for some clients considering the shelf life of autoinjectors and how infrequently they are likely to be used.

3.3.5 | Knowledge Gaps

There is no literature regarding the role of prehospital epinephrine in dogs or cats with anaphylactic reactions, and such information is needed.

The ideal method to ensure optimal prehospital administration of epinephrine during an anaphylactic reaction in a dog or cat has not been determined (e.g., epinephrine autoinjector vs. prefilled syringe vs. rubber-stopper vials of epinephrine and instructions for use; requirement for IM dosing vs. SC; ideal location for injection considering efficacy and owner safety).

3.4 | Prehospital Antihistamines for Acute Allergic Reaction Affecting Breathing (FA-13)

In cats and dogs in the prehospital setting with acute allergic reactions affecting breathing (P), does oral antihistamine administration (I), compared to no oral antihistamine administration (C), result in improved outcome (O)?

3.4.1 | Introduction

Allergic reactions can be life-threatening reactions (anaphylaxis) that include problems such as bronchoconstriction with respiratory distress or cardiovascular collapse. H1R antagonists such as diphenhydramine are commonly recommended in people and dogs to treat uncomplicated allergic reactions [3, 5, 34, 35]; however, it is unclear whether H1R antagonists are effective at treating anaphylaxis involving respiratory difficulty, or if their administration can help prevent evolution of severe anaphylaxis in small animals. This PICO question was designed to help determine whether the prehospital treatment of cats and dogs experiencing acute allergic reactions impairing breathing with oral antihistamine would improve outcome.

3.4.2 | Consensus on Science

3.4.2.1 | Outcomes 1 and 2: Survival to Discharge and Incidence of CPA. For the most critical outcomes of survival to discharge and incidence of CPA, we identified one OS (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) and two ESs (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question [7, 36, 37]. Smith et al. performed a retrospective OS of 67 dogs with severe anaphylaxis seen at a single university veterinary hospital between 2016 and 2018. This study found that the in-hospital use of diphenhydramine in dogs with severe anaphylaxis did not affect survival, though mortality was low (10/67; 15%), nonsurvival cases included euthanized dogs, and the study was small [7]. An ES by Campbell et al. found that diphenhydramine pretreatment did not improve survival/prevent CPA in rabbit or guinea pig models of anaphylaxis [36]. Using a guinea pig model of anaphylaxis, Felix et al. similarly found that while pretreatment with an H1R antagonist delayed CPA from anaphylaxis in antigen-exposed guinea pigs, it did not improve survival in this setting and species [37].

3.4.2.2 | Outcome 3: Severity of Clinical Signs. For the critical outcome of severity of clinical signs, we identified one CT (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision), two OSs (low quality of evidence, downgraded for serious indirectness and upgraded for large effect), and four ESs (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, imprecision, and inconsistency) that addressed the PICO question [37–43]. Runge et al. performed a small randomized, double-blinded clinical trial in 39 people comparing the impact of placebo plus IV diphenhydramine (14 people), placebo plus IV cimetidine (12), or IV diphenhydramine plus IV cimetidine (13) on acute allergic severity using a standardized visual analog scale [38]. This trial found that diphenhydramine with placebo led to more improvement in pruritus (35 patients) than cimetidine with placebo ($p = 0.03$); combination therapy did not differ from either single therapy for treatment of pruritus. Of the 33 people with urticaria, 5 of 11 (46%) receiving diphenhydramine plus placebo had clinically significant relief compared with 8 of 10 (80%) receiving cimetidine plus placebo ($p = 0.18$). Eleven of 12 patients (92%) receiving diphenhydramine plus cimetidine

had relief, which performed better than diphenhydramine plus placebo ($p = 0.027$) [38].

Two large, retrospective OSs in people were identified in the search. Kawano et al. compared practitioner-administered (emergency medical services or ED) H1R antagonist influence on the incidence of anaphylaxis in 2376 adults presenting to the ED for uncomplicated allergic reactions (i.e., not experiencing anaphylaxis at ED presentation). This study found that of the 1880 people managed with an H1R antagonist, 36 of 1880 (1.9%) developed anaphylaxis, compared to 17 of 496 (3.4%) in the non-H1R antagonist-treated group (aOR 0.34, 95% CI 0.17–0.70); thus, adult people experiencing uncomplicated allergic reactions were less likely to progress to anaphylaxis if treated with an H1R antagonist [39]. Gabrielli et al. performed a retrospective observational, registry-based study including 3498 adult and pediatric (80.3%) cases of anaphylaxis presenting to the ED [40]. Among other analyses, this study evaluated associations between prehospital treatment with antihistamine and "uncontrolled reaction," defined as the need for two or more doses of epinephrine in the ED, and found that prehospital treatment with antihistamine decreased the likelihood of receiving multiple doses of epinephrine in the ED (aOR 0.61, 95% CI 0.44–0.85). However, prehospital treatment with antihistamine was not associated with IV fluid administration in the ED, suggesting no decrease in need for fluid support [40].

An additional, large, combined retrospective and prospective OS relevant to this outcome was identified in the bridge search and thus is included here, though the study did not undergo full GRADE evaluation [44]. This study of 5364 allergic reactions in 11 EDs across Canada and Israel found that, when adjusting for antigen, pre-existing asthma, and other treatments, patients were less likely to require two or more doses of epinephrine in the ED (i.e., to have an "uncontrolled reaction") if treated prehospital with antihistamines (aOR 0.9786, 95% CI 0.9675–0.9898) [44].

Four experimental studies were identified; the one identified study that included a species of interest (dogs) and H1R antagonist administration is described here [41]. Silverman et al. divided 24 anesthetized dogs into three equal groups and pretreated them with placebo, chlorpheniramine, or chlorpheniramine plus cimetidine before administering histamine. Antihistamine pre-administration prevented the cardiopulmonary signs associated with histamine administration. However, when the same pre-treatments were given and followed by pre-sensitized antigen, antihistamine pretreatment did not prevent cardiopulmonary changes of anaphylaxis, and dogs still experienced hypotension, decreased cardiac output, decreased lung compliance, increased pulmonary vascular resistance, and markedly increased airway resistance [41].

3.4.2.3 | Outcome 4: Length of Stay. For the important outcome of need for intervention from a medical professional, we identified one OS (very low quality of evidence, downgraded for serious indirectness) that addressed the PICO question [40]. As detailed above, Gabrielli et al. performed a retrospective observational, registry-based study including 3498 adult and pediatric (80.3%) cases of anaphylaxis presenting to the ED. This study found that prehospital treatment with antihistamine was not associated with admission to the hospital or the ICU [40].

Additionally, the Delli Colli study identified in the bridge search addressed this outcome [44]. This study of 5364 allergic reactions in 11 EDs across Canada and Israel found that, when adjusting for antigen, pre-existing asthma, and other treatments, patients were less likely to require hospital admission for their allergic reaction (aOR 0.963, 95% CI 0.949–0.977) [44].

3.4.3 | Treatment Recommendation

In dogs and cats in the prehospital setting with acute allergic reactions affecting breathing, we suggest against oral administration of antihistamines (weak recommendation, expert opinion).

3.4.4 | Justification of Treatment Recommendation

There is currently insufficient evidence to support the use of oral antihistamines for acute allergic reactions in dogs and cats with respiratory difficulty. An acute allergy including respiratory signs is by definition an anaphylactic reaction, as it includes systemic signs; thus, epinephrine is the treatment of choice, and evidence for H1R antagonists in this setting is lacking. The majority of the evidence originates from experimental studies investigating the effect of parenteral antihistamine pretreatment prior to induced anaphylaxis, thus extrapolation to clinical veterinary medicine is difficult.

Also, from a practical perspective, the committee had concerns that client attempts to administer H1R antagonists to dogs and cats having trouble breathing associated with an acute allergic reaction may (a) delay presentation to a veterinary hospital; (b) delay or replace use of prehospital IM epinephrine (for which there is evidence of benefit during early anaphylaxis in people) [44, 68, 69]; and (c) increase the risk of bite injuries to the caretaker.

3.4.5 | Knowledge Gaps

No current evidence clearly demonstrates a benefit of antihistamine administration in the prehospital setting in cats and dogs suffering breathing difficulties from acute allergic reactions. Experimental data are related to pretreatment (before induction of anaphylaxis by IV antigen administration), and observational data are based on in-hospital population presenting without respiratory signs (i.e., with uncomplicated acute allergic reaction). Randomized, placebo-controlled, clinical trials of H1R antagonists in dogs and cats experiencing allergic reactions with respiratory distress could be helpful.

3.5 | In-Hospital IM Versus IV Epinephrine for Anaphylaxis (FA-02)

In cats and dogs experiencing anaphylaxis in the hospital (P), does administration of IV epinephrine (I), compared to IM epinephrine (C), result in improved outcome (O)?

3.5.1 | Introduction

Anaphylaxis is a severe and potentially life-threatening hypersensitivity reaction that may include collapse, circulatory shock,

respiratory distress, gastrointestinal distress, and cutaneous signs like urticaria, flushing, and angioedema. Epinephrine is considered first-line treatment for people with anaphylaxis [18, 56, 57]; however, evidence-based guidelines for the treatment of anaphylaxis in dogs and cats are lacking. Specifically, the optimal route of epinephrine administration in dogs and cats is unknown. This PICO question was created to investigate whether epinephrine should be given by the IM or the IV route to dogs and cats experiencing anaphylaxis.

3.5.2 | Consensus on Science

3.5.2.1 | Outcome 1: Survival to Discharge. For the most critical outcome of survival to discharge, we identified one OS (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) that addressed the PICO question [76]. In this study of 91 pediatric patients with drug-induced anaphylaxis, 62 (68%) received epinephrine, though only 49 (54%) received it as an initial therapy. Of the 48 early epinephrine cases in which administration route was recorded, 15 (31%) received epinephrine as an IV bolus and six (13%) as a continuous rate infusion (CRI); 11 of 48 (23%) received epinephrine IM. Only 1 of 91 patients died, and so the impact of epinephrine route on survival to discharge could not be determined. However, supratherapeutic epinephrine dosing (administration above recommended dose) was more common in the IV bolus group compared to IM (5/14, OR 19.25, 95% CI 1.77, 209.55, $p = 0.009$) and SC administration groups (4/11, OR 19.80, 95% CI 1.94, 201.63, $p = 0.005$). Overdosing was not associated with severity of presenting signs [76]. No other primary evidence regarding impact of epinephrine route on survival to discharge was identified (including in the bridge search performed September 2025).

3.5.2.2 | Outcome 2: Incidence of CPA. For the critical outcome of incidence of CPA, we identified no studies that addressed the PICO question.

3.5.2.3 | Outcome 3: Severity of Clinical Signs. For the critical outcome of severity of clinical signs, we identified two OSs (very low quality of evidence, downgraded for serious risk of bias and serious indirectness, upgraded for large effect) and two ESs (very low quality of evidence, downgraded for serious risk of bias and imprecision) that addressed the PICO question [20, 22, 77, 78]. A retrospective OS of 301 people presenting to an ED with anaphylaxis found that adverse cardiovascular events were more likely with IV bolus (bolus only) epinephrine administration when compared with IM dosing (OR 8.7, 95% CI 1.8–40.7, $p = 0.006$); similarly, adverse cardiovascular events were more common with epinephrine via the IV route (combining IV bolus and IV CRI) compared with the IM route (9.7% vs. 1.3%; OR 7.5, 95% CI 1.6–35.3, $p = 0.01$) [77]. This same study also found that epinephrine overdose was more likely with IV bolus (bolus only) epinephrine when compared with IM (OR 61.3, 95% CI 7.5 to infinity, $p < 0.001$), and the same held true with epinephrine via the IV route (combining IV bolus and IV CRI) for odds of overdose compared to the IM route (11.8% vs. 0%; OR 53.4, 95% CI 6.5 to infinity, $p < 0.001$) [77]. Indeed, all cases ($n = 4$) of supratherapeutic dosing in this study occurred when epinephrine was given as an IV bolus [77]. Similarly, in a retrospective, registry-based study of 268 human anaphylaxis cases, Cardona et al. found that IV epinephrine was associated with development of more adverse effects (5/9 cases) than IM epinephrine (51/251 cases; $p = 0.035$) and that severe adverse events were noted in 3 of 9 patients treated with IV epinephrine versus only 4 of 256 cases treated with epinephrine by other routes ($p < 0.01$) [78].

Both identified experimental studies were in anesthetized, mechanically ventilated dogs exposed to ragweed antigen and treated with epinephrine by various routes or placebo, only after anaphylactic shock was advanced or "maximal" (i.e., MAP 50% of baseline). Bautista et al. found that an IV epinephrine bolus (0.01 mg/kg IV) caused an immediate increase in MAP, stroke volume, and pulmonary capillary wedge pressure; however, this effect was sustained for less than 15 min, after which time these parameters were similar to the placebo group. Hemodynamic parameters of dogs receiving IM or SC epinephrine once in full anaphylactic shock were no different at any time point than those in dogs receiving placebo [20]. The same investigators using the same canine anaphylactic shock model compared bolus epinephrine (0.01 mg/kg) via the IM, IV, or SC routes to epinephrine given as an IV CRI targeting MAP 70% of baseline (using a previously established placebo group) [22]. In dogs receiving bolus epinephrine only by the IV route, there was a brief increase in MAP at the 5 min time point; all other time points for all bolus routes of administration were equivalent to placebo [22]. In contrast, dogs receiving epinephrine as an IV CRI achieved MAP (to 70% of baseline) (significantly higher than placebo or any bolus route) with lower total epinephrine doses [22].

An additional ES in dogs was provided during the comment period for consensus building [21]. This study, performed by the same group (i.e., Mink, Bautista), used the same ragweed antigen anaphylactic shock protocol in eight sensitized dogs in a crossover design. Similar to the others, this study found that a bolus of epinephrine of either 0.01 or 0.025 mg/kg administered at the time of maximum hypotension following antigen exposure led to only a transient increase in MAP and cardiac output that persisted only 20 min. Left ventricular stroke work was lower in the epinephrine-treated dogs after the initial increase in MAP and cardiac output than in the saline placebo control group [21].

3.5.2.4 | Outcome 4: Length of Stay. For the important outcome of LOS, we identified no studies that addressed the PICO question.

3.5.3 | Treatment Recommendations

In dogs and cats experiencing acute anaphylaxis without hypotension (moderate anaphylaxis) in the hospital setting, we suggest that epinephrine be administered as early as possible by the IM route (weak recommendation, very low quality of evidence).

In dogs and cats in the hospital experiencing anaphylaxis with hypotension (severe anaphylaxis), we suggest epinephrine be given by continuous IV infusion targeting MAP 70 mm Hg rather than by IV bolus dosing (weak recommendation, very low quality of evidence).

3.5.4 | Justification of Treatment Recommendations

The committee's recommendation for early IM epinephrine in canine and feline nonhypotensive (moderate) anaphylaxis is aligned with current human guidelines, in which epinephrine given IM at a dose of ~0.01 mg/kg is considered a first-line treatment for anaphylaxis [18, 56, 57]. Studies in people suggest that early epinephrine decreases morbidity and hospital admissions in human anaphylaxis, and the IM route appears preferable due to its efficacy and favorable safety profile compared to the IV route [44, 63, 66, 68, 69, 77, 78]. Another advantage of the IM route for anaphylaxis without hypotension is that it allows for rapid epinephrine administration without the need for IV access. No studies were available regarding the route of epinephrine in nonhypotensive anaphylaxis in dogs, and no primary literature was identified about epinephrine for anaphylaxis in cats.

Interestingly, data available regarding epinephrine route in dogs experiencing severe anaphylaxis (hypotension, cardiovascular collapse) suggest that epinephrine is not effective via any studied route (IV, IM, SC) when administered by single bolus of 0.01 mg/kg [20–22]. Whether this lack of efficacy is related to dose or timing is unclear, but in these severe cases, epinephrine as an IV CRI appears effective at maintaining MAP, at least in the dog [22]. A recent, double-blind, randomized, crossover ES in healthy human volunteers similarly found that a single dose of epinephrine IM led to a transient increase in MAP during histamine-mediated hypotension in only 5 of 20 participants (25%; 95% CI 8.7%–49.1%) [79]. A second IM epinephrine dose given to subjects with persistent hypotension (MAP $\leq$ 60 mm Hg) despite this single IM epinephrine injection also failed to reverse hypotension. The area under the effect curve for change in MAP was not different between epinephrine versus placebo (7 mm Hg·min, 95% CI −2 to 25, $p = 0.06$) in this study. These findings are similar to those in dogs [20].

Two more recent, retrospective clinical studies of canine anaphylaxis from a single institution shed some light on their in-hospital use of epinephrine in dogs with anaphylaxis, though epinephrine route was not investigated in either study [6, 7]. Smith et al. investigated risk factors for mortality in 67 dogs with severe anaphylaxis [7]. The study reported that some dogs at their institution with severe anaphylaxis received epinephrine either as IM or IV bolus (0.1–0.2 mg/kg) or as an IV bolus (0.1–0.2 mg/kg) followed by IV CRI (0.05–0.1 μg/kg/min); other dogs did not receive epinephrine, though the numbers of dogs that did and did not receive epinephrine (or by which route) are not reported. The study found that epinephrine use did not differ between dogs that survived (57/67 dogs) and those that did not survive (10/67 dogs) [7]. Finally, Kadowaki et al. studied 49 dogs with severe anaphylaxis that did not receive epinephrine within 6 h of onset of clinical signs [6]. Of these 49 dogs, 45 survived (91.8%; two died, two euthanized for severity of illness) despite none of them receiving early epinephrine; all were treated with fluid therapy and other supportive measures, and 9 of 49 (18%) were treated with norepinephrine (and one with late epinephrine) CRI. The institution's protocol for canine anaphylaxis does not include early in-hospital epinephrine, and so only three dogs were excluded for having received it; this mitigates to large extent confounding by indication for epinephrine [6]. This study shows that many dogs can survive severe anaphylaxis with supportive measures such as fluid therapy and, when required, non-epinephrine pressor CRIs; however, survival outcome for the four dogs that died in this study may have been different if early epinephrine had been provided. Overall, the committee suggests that dogs and cats with severe anaphylaxis (anaphylaxis with hypotension) be treated with an epinephrine IV CRI in addition to other supportive measures.

3.5.5 | Knowledge Gaps

Very few studies were identified that addressed this PICO for dogs, and none were identified that involved cats. Prospective randomized CTs comparing routes of epinephrine administration in dogs and cats with early and severe anaphylaxis are needed to determine the optimal route of administration in each situation.

3.6 | In-Hospital Use of Glucocorticoids for Anaphylaxis (FA-30)

In cats and dogs experiencing anaphylaxis in the hospital (P), does administration of systemic glucocorticoids (I), compared to no administration of systemic glucocorticoids (C), result in improved outcome (O)?

3.6.1 | Introduction

Anaphylaxis is a severe and potentially life-threatening hypersensitivity reaction that may include collapse, circulatory shock, respiratory distress, gastrointestinal distress, and cutaneous signs like urticaria and flushing. While early epinephrine is the recommended first-line treatment for anaphylaxis in people [18, 56–59] and dogs and cats [21, 22], the role of glucocorticoids in anaphylaxis is less clear [10, 80]. Glucocorticoids have been used in human and veterinary medicine in an attempt to mitigate the clinical course of or prevent a biphasic reaction in anaphylaxis, though evidence of such treatment effect is lacking [5, 81]. Of concern are common contraindications such as concurrent NSAID use or diabetes mellitus and possible adverse events like immune compromise, poor wound healing, and prothrombotic tendency associated with even short courses of glucocorticoids [46–48]. This PICO question was developed to investigate whether routine administration of glucocorticoids to small animals experiencing anaphylaxis affects survival, severity of clinical signs, or LOS.

3.6.2 | Consensus on Science

3.6.2.1 | Outcome 1: Survival to Discharge. For the most critical outcome of survival to discharge, we identified one OS (very low quality of evidence, downgraded for serious risk of bias and imprecision) that addressed the PICO question [7]. Smith et al. investigated risk factors for mortality in 67 dogs with severe anaphylaxis [7]. Fifty-seven dogs survived and 10 died; four nonsurvivors died and six were euthanized. The study reported that corticosteroid administration did not differ between dogs that survived (57/67 dogs) and those that did not survive (10/67). Direct correspondence with the primary author confirmed that 41 of 67 dogs with anaphylaxis in the study were treated with

corticosteroids: 7 of 10 nonsurvivors and 34 of 57 survivors (Fisher exact OR 0.69, 95% CI 0.17–2.70, $p = 0.73$) [7].

All of the human studies identified included adults or children presented to EDs or hospitalized for treatment of anaphylaxis. None of them included survival as an outcome, and survival from anaphylaxis was 100% or nearly 100% in every identified human study.

3.6.2.2 | Outcome 2: Severity of Clinical Signs. For the important outcome of severity of clinical signs, we used the Shaker et al. 2020 meta-analysis (which includes 26 OSs, overall very low certainty of evidence for recommendation) and thereafter identified one CT (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) and seven additional OSs published after Shaker's analysis (very low quality of evidence, downgraded for serious risk of bias and serious indirectness) that addressed the PICO question [33, 40, 44, 82–87]. The Shaker meta-analysis of 26 human OSs, which included a total of 15,633 patients with anaphylaxis, posed the specific clinical question of whether patients with anaphylaxis should be treated with glucocorticoids to prevent a biphasic anaphylactic reaction (BAR), considered an increase in severity [33]. Using seven of the 26 OSs specifically addressing pediatric anaphylaxis, Shaker found that children with anaphylaxis ($n = 1203$) who experience a BAR ($n = 114$) were more likely to have been treated with glucocorticoids (78/114, 68.4% vs. 632/1089, 58%; OR 1.55, 95% CI 1.01–2.38); however, these findings are likely confounded by indication for the glucocorticoid (i.e., initial severity). When all 26 human OSs were analyzed together, glucocorticoid treatment was not associated with a BAR (OR 0.87, 95% CI 0.74–1.02). Shaker et al. suggest against administering glucocorticoids as an intervention to prevent biphasic anaphylaxis; however, authors cite very low certainty of evidence and acknowledge continued equipoise as of 2020 [33].

The single CT identified in the literature search compared the likelihood of re-visit for anaphylaxis within 7 days in 152 children with anaphylaxis presenting to an ED in Qatar who were randomized either to oral dexamethasone 0.3 mg/kg ($n = 68$ analyzed of 75 initially randomized) or to an identical placebo ($n = 75$ analyzed of 77 initially randomized) [82]. All children were treated upon ED arrival with epinephrine and an H1R antagonist, and were given study medication in the hospital's short-stay unit. Three of 68 (4.4%) children treated with dexamethasone and 5 of 75 (6.7%) treated with placebo sought additional care for anaphylaxis within 7 days ($p = 0.7$) [82].

In the first of the seven OSs, Gabrielli et al. conducted a retrospective study of 3498 Canadian registry cases of adult and pediatric (80.3% of cases) anaphylaxis to assess the impact of prehospital glucocorticoids on the requirement for hospitalization, multiple doses of epinephrine, or IV fluids [40]. In this study, 2% of people with anaphylaxis were treated with corticosteroids prior to hospital arrival; prehospital corticosteroid administration was associated with increased odds of hospital admission (aOR 2.88, 95% CI 1.13–7.36, $p < 0.05$) and had no impact on the need for two or more doses of epinephrine or the need for IV fluids in the ED [40].

Similarly, Okubo et al. performed a retrospective analysis of the impact of glucocorticoids in 6161 children hospitalized for anaphylaxis in a network of >1000 hospitals in Japan between 2010 and 2015 [86]. This study compared the risk of 10-day readmission using two different adjustment models to account for confounders. There was no difference in 10-day readmission when patients received glucocorticoids using either adjustment model (risk ratio 1.13, 95% CI 0.60–2.16, $p = 0.71$; risk difference −0.011 [95% CI −0.026 to 0.004], $p = 0.16$).

A large study out of Japan compared the incidence of BAR in 13,700 propensity score-matched patients hospitalized for anaphylaxis who were treated with glucocorticoids to 3425 patients not treated with glucocorticoids [84]. All patients had received epinephrine in the ED, and those in the glucocorticoid group had also received a glucocorticoid in the ED. There was no difference in the rate of BAR (10.7% in the glucocorticoids group vs. 10.5% in the control group; OR 1.03, 95% CI 0.85–1.24, $p = 0.77$) between patients with anaphylaxis treated with and without glucocorticoids on the day of admission [84].

A retrospective and prospective OS by Delli Colli et al. assessed the impact of prehospital corticosteroid administration on the need for two or more doses of epinephrine in the ED in 5364 anaphylactic reactions in people of all ages between 2011 and 2022 from 10 Canadian and one Israeli ED [44]. This study found that patients treated with prehospital corticosteroids were more likely to require IV fluids in the ED (aOR 1.059, 95% CI 1.013–1.107) and be admitted (aOR 1.232, 95% CI 1.181–1.286) when adjusted for sex, severity of reaction, trigger, other treatments, and history of allergies and asthma [44].

In the largest study on corticosteroids in anaphylaxis to date, Dribin et al. reviewed 42,909 pediatric ED visits for anaphylaxis from 2016 to 2022 across 48 hospitals in the United States [83]. In this investigation, 28,125 (73.8%, IQR 63.9%–81.4%) people received systemic steroids for anaphylaxis with a decreasing trend over the course of the study (−19.6% over study course, IQR −26.3% to −12.4%). In a multivariable model, glucocorticoid administration was found to be associated with the development of a severe reaction (OR, 1.9; IQR, 1.4–2.6); however, severity of the initial reaction was not considered in the model and thus it is possible that steroids were administered more commonly to children with more severe initial clinical signs [83].

Two additional, smaller OSs were found. A retrospective, single-center study of 120 patients ≥16 years old with anaphylaxis admitted to the hospital from the ED from 2008 to 2015 found that ED administration of hydrocortisone or methylprednisolone had no effect on the incidence of BAR [85]. Glucocorticoid was given to 98 of 107 (91.6%) patients with uniphasic reactions and to 13 of 13 (100%) patients with BAR ($p = 0.595$) [85]. Finally, a study of 557 patients with allergy or anaphylaxis in the Netherlands between 2015 and 2019 found that only eight patients experienced a BAR, all of whom had received steroids. No statistical comparisons were made [87].

3.6.2.3 | Outcome 3: Length of Stay. Given that the Shaker et al. meta-analysis used as the anchor paper for this PICO did not evaluate LOS as an outcome, another, slightly older but more general meta-analysis was also used in this literature search

[33, 88]. Liyanage et al. reviewed 30 papers—22 in people and eight experimental animal studies—about the use of glucocorticoids in anaphylaxis, and its newest reference is from 2016. Only one study included in Liyanage investigated corticosteroids and LOS in anaphylaxis, which was Michelson et al. [88, 89]. To ensure literature capture between the end of Liyanage's literature search and our current literature search (date limited January 1, 2018 to February 2, 2026), references from 2015 forward that were included in Shaker et al. 2020 were manually reviewed for information about LOS. One additional study found in Shaker et al. 2020 investigated corticosteroids and reported LOS [90]. Finally, literature from the current search, described above in the Literature Search Methodology, was reviewed, and pertinent studies were included. In all, five OSs (very low quality of evidence, downgraded for serious indirectness) were identified that addressed this outcome [40, 44, 86, 89, 90].

A retrospective, 35-hospital database review of pediatric anaphylaxis in the United States from 2009 to 2013 included 5203 children hospitalized for anaphylaxis [89]. Of the 5203 patients, 424 (8.2%) had prolonged LOS. Glucocorticoid administration was inversely associated with prolonged LOS (aOR 0.61, 95% CI 0.41–0.93) [89]. However, when these cases were combined with discharged children and the other 25 OSs in Shaker's meta-analysis, glucocorticoid administration in pediatrics was found to predispose to the more clinically serious outcome of BAR, as reported above [33].

In a single-center, retrospective study from 2011 to 2013 in the United States, Guiot et al. described care practices in inpatient management and LOS in 287 children treated as inpatients for anaphylaxis [90]. Median LOS in this study was 15 h (IQR, 8 h); corticosteroids were administered in the ED to 60% of patients and to 0 during inpatient hospitalization. There was no comparison of LOS between children who had received corticosteroids in the ED and those who had not [90].

Three OSs that were presented above also included LOS as an outcome. As mentioned above for Outcome 2: Severity of Clinical Signs, Gabrielli et al. found in a retrospective study of 3498 Canadian registry cases of adult and pediatric (80.3% of cases) anaphylaxis that prehospital glucocorticoid administration was associated with increased odds of hospital admission (aOR 2.88, 95% CI 1.13–7.36, $p < 0.05$) [40]. Okubo et al.'s retrospective analysis of the impact of glucocorticoids in 6161 children hospitalized for anaphylaxis in Japan between 2010 and 2015 found that LOS was longer in patients who received glucocorticoids using two different adjustment models to account for confounders [86]. In one model, LOS was found to be longer in the glucocorticoid group by 0.39 days (95% CI 0.29–0.49, $p < 0.001$), and in the other model, LOS difference was found to be 1.01 days for patients receiving glucocorticoids (95% CI 0.83–1.16 days longer, $p < 0.001$) [86]. The retrospective and prospective OS by Delli Colli et al. that assessed the impact of prehospital corticosteroid administration in 5364 anaphylactic reactions in people of all ages found that patients treated with prehospital corticosteroids were more likely to be admitted to the hospital (aOR 1.232, 95% CI 1.181–1.286) when adjusted for sex, severity of reaction, trigger, other treatments, and history of allergies and asthma [44].

3.6.3 | Treatment Recommendation

In cats and dogs experiencing anaphylaxis in the hospital, we recommend against routine administration of systemic glucocorticoids (strong recommendation, very low quality of evidence).

3.6.4 | Justification of Treatment Recommendation

Taken together, the one CT and seven OSs published since Shaker et al.'s meta-analysis included nearly 76,000 patients, approximately five times the number of cases ($n = 15{,}633$) included in the meta-analysis. Shaker et al. suggested against the routine administration of glucocorticoids to people with anaphylaxis. Thereafter, all eight post-Shaker studies found either no association between glucocorticoid administration and severity of clinical signs (often identified as a BAR) or that patients treated with glucocorticoids experienced more severe clinical signs. Even studies that adjusted for baseline patient characteristics, including illness severity, found either no difference in clinical course between patients who did or did not receive glucocorticoids [84, 86] or an association between early glucocorticoid administration and more severe clinical course [40, 44].

Given the consistent evidence of lack of benefit from glucocorticoid administration during anaphylaxis even when adjusted for illness severity [84, 86], and the suggestion that glucocorticoids both in anaphylaxis [40, 44] and in general [47, 48, 91, 92] can cause adverse effects, the committee decided to recommend against their routine use in this setting in dogs and cats. Additionally, there is strong evidence in people that even short courses of glucocorticoids can cause harm, further suggesting that the risk:benefit ratio of glucocorticoids in anaphylaxis is unfavorable [47, 48].

These recommendations are aligned with those in people [33], and evidence is arguably even stronger now than it was at the time of that meta-analysis, given the >75,000 cases represented in the literature between Shaker's publication and the time of this writing. The literature search identified two studies in which investigators reported on campaigns to reduce glucocorticoid use in anaphylaxis with moderate success [93, 94].

3.6.5 | Knowledge Gaps

The effect of glucocorticoid administration on outcomes in small animal anaphylaxis is largely unknown, and observational studies are warranted.

4 | Clinical Guidelines for Management of Uncomplicated Allergic Reaction and Anaphylaxis in Dogs and Cats

Evidence- and consensus-based treatment recommendations for uncomplicated allergic reaction versus anaphylaxis in small animals are different, based on evidence of benefit from H1R antagonists in uncomplicated allergic reaction versus evidence of

benefit from epinephrine in anaphylaxis. Therefore, recognizing these hypersensitivity reactions and distinguishing uncomplicated allergic reactions from anaphylaxis are important for optimizing timely and appropriate management. Therefore, we developed a treatment-based grading system of acute hypersensitivity reactions in dogs and cats (Table 1). This table is intended to provide concise information for the veterinary team to recognize these distinct clinical presentations and consider administration of the drug (and route) with the best evidence of benefit for the situation.

4.1 | RECOVER First Aid Acute Hypersensitivity Reaction Algorithm

The FA Domain working group developed the RECOVER First Aid Acute Hypersensitivity Reaction Algorithm in decision tree format for ease of clinical use (Figure 1). This resource is intended to take clinicians step by step through cases of possible acute hypersensitivity and to distinguish uncomplicated allergic reaction from anaphylaxis in an efficient way. Recognizing anaphylaxis can be challenging because in many cases, the inciting cause (allergen) is unknown and cutaneous signs are often absent, so the condition must be recognized based on the peracute presentation of appropriate clinical signs with no other clear cause [4, 5].

The Algorithm starts with this pairing of peracute (e.g., all signs appear within minutes to a few hours) onset clinical signs with possible (or known) antigen exposure. Certainly, if the animal encountered a likely allergen such as a vaccine or a *Hymenoptera* species, acute hypersensitivity should be highly suspected if appropriate clinical signs arise within minutes to hours of exposure. Even without suspected antigen exposure, with peracute onset of appropriate clinical signs, one should consider whether acute hypersensitivity is possible since many exposures are unwitnessed [4, 5]; following the "Yes" pathway, one would then score the patient from 0 to 3 based on the number of non-cutaneous body systems affected. If clinical sign onset is not peracute, the animal is unlikely to have an acute hypersensitivity reaction, and the clinician would follow the "No" pathway and continue diagnostic workup and management for other conditions.

Once the animal is scored for multiple episodes of vomiting or diarrhea, respiratory signs, and cardiovascular signs, the total points are added to yield a score from 0 to 3, and that score is considered in light of the presence of cutaneous signs. Common cutaneous signs of acute hypersensitivity reactions in dogs and cats include urticaria (e.g., wheals, angioedema), flushing, or pruritus [3, 5, 14, 15]. A score of 0 paired with no appropriate cutaneous signs is unlikely to be an acute hypersensitivity reaction (gray box on the Algorithm), while a score of 0 with appropriate cutaneous signs is an *uncomplicated allergic reaction* (blue box on the Algorithm). We recommend treating uncomplicated allergic reactions with an H1R antagonist (e.g., diphenhydramine, cetirizine). The animal with self-limiting, mild vomiting or diarrhea (e.g., a single episode) would also score a 0 and, if cutaneous signs were present, would also be classified as having an *uncomplicated allergic reaction* (blue box on the Algorithm), and we recommend treating with an H1R antagonist. Other supportive care should be given if indicated.

An animal that *scores a 1, 2, or 3 with appropriate cutaneous signs* (i.e., urticaria, flushing, or pruritus) has *anaphylaxis* (dark pink box on the Algorithm). If such animal is not collapsed, hypotensive, or in severe respiratory distress, the anaphylaxis is scored as *moderate*, and we suggest IM epinephrine in such cases, in addition to appropriate supportive care. If the animal scoring 1, 2, or 3, with cutaneous signs or with appropriate supportive findings, has *collapse, hypotension, or severe respiratory distress*, this animal has *severe anaphylaxis*, and we suggest treating with an epinephrine CRI, targeting a MAP of 70 mm Hg. Because of the evidence that dogs with hypotension due to severe anaphylaxis do not respond adequately to IM epinephrine or to bolus doses of epinephrine [20–22], the epinephrine CRI seems particularly important in this patient set. However, a cat with severe anaphylaxis manifesting as severe respiratory distress may not be amenable to IV catheter placement. There is nearly no feline anaphylaxis evidence available, and it seems reasonable to give a dose of epinephrine IM to cats with severe anaphylaxis manifesting as respiratory distress if IV access and epinephrine CRI are not possible.

An animal that *scores a 1, 2, or 3 with no cutaneous signs* poses more of a diagnostic challenge; in such cases, it is reasonable to seek further supportive findings to solidify the diagnosis. Such findings might include history of prior acute hypersensitivity reactions or known/suspected recent exposure; physical inspection for the presence of a stinger; point-of-care ultrasound examination for gallbladder wall edema or unexplained peritoneal effusion; or otherwise unexplained hemoabdomen [4, 14]. If the animal *scoring 1, 2, or 3 without cutaneous signs has supporting findings*, it is likely *anaphylaxis*. Anaphylaxis would be considered *moderate* in the absence of collapse, hypotension, or severe respiratory distress, and we suggest IM epinephrine; it would be considered *severe anaphylaxis* if this animal has *collapse, hypotension, or severe respiratory distress*, and we suggest IV epinephrine as a CRI to achieve a MAP of 70 mm Hg.

An animal with peracute onset of clinical signs (i.e., is being considered in the Algorithm) that scores a 1 with no cutaneous signs and no supporting findings could still have anaphylaxis. In the human grading system, anaphylaxis would only be prioritized for such an individual if the patient had collapse, hypotension, or severe respiratory distress after exposure to a known or highly probable allergen for that individual [18, 19]. Such an individual with peracute onset of collapse/hypotension *or* severe respiratory distress, with only one system involved, with highly likely allergen exposure, but without other supporting findings, would have *severe anaphylaxis*, and we suggest IV epinephrine as a CRI to achieve a MAP of 70 mm Hg. It is unclear how many small animal anaphylaxis cases present with this peracute, profound, "single-system" form of severe anaphylaxis.

Supportive care beyond epinephrine should be given to patients with anaphylaxis as clinically indicated. There is evidence that glucocorticoids are not beneficial in either uncomplicated allergic reaction or in anaphylaxis, and some evidence of worse outcomes with glucocorticoids in anaphylaxis, even when populations are adjusted for illness severity [84, 86]. We suggest against routine

use of glucocorticoids in uncomplicated allergic reaction and recommend against routine use of glucocorticoids in anaphylaxis.

If the animal with peracute onset of clinical signs scoring 1, 2, or 3 has no cutaneous signs, no supporting findings, and is not collapsed, hypotensive, or severely respiratory distressed, anaphylaxis is still possible but other conditions may be more strongly considered. Acute hypersensitivity is unlikely the cause when different body systems become involved over time (e.g., vomiting started yesterday and increased respiratory effort started today), or if signs are chronic (e.g., weeks of diarrhea).

5 | Discussion

This paper describes the development of, evidence regarding, and rationale behind the first evidence- and consensus-based treatment recommendations for the management of acute hypersensitivity reactions in dogs and cats. It contains the 12 treatment recommendations and the RECOVER First Aid Acute Hypersensitivity Reaction Algorithm for the RECOVER First Aid: Acute Allergy and Anaphylaxis subdomain, and complements the series of RECOVER consensus guidelines papers [8, 9, 23, 95]. The series of RECOVER consensus guidelines papers are important elements in the pathway from scientific knowledge to clinical decision-making in veterinary resuscitation; the pathway begins with generating evidence from research, synthesizing that evidence to generate guidelines, and then applying the guidelines in practice to inform clinical decisions.

During this process, we extracted a large amount of scientific information from primary, peer-reviewed literature to address high-priority clinical questions pertaining to the treatment of acute hypersensitivity in dogs and cats. The resulting evidence- and consensus-based treatment recommendations and clinical guidelines provide guidance to veterinary professionals and provide a basis for instructions to clients or paraprofessionals when they contact a veterinary clinic for guidance from the prehospital setting. These consensus guidelines will also serve as a foundation for standardized educational programs for veterinary professionals, animal owners, canine handlers, and paraprofessionals regarding the early management of canine and feline acute hypersensitivity reactions.

We used methodology to develop the current treatment recommendations similar to what we used to generate the 2024 RECOVER CPR Guidelines for dogs and cats [24]. However, for PICOs FA-01, FA-02, FA-12, and FA-13, additional literature searches were performed to bridge the time gap between the original 2020 literature searches and late 2025, when these Evidence Profile Worksheets were written. Also, two PICOs (FA-29, FA-30) were developed, and their literature was searched and evaluated only from late 2025 to early 2026. The GRADE method for guidelines generation in health care is a rigorous, comprehensive approach to ensure evidence is considered and applied in a systematic way to inform actionable treatment recommendations [25]. In developing the recommendations presented in this document, relevant peer-reviewed literature was reviewed and assessed for indirectness, imprecision, inconsistency, and bias to assign a strength to the treatment recommendations. All evidence identified, screened, and evaluated for content and quality through the bridge and FA-29/-30 searches in the late 2025 to early 2026 timeframe was initially evaluated by only one (rather than two independent) EE and thus was assigned one lower degree of quality/certainty during GRADE evaluation in an attempt to mitigate overstatements due to bias. Because we applied this rigorous GRADE approach to the six acute hypersensitivity PICO questions addressed in this paper, 7 of 12 recommendations were developed based on low- or very-low-quality evidence and 5 were based on expert opinion.

Much of the evidence uncertainty in this subdomain was a consequence of the dearth of clinical trials or prospective data regarding treatment of acute hypersensitivity in any species. The large studies regarding acute hypersensitivity in people are mostly retrospective and all observational, and the few available prospective clinical trials are quite small or lower in quality due to risk of bias and species indirectness [38, 49–53, 82]. Veterinary studies are all observational and all but two [4, 35] include fewer than 100 animals [2, 3, 6, 7, 14]. Consequently, many of the treatment recommendations are supported by expert opinion based on assessment of the limited evidence available, input received during the consensus process, and a careful risk–benefit analysis of the treatments as considered by the writing group.

Additionally, some treatment recommendations are topically tangential to the original PICO question; such treatment recommendations were based on evidence found during literature search and evaluation for the original PICO question. The Information Specialists develop literature search strategies that are highly sensitive rather than specific to the PICO questions, in order to identify as much relevant literature as possible. Considering this robust literature search strategy in combination with an international consensus process that provided further relevant articles, we believe key literature was considered and that large deficits are unlikely. Ultimately, the recommendations presented agree in many ways with previously published recommendations for the treatment of acute hypersensitivity dogs and cats [10, 11, 13].

Despite low or very low quality of evidence, or lack of directly applicable evidence, we provide treatment recommendations because of the need for clear, consistent standards for managing acute hypersensitivity reactions in dogs and cats. While treatment recommendations supported by low or very-low-quality evidence or expert opinion would usually be accompanied by a "weak" or "conditional" suggestion for treatment, the writing group made some "strong" treatment recommendations, which were upheld through the consensus process. We provided reasoning for such deviations in the justification section of each PICO question. One example is the strong recommendation for H1R antagonist (e.g., diphenhydramine, cetirizine) administration to small animals with uncomplicated allergic reactions despite low quality of evidence [39, 40, 44]. The potential benefit in decreased morbidity associated with H1R antagonist administration was considered to outweigh the risk of these medications, and thus a strong recommendation was made.

The RECOVER First Aid Acute Hypersensitivity Reaction Algorithm is intended to be sensitive to catch most cases of acute hypersensitivity, and so it should be applied only to cases in which the clinician has an index of suspicion. Its lack of specificity could

lead to misdiagnosis in certain circumstances. For example, a dog with a pyloric outflow obstruction with repeated vomiting leading to hypovolemic shock and aspiration pneumonia may be affected in 3 of 4 anaphylaxis candidate body systems, despite not having an acute hypersensitivity reaction. This example underscores the importance of the peracute, near-simultaneous onset of appropriate clinical signs with either no other inciting cause (i.e. "possible" antigen exposure) or known allergen exposure. This example case of pyloric outflow obstruction is more likely to have signs that progress incrementally (i.e., from vomiting first to eventual cardiovascular and respiratory signs over hours to a few days) rather than appear in a near-simultaneous, peracute way within minutes to a few hours. Moreover, the RECOVER First Aid Acute Hypersensitivity Reaction Algorithm should be used when an acute hypersensitivity reaction is suspected rather than as a broad screening tool, because of its lower specificity for acute hypersensitivity.

Considering the breadth of clinical presentation spanned by uncomplicated allergic reaction, moderate anaphylaxis, and severe anaphylaxis, there was little information available in dogs and very little in cats. In the scant literature available lies a suggestion that cardiovascular and gastrointestinal signs may predominate in canine anaphylaxis [4], while respiratory and gastrointestinal signs may predominate in feline anaphylaxis [2]. Prospectively collected data of many more animals affected by various identified allergens across multiple institutions will be needed to determine whether there is a difference between the presentation of anaphylaxis in the two species; if so, optimal treatments may differ between the species.

There were many knowledge gaps regarding management of acute hypersensitivity in dogs and cats. Key knowledge gaps considered high priority for study are listed in Box 1. It is our hope that the knowledge gaps that emerged in the process will serve as a basis for collaborative research initiatives to gather evidence regarding treatment of acute hypersensitivity in dogs and cats. It is expected that the RECOVER First Aid: Acute Allergy and Anaphylaxis treatment recommendations will be updated as new information becomes available.

BOX 1 | Key knowledge gaps in the management of acute hypersensitivity reactions in dogs and cats.

What is the ideal administration route for histamine-1 receptor antagonist administration in small animals with an uncomplicated allergic reaction in the urgent/emergency care setting?
Do histamine-2 receptor antagonists improve outcomes in small animals with uncomplicated allergic reaction?
Do glucocorticoids improve outcomes for small animals with persistent urticaria in uncomplicated allergic reaction?
In dogs and cats with moderate anaphylaxis, how does supportive care alone, compared to epinephrine plus supportive care, affect outcomes?
Does prehospital administration of IM epinephrine for dogs and cats with anaphylaxis improve outcomes?
In cats with severe anaphylaxis that have severe respiratory distress but not hypotension, how does IM epinephrine, compared to an epinephrine CRI, affect outcome?
What is the ideal format of epinephrine to prescribe (e.g., autoinjector, prefilled syringes, epinephrine in ampules with syringes) for home use in dogs and cats for anaphylaxis?
In dogs and cats with anaphylaxis in the prehospital setting, how does subcutaneous epinephrine, compared to intramuscular epinephrine, affect outcome?

Author Contributions

Jamie M. Burkitt-Creedon: conceptualization, writing – original draft, methodology, writing – review and editing, project administration, supervision, investigation, formal analysis. **Deborah C. Mandell**: conceptualization, investigation, writing – review and editing, supervision, formal analysis. **Vincent J. Thawley**: conceptualization, investigation, writing – review and editing, supervision, formal analysis. **Daniel J. Fletcher**: conceptualization, investigation, funding acquisition, methodology, writing – review and editing, software, formal analysis, project administration, supervision. **Manuel Boller**: conceptualization, investigation, funding acquisition, methodology, writing – review and editing. **Jonathan Ball**: writing – review and editing, data curation. **Corrin J. Boyd**: data curation, writing – review and editing. **Fiona J. L. Brown**: writing – review and editing, resources. **Melissa Evans**: writing – review and editing, data curation. **Erik Fausak**: methodology. **Thomas Hackney**: writing – review and editing, data curation. **Jiwoong Her**: writing – review and editing, data curation. **Heather K. Moberly**: writing – review and editing, resources. **Lee E. Palmer**: writing – review and editing, data curation. **Laura M. Rey**: writing – review and editing, resources. **Amanda Witsil**: writing – review and editing, data curation. **Ivayla Yozova**: writing – review and editing, data curation.

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Conflicts of Interest

Drs. Boller, Burkitt-Creedon, and Fletcher are Executive Board members of The RECOVER Initiative, a nonprofit organization. Dr. Burkitt-Creedon is the Chief Editor of the Journal but only participated in the peer review process as an author. The authors declare no other conflicts of interest.

Endnotes

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