The Egyptian Guidelines for Managing Anaphylaxis in the Emergency Department

Contents

Committee

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Abbreviations

AGREE II	Appraisal of Guidelines For Research & Evaluation
ED	Emergency department
EKB	Egyptian Knowledge Bank
EtD	Evidence to decision
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IM	Intramuscular
IV	Intra-Venous
RCUK	Resuscitation Council United Kingdom

Glossary

Anaphylaxis	A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially life-threatening compromise in airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present.
Antihistamine drugs	Class of drugs that blocks the action of histamines, for symptomatic relief of associated manifestations such as fever, skin rash, itching, sneezing, a runny nose, and watery eyes.
Bronchia Asthma	A chronic inflammatory disease of the airways characterized by bronchial hyperreactivity and a variable degree of airway obstruction. It is diagnosed on the basis of the clinical history, physical examination, and pulmonary function tests, including reversibility testing and measurement of bronchial reactivity.
Corticosteroids drugs	Corticosteroids are synthetic analogues of the natural steroid hormones produced by the adrenal cortex, specifically glucocorticoids, which act by binding to intracellular receptors. Upon activation, it inhibits gene expression and translation in inflammatory leukocytes and structural cells, such as epithelium.

Executive Summary

This guideline is the key for the initial management of anaphylaxis (a life-threatening condition compromising the airway, breathing, and/or circulation) in the emergency department (ED), to be used by emergency physicians and any physician who works in the ED, whatever the specialty. It has been made in a simple concise way to go through in a quick stepping manner giving the clues to most critical points of such a critical condition in the ED.

The guideline was developed through adoption and adaptation methodology by a consensus of expert field group, Guideline Development Group (GDG) of the Egyptian National Clinical Guidelines Centre, supporting the 2021 update of the Resuscitation Council United Kingdom (RCUK). Because of lacking randomized clinical trials, the certainty of evidence for these recommendations was moderate or less.

We recommend	Strength
1- giving adrenaline as the first line of treatment	**Strong**
2- early administration of adrenaline once symptoms of anaphylaxis are recognized or suspected	**Weak**
3- giving adrenaline by intramuscular route as the initial treatment of anaphylaxis	**Strong**
4- following the list of adrenaline doses according to age	**Strong**
5- repeating intramuscular adrenaline every 5-15 min in cases of refractory anaphylaxis	**Weak**
6- iv bolus of crystalloid in case of hemodynamic instability and in refractory anaphylaxis	**Weak**
7- against using antihistamines as initial treatment of anaphylaxis	**Weak**
8- against using corticosteroids in initial treatment of anaphylaxis	**Weak**
9 - giving inhalational beta2 agonist as part of treatment in the presence of wheezy chest	**Weak**
10- a minimum of 6 hours of observation after resolution of symptoms for all patients with a confirmed diagnosis.	**Weak**

Introduction

Anaphylaxis is an acute, life-threatening systemic hypersensitivity reaction that compromises the airway, respiration, and/or circulation. It may occur without typical skin features, circulatory shock, or compromised breathing being present [1]. Anaphylaxis should be recognized and treated immediately [2]. Emergency department (ED) anaphylaxis care involves proper triage, administration of adrenaline, and the general management of airway, breathing, and circulation [3]. Therefore, guidelines for managing anaphylaxis in the ED must be based on the best available research evidence, theory, and expert consensus.

This evidence review was undertaken by the Anaphylaxis Guideline Development Group (GDG) of the Egyptian National Clinical Guidelines Centre, supporting the 2021 update of the Resuscitation Council United Kingdom (RCUK). The GDG used an internationally accepted approach for adoption, adaptation, and de novo guideline development based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence to decision (EtD) framework, referred to as GRADE-ADOLOPMENT [4]. The EtD framework

facilitates the use of evidence in a structured and transparent way to inform decisions in the context of clinical and public health recommendations and decisions [5].

Purpose

To our knowledge, few registries of anaphylaxis exist in Egypt, and no specific Egyptian guidelines are available. Therefore, we aimed to design Egyptian guidelines to prevent treatment errors in the ED among Egyptians. This guideline may also benefit institutions worldwide, particularly in low-middle-income countries.

Intramuscular (IM) adrenaline is considered the first-line drug for the treatment of anaphylaxis [6], but there is considerable divergence between published guidelines regarding the role of adrenaline in comparison to other available medications [7]. This may be due to a lack of high-certainty evidence to support treatment recommendations [8]. However, based on prior publications and the experience of experts, this guideline selects and answers key questions that are key to multidisciplinary healthcare providers in the ED. Adherence to this guideline should improve the care of anaphylaxis patients at Egyptian medical institutions.

Scope and Target Audience

This document's recommendations are directed to emergency physicians and other specialists working in the ED of Egyptian hospitals in the different sectors of the Egyptian healthcare system. The key research questions were identified from the previous RCUK guidelines. The EtD framework for each question/topic was discussed by the expert in emergency medicine to adapt those recommendations in the Egyptian ED setting (see **Annex 1**).

Methods

Multiple sources provided by the Egyptian Knowledge Bank (EKB) platform were used to identify up-to-date international guidelines. We searched for guidelines covering ED management of anaphylaxis. We included international guidelines regardless of whether they used the GRADE EtD framework (and some guidelines preceded the EtD methodology) or not.

After applying the Appraisal of Guidelines For Research & Evaluation (AGREE II) tool [9], we chose two initial guidelines: one developed by medical Chinese societies [10]and the other by the RCUK [11]. We decided to choose the RCUK guideline because it was more suitable for applying the GRADE ADOLOPMENT process.

Each committee member chose one or two recommendations and searched for any key studies related to those recommendations published after the date of the RCUK guideline publication. The studies that could potentially influence the recommendation strength or the level of certainty of evidence were shared among the working group.

The GRADE-PRO web-based application was used to create the draft of the evidence-to-decision (EtD) tables and to facilitate the committee members' voting for each recommendation [12]. The template provided by RCUK guidelines was used to guide the discussion. The EtD tables were then reviewed by the GDG, and a consensus was reached on whether to support the previous recommendation ("adopted") or indicate a need to update the recommendation ("adapted"). If there was no consensus regarding the strength of the recommendation, the GDG chair led a thorough discussion to achieve a final agreement. The strength for each recommendation was assigned as either strong or weak (**see Annex 1**).[6]

Summary of the Evidence

The certainty of evidence for each recommendation was determined as High, Moderate, Low, or Very Low (**Table 1**), according to the available evidence in RCUK guidelines in addition to the updated literature review conducted by the committee members.

Table 1 – Certainty of evidence [4]

Certainty of evidence	Explanation
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Contextual Factors Considerations

Although evidence regarding the performance, efficacy, and safety of interventions is crucial for all guidelines, it's important to consider contextual factors of the EtD framework when formulating recommendations. These considerations include the feasibility and acceptability of an intervention in each setting, its cost-effectiveness, and the potential impact on reducing or increasing inequities. Patients' values and preferences should also be considered. All these contextual factors were discussed by the GDG, considering the Egyptian context.

Recommendations

GDG adapted 10 recommendations. Five of them relate to adrenaline as a first line for anaphylaxis treatments, adrenaline timing, dosage, method of administration, and subsequent usage in refractory cases. The other 5 recommendations focused on the role of potential adjuvant therapies (i.e., intravenous fluid, antihistamine, corticosteroids, and beta2 agonist) in addition to patients' disposition from ED. The guideline recommends against using antihistamines and corticosteroids as part of the initial therapy.

The intravenous (IV) route is not recommended for initial management of anaphylaxis, except by senior physicians who hold the privilege of using IV adrenaline. Also, the privilege of using IV adrenaline infusion to treat refractory anaphylaxis should be available for the treating physician. Although GDG advised against using antihistamines or corticosteroids as part of the initial anaphylaxis treatment, antihistamines could be used to manage skin manifestations, and corticosteroids could be given with IV crystalloids in case of hemodynamic instability and in refractory anaphylaxis, provided that their administration is not delaying adrenaline administration.

The GDG does not recommend fast-track discharge (after 2 h of observation from the resolution of anaphylaxis). Most of the Egyptian patients do not have access to adrenaline auto-injectors to be safely discharged on them. Also, adequate supervision following discharge is not guaranteed. Also, we are not sure about adequate medical supervision following discharge. Key research questions, recommendations, a summary of the evidence, and remarks related to the implementation are summarized in **Table 2.**

Table 2, Key research questions, recommendations, a summary of the evidence, and remarks related to the implementation

	The question	The recommendation (strength/ certainty)	Summary of evidence (the most important references)	Remarks (for implementation)
1.	**Is adrenaline effective for the treatment of anaphylaxis?**	We recommend adrenaline as the first line treatment for anaphylaxis in ED *(strong recommendation, moderate certainty evidence)*	There is little doubt that sufficient levels of adrenaline lead to the resolution of symptoms, while delayed administration can lead to prolonged reactions, hypotension, and fatal outcomes [13 14].	A clear definition of anaphylaxis should be provided and demonstrated through the ABCDE approach (see **Annex 2,3**), to discriminate it from allergic skin reaction which is not an emergency.
2.	**What is the optimal timing of adrenaline in the treatment of anaphylaxis?**	We recommend that adrenaline should be administered early once symptoms of anaphylaxis have been recognized or suspected *(weak recommendation, very low certainty evidence).*	Although there is a lack of high-certainty evidence to differentiate the effect of early versus delayed administration of adrenaline on clinical outcomes, it is reasonable to recommend administering adrenaline as soon as symptoms of anaphylaxis appear [7 13].	It seems reasonable to ensure the availability of adrenaline in ED to be given as soon as features of anaphylaxis are apparent.
3.	**What is the optimal route of adrenaline to treat anaphylaxis?**	The intramuscular (IM) route is recommended for initial adrenaline treatment for anaphylaxis *(strong recommendation, very low certainty evidence).*	There are currently no trials comparing the effectiveness of different ways of administering adrenaline to patients during anaphylaxis. The use of IM adrenaline as the initial treatment for anaphylaxis due to its favourable safety profile, especially for patients with cardiovascular issues [15].	The IV route is not recommended for initial management of anaphylaxis, except by those skilled and experienced in its use.

4.	**What is the optimal dose of intramuscular adrenaline in the treatment of anaphylaxis?**	We recommend IM adrenaline dosage listed according to age (*strong recommendation, low certainty evidence*)	The dosing regimen listed has been proven safe and effective in clinical practice for over 20 years. International guidelines recommend a dose of 0.01 mg/kg (maximum 500 micrograms) for children, which should be titrated to achieve a clinical response. Several guidelines also recommend simplifying the dosing schedule based on age categories, making it safer and more practical for emergency use by simplifying the preparation and injection process [1 16 17]. .	Table with doses and equivalent ml should be available in ED. **Adults:** 500 ug (0.5 mg) IM (0.5 mL of 1 mg/ml [1:1000]) **Children >12 years:** same as adult dose and 300 ug (0.3 ml) if child is small **Children 6-12 years:** 300 micrograms IM (0.3 mL) **Children 6 months-6 years:** 150 micrograms IM (0.15ml) **Children <6 months:** 100-150 micrograms IM (0.1 0.15 mL)
5.	**Is adrenaline effective in the treatment of anaphylaxis reactions refractory to initial treatment with adrenaline?**	We recommend that: 1- Subsequent doses of IM adrenaline should be given every 5 min, titrated to clinical response, in patients whose symptoms are refractory to initial treatment (*weak recommendation, very low certainty evidence*). 2- Low dose intravenous (IV) adrenaline infusions appear to be effective and safe to treat refractory anaphylaxis. (*weak recommendation, very low certainty evidence*).	The absorption of adrenaline following intramuscular injection follows a biphasic profile, with the initial peak occurring within 5-10 minutes [18]. Therefore, IM adrenaline should be repeated every 5-15 min where features of anaphylaxis persist [15]. The rationale for waiting longer than 5 min when symptoms have failed to respond to adrenaline is unclear. Low-dose adrenaline infusions are effective in case series of human anaphylaxis [19 20] and are included as the treatment of choice for refractory anaphylaxis in national guidelines in Australia for the acute management of anaphylaxis; 2024 [21].	Where respiratory and/or cardiovascular features of anaphylaxis persist despite 2 appropriate doses of adrenaline (administered by IM or IV route), urgent expert help (e.g. from experienced critical care clinicians) should be sleeked to establish an intravenous adrenaline infusion to treat refractory anaphylaxis. Complications due to adrenaline occur regardless of route but are more common after IV administration.

6.	**Are intravenous fluids effective as an adjuvant treatment for anaphylaxis?**	In case of anaphylaxis with haemodynamic instability, IV crystalloid fluids should be given. (*weak recommendation, very low certainty evidence*)	Crystalloid infusion was more effective in restoring venous return when compared to a single dose of IM adrenaline [22].	IV access should be obtained as early as possible, as a single bolus of IV crystalloid can be used in refractory anaphylaxis.
7.	**Are antihistamines effective in the treatment of anaphylaxis?**	We advise against using antihistamines as part of the initial emergency treatment for anaphylaxis. *(weak recommendation, low certainty evidence)*	Antihistamines are not to be utilized in the treatment of respiratory or cardiovascular symptoms associated with anaphylaxis. Their application should not impede the timely administration of adrenaline and intravenous fluids required to address such symptoms [1 17 21].	We suggest antihistamines are used to treat skin symptoms which often occur as part of allergic reactions without delaying timely and appropriate use of adrenaline to treat anaphylaxis
8.	**Are corticosteroids effective in the treatment of anaphylaxis?**	We advise against using corticosteroids as part of initial emergency treatment for anaphylaxis (*weak recommendation; low certainty of evidence)*	Corticosteroids increased the admission rate in the intensive care units and Hospital in a Canadian Emergency Department Anaphylaxis Cohort [23]. Also, corticosteroids may postpone the use of adrenaline which is life saving [24].	Corticosteroids could be included in the management of refractory anaphylaxis and shock.
9.	**Are inhaled beta-2 agonists effective in the treatment of anaphylaxis?**	We suggest that inhaled beta2 agonist can only be used as an adjunct treatment to adrenalin in the presence of wheezing for anaphylaxis (*weak recommendation low certainty of evidence*)	Short-acting beta-2 agonists (inhaled through a nebulizer or spacer) can be used to relieve lower respiratory symptoms and anaphylaxis, such as wheezing and coughing [25]. But it should not be used instead of adrenaline as a first line of treatment for anaphylaxis [21].	Considering bronchial asthma as an important differential diagnosis of acute onset dyspnea and wheezes. Beta 2 agonist should not be used as a treatment for persistent wheezing instead of repeating the IM adrenaline.

10.	**How long should patients be observed in hospital following anaphylaxis?**	We recommend, minimum 6 hours observation after resolution of symptoms for all patients. Observation for at least 12 hours after the symptoms have resolved should be ensured in the following cases: - A severe reaction that necessitated more than 2 doses of adrenaline. - Patients with severe asthma or those who experienced severe respiratory compromise during the reaction. - Possibility of continued absorption of allergen, such as with slow-release medications. - Patients who present late at night or may not be able to respond to any deterioration. - Patients in areas where access to emergency care is difficult. (*weak recommendation, very low certainty evidence*)	The optimal duration of observation following anaphylaxis is unknown. We suggest using a risk-stratified approach for discharging patients after anaphylaxis [24 26] .	The rapid discharge of patients within 2-6 hours after anaphylaxis symptoms have been resolved is not considered a safe approach. However, relatively early discharge of stable patients or arranging for safe transfer to another hospital should be considered in the event of limited capacity at busy ED and small hospitals during a medical crisis.

Research Gaps

Anaphylaxis is a severe, life-threatening, multisystem hypersensitivity reaction that affects multiple systems. The distribution of anaphylaxis varies based on age, gender, race, geographical location, and socioeconomic status of the individuals involved; therefore, describing the epidemiology of anaphylaxis in developing countries is very crucial [27]. The incidence of anaphylaxis is often underestimated in various studies due to difficulties in recognizing it and variations in diagnostic criteria among different studies and countries [28]. Furthermore, the underestimation of anaphylaxis diagnosis is more pronounced in developing countries, and when diagnosed, proper management is sometimes lacking [29].

The overall prognosis for anaphylaxis is generally good. Injecting adrenaline early in the case of anaphylaxis (i.e., before arriving at the emergency department) can substantially reduce the chances of being admitted to the hospital. On the other hand, delayed administration of adrenaline has been linked to numerous cases of anaphylaxis-related fatalities in a large series of cases [30]. The impact of the lack of auto-injectable devices that deliver adrenaline in the pre-hospital phase on anaphylaxis prognosis is not well studied. Cost-effectiveness analysis to study the impact of incorporating adrenaline auto- injectable adrenaline devices in the Egyptian Healthcare system should be conducted.

Guidelines for both adults and children stress the importance of prompt diagnosis for optimal treatment [31]. Mistakes in diagnosing anaphylaxis can happen due to the limited time available for diagnosis, the stressful environment of the emergency room, incomplete clinical features in early anaphylaxis, and the lack of useful laboratory markers. Sensitive and specific biomarkers for anaphylaxis diagnosis will reduce its misdiagnosis [32].

A simplified universal anaphylaxis guideline dedicated to recognizing, diagnosing, and risk stratification of this condition is still unmet (see **annex 3**)[33]. Future implementation research is necessary to minimize discrepancies between guidelines and elucidate reasons for differences [34].

Monitoring and Evaluation

Clinical indicators for recommendations monitoring are needed to ensure achieving the impact of guidelines **(Table 3).**

Table 3: Clinical indicators for recommendations

Recommendation	**Clinical indicators**
Adrenaline as the first line treatment for anaphylaxis.	100 % of patient presented with anaphylaxis shock should be treated with adrenaline.
Adrenaline should be administered early once symptoms of anaphylaxis have been recognized or suspected.	Percentage of experiencing anaphylaxis who are promptly treated with adrenaline.
The IM route is recommended for initial adrenaline treatment.	Percentage of patients treated with adrenaline in ED by appropriate route.
IM adrenaline dosage listed according to age	100 % of patients prescribed adrenaline in treatment anaphylaxis should be for the correct dose
Subsequent doses of adrenaline, titrated to clinical response, in patients whose symptoms are refractory	Percentage of patients with anaphylaxis who received adrenaline 2nd dose due to refractory reaction after initial dose of adrenaline
IV crystalloid for treating anaphylaxis with haemodynamic instability	Percentage of patients with anaphylaxis who received IV fluid (bolus and maintenance)
Antihistamines shouldn't be the initial emergency treatment for anaphylaxis	Percentage of patients with anaphylaxis who administrated antihistamines prior to adrenaline
Corticosteroids shouldn't be the initial emergency treatment for anaphylaxis	Percentage of patients with anaphylaxis who administrated corticosteroids prior to adrenaline
Inhaled beta2 agonist as an adjunct treatment to adrenaline in the presence of wheezing for anaphylaxis	Percentage of patients with lower respiratory symptoms in the context of anaphylaxis inhaled beta-2 agonists

Minimum 6- 12 hours observation after resolution of symptoms of anaphylaxis according to the associated risk	Percentage of patients with an acute episode of anaphylaxis are observed in hospital for duration less than 6 hours. Hospital revisit or mortality after 6 hours of observations

Update to guidelines

The guidelines will be continuously updated based on new and relevant evidence.

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Annex1- EtD Tables

QUESTION

Should Adrenaline by any route vs. No adrenaline be used for patients presented to ED with suspected anaphylaxis.?	
POPULATION:	patients presented to ED with suspected anaphylaxis.
INTERVENTION:	Adrenaline by any route
COMPARISON:	No adrenaline
MAIN OUTCOMES:	Symptom resolution; Survival with good functional outcome, survival with complications; Occurrence of biphasic reaction; Biphasic reaction which prompts return visit to Emergency Department;
SETTING:	Emergency department setting

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

QUESTION

Should Administration of adrenaline by any route within 30mins of symptom onset vs. delayed administration be used for patients presented to ED with suspected anaphylaxis.?	
POPULATION:	patients presented to ED with suspected anaphylaxis.
INTERVENTION:	Administration of adrenaline by any route within 30mins of symptom onset
COMPARISON:	delayed administration
MAIN OUTCOMES:	New outcome;
SETTING:	Emergency department setting

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

QUESTION

Should Adrenaline by the intramuscular (IM) route vs. Adrenaline by an alternative route be used for patients presented to ED with suspected anaphylaxis.?	
POPULATION:	patients presented to ED with suspected anaphylaxis.
INTERVENTION:	Adrenaline by the intramuscular (IM) route
COMPARISON:	Adrenaline by an alternative route
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

QUESTION

Should Intramuscular adrenaline dosage table vs. other dosage be used for patients presented to ED with suspected anaphylaxis.?	
POPULATION:	patients presented to ED with suspected anaphylaxis.
INTERVENTION:	Intramuscular adrenaline dosage table
COMPARISON:	other dosage
MAIN OUTCOMES:	Pharmacokinetic profile (plasma concentration of adrenaline); Safety / adverse events; Speed of administration;
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

QUESTION

Should Repeating adrenaline by any route vs. Other interventions be used for patients with refractory anaphylaxis in ED.?	
POPULATION:	patients with refractory anaphylaxis in ED.
INTERVENTION:	Repeating adrenaline by any route
COMPARISON:	Other interventions
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

QUESTION

Should Intravenous fluids as an adjuvant for anaphylaxis vs. no intravenous fluids be used for patients presented to ED with suspected anaphylaxis.?	
POPULATION:	patients presented to ED with suspected anaphylaxis.
INTERVENTION:	Intravenous fluids as an adjuvant for anaphylaxis
COMPARISON:	no intravenous fluids
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

QUESTION

Should Antihistamine vs. no antihistamine be used for patients presented to ED with suspected anaphylaxis?	
POPULATION:	patients presented to ED with suspected anaphylaxis
INTERVENTION:	Antihistamine
COMPARISON:	no antihistamine
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

QUESTION

Should Corticosteroid (hydrocortisone, dexamethasone) vs. no corticosteroid be used for patients presented to ED with suspected anaphylaxis?	
POPULATION:	patients presented to ED with suspected anaphylaxis
INTERVENTION:	Corticosteroid (hydrocortisone, dexamethasone)
COMPARISON:	no corticosteroid
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

QUESTION

Should Inhaled bronchodilators e.g. salbutamol vs. no inhaled bronchodilators be used for patients presented to ED with suspected anaphylaxis?	
POPULATION:	patients presented to ED with suspected anaphylaxis
INTERVENTION:	Inhaled bronchodilators e.g. salbutamol
COMPARISON:	no inhaled bronchodilators
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

QUESTION

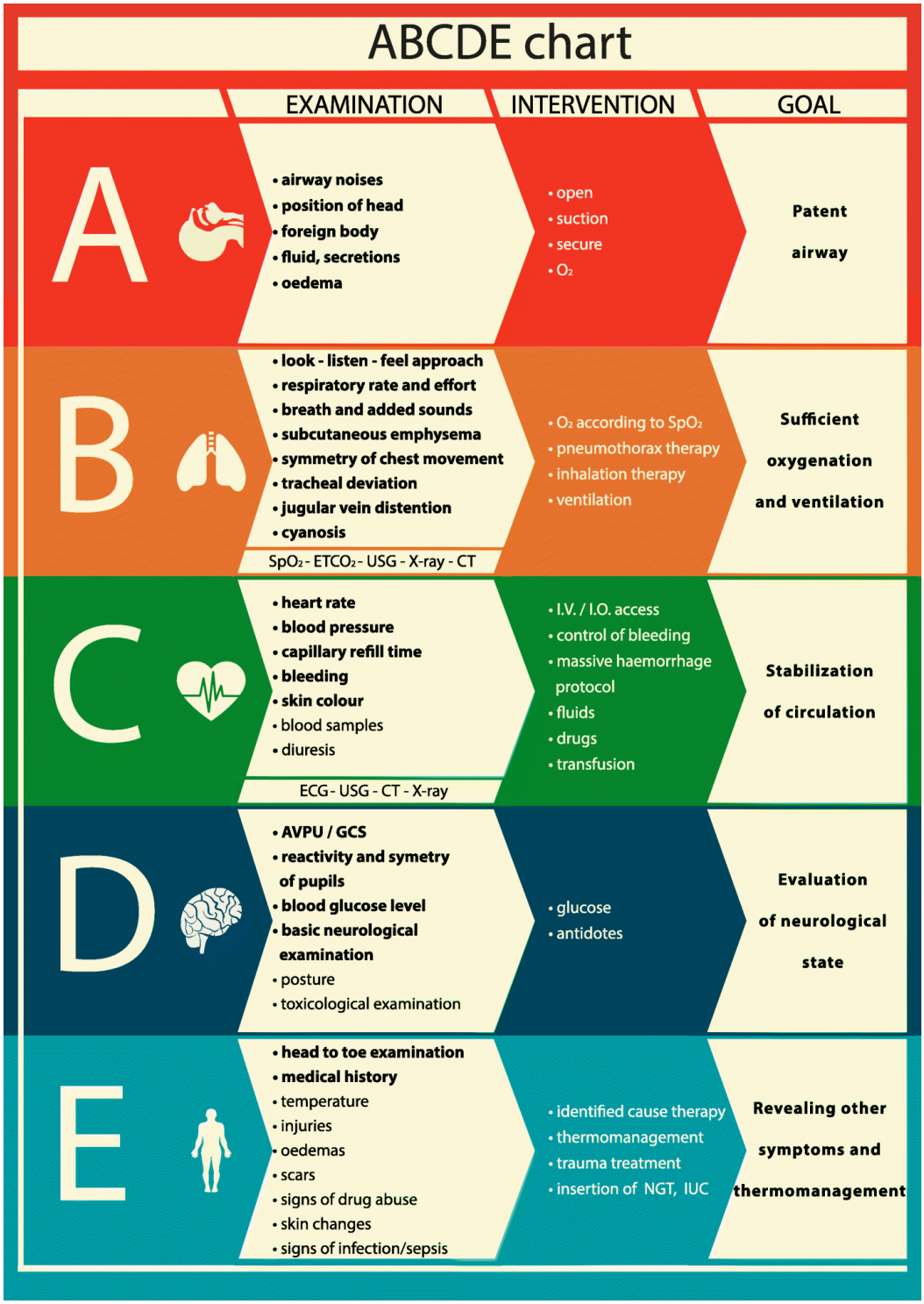
Should “Prolonged” observation in hospital vs. discharge following resolution of symptoms of anaphylaxis be used for patients with treated anaphylaxis in ED?	
POPULATION:	patients with treated anaphylaxis in ED
INTERVENTION:	“Prolonged” observation in hospital
COMPARISON:	discharge following resolution of symptoms of anaphylaxis
MAIN OUTCOMES:	
SETTING:	

PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

Annex 2: Recommended ABCDE Approach for managing critically ill patients



Peran, D., Kodet, J., Pekara, J., Mala, L., Truhlar, A., Cmorej, P.C., Lauridsen, K.G., Sari, F., Sykora, R., 2020. ABCDE cognitive aid tool in patient assessment – development and validation in a multicenter pilot simulation study. BMC Emergency Medicine 20.. https://doi.org/10.1186/s12873-020-00390

Annex 3: Most recent definitions used for anaphylaxis

WHO ICD-11	2019	Anaphylaxis is a severe, life-threatening systemic hypersensitivity reaction characterized by being rapid in onset with potentially life-threatening airway, breathing, or circulatory problems and is usually, although not always, associated with skin and mucosal changes.
WAO	2019 2020	Anaphylaxis is a serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially life-threatening compromise in breathing and/or the circulation and may occur without typical skin features or circulatory shock being present.
EAACI	2020	Anaphylaxis is a severe allergic reaction. [Defined in the context of when to use epinephrine autoinjectors]
ASCIA	2021	Any acute-onset illness with typical skin features (urticarial rash or erythema/flushing and/or angioedema), plus involvement of respiratory and/or cardiovascular and/or persistent severe gastrointestinal symptoms; or any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present.
Brighton Collaboration Working Group	2022	Anaphylaxis presents acutely and leads to a marked change in an individual's previous stable condition and is characterized by the following: rapid progression of symptoms and signs which typically affects multiple body systems (skin/mucosa/respiratory/cardiovascular/gastrointestinal) at the same time or sequentially but occurring in a short period of time (within 1 hour of onset of the first symptoms or signs).

ASCIA, Australian Society of Clinical Immunology and Allergy; EAACI, European Academy Allergy and Clinical Immunology; WAO, World Allergy Organization; WHO, World Health Organization. Golden DBK, Wang J, Waserman S, et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology 2024;132(2):124-76. doi: 10.1016/j.anai.2023.09.015