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Hong Kong Anaphylaxis Consortium Consensus Statements on prescription of adrenaline autoinjectors in the acute care setting

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ABSTRACT

Background: Adrenaline autoinjectors (AAInj) facilitates early administration of adrenaline and remains the first-line treatment for anaphylaxis. However, only a minority of anaphylaxis survivors in Hong Kong are prescribed AAIInj and formal guidance do not exist. International anaphylaxis guidelines have been largely based on Western studies, which may not be as relevant for non-Western populations.

Objective: To formulate a set of consensus statements on the prescription of AAIInj in Hong Kong.

Methods: Consensus statements were formulated by the Hong Kong Anaphylaxis Consortium by the Delphi method. Agreement was defined as greater than or equal to 80% consensus. Subgroup analysis was performed to investigate differences between allergy and emergency medicine physicians.

Results: A total of 7 statements met criteria for consensus with good overall agreement between allergy and emergency medicine physicians. AAIInj should be used as first-line treatment and prescribed for all patients at risk of anaphylaxis. This should be prescribed prior to discharge from the Accident and Emergency Department together with an immediate referral to an allergy center. The decision for prescribing AAIInj should be based

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on the severity of previous reactions; including objective signs of respiratory involvement, objective signs of cardiovascular involvement and multiorgan involvement (regardless of severity). Patient demographics and comorbidities, specifically history of asthma or chronic obstructive pulmonary disease, should also be considered. Patients deemed eligible for AAInj should be offered avoidance advice and prescribed one AAInj while awaiting review by allergists. AAInj technique should be demonstrated by a healthcare professional or instruction video, and a return demonstration by the patient is required. The patient should also be counseled that the decision on the continued need of AAInj prescription in the long-term should be reviewed by an allergist.

Conclusion: Consensus statements support the prescription of AAInj by front-line physicians with subsequent allergist review when treating patients at risk of anaphylaxis in Hong Kong.

Keywords: Adrenaline; Anaphylaxis; Autoinjector; Consensus; Consortium; Hong Kong

INTRODUCTION

Anaphylaxis is defined as a potentially fatal, severe, and systemic allergic reaction in which adrenaline (also known as epinephrine) remains the first-line treatment of choice [1]. One of the most important breakthroughs in anaphylaxis management came in the 1970s with the invention of adrenaline autoinjectors (AAInj), which allowed patients to readily self-inject adrenaline without the need for medical training [2]. AAInj can facilitate early administration of adrenaline and improve the outcomes from an anaphylactic episode [3, 4]. Anaphylaxis registries and large cohorts have consistently reported an increasing rate of anaphylaxis worldwide [5, 6]. Fortunately, this growing incidence has not been paralleled with an increase in anaphylaxis-related mortality [7]. This can be attributed to the improvement in anaphylaxis management with AAInj prescriptions being a key component and uniformly recommended across different international guidelines [8-12].

Similar to Western populations, the estimated incidence rate of anaphylaxis in Hong Kong is around 3.57 per 100,000 person-years and admissions for anaphylaxis have increased significantly [13]. However, only a minority of patients in Hong Kong diagnosed with anaphylaxis are prescribed AAInj despite the recommendation to provide AAInj following anaphylaxis in the Hospital Authority's *Handbook of Internal Medicine* [14, 15]. Despite a continued increase in anaphylaxis incidence, fewer than 15% of anaphylaxis survivors were prescribed AAInj prior to hospital discharge between 2009 and 2019 [16]. Formal guidance does not exist locally and there may be several reasons for this omission. Most international anaphylaxis guidelines were predominantly evidence-based on Western studies and may not be as relevant for non-Western populations. For example, as compared to Western populations, Hong Kong has a higher proportion of shellfish and lower proportion of beta-lactam antibiotic allergies [17-19]. Traditional Chinese medicine has been implicated to trigger anaphylaxis [17]. Clinical presentations and patient adherence to allergen avoidance also differ from other populations [15]. Remoteness from emergency care is less of a concern with the HK Fire Service Department's service pledge of just 12 minutes from time of call to arrival of an ambulance [20]. Hong Kong is in severe shortage of allergy services and allergy training, with an allergist-per-population ratio being one of the lowest in the world so many patients surviving anaphylaxis are discharged without an AAInj prescription and subsequent follow-up by allergists [21].

In light of this background, local experts were nominated by the Hong Kong Institute of Allergy (HKIA) and Hong Kong College of Emergency Medicine (HKCEM) to establish the "Hong Kong Anaphylaxis Consortium" to investigate and formulate using the Delphi method a set of consensus statements on the use and prescription of AAInj in Hong Kong.

MATERIALS AND METHODS

Consensus statements were formulated by the Delphi method, soliciting the opinions of experts managing patients with anaphylaxis in Hong Kong [22]. "Patients at risk of anaphylaxis" was defined as patients with suspected allergens which may not completely or easily avoidable, and therefore remain at risk of future re-exposure. In the first Delphi round, a structured questionnaire containing a set of proposed consensus statements encompassing important issues around the prescription of AAInj was developed by the Steering Committee of the Hong Kong Anaphylaxis Consortium. Consensus statements were formed in response to 7 key questions ("who, what, when, where, why, and how") on AAInj prescriptions. All members of the Steering Committee were nominated representatives of the HKIA and HKCEM and consisted of: a facilitator (PHL, adult allergist), 2 adult allergists (AYYW and THL) 3 pediatricians (GTC, ASYL, and MHKH), 2 emergency medicine (EM) physicians (Y-CC and AYCS) and 1 lay representative (EHL).

In the second round of Delphi, an expert panel was invited by the HKIA and HKCEM to participate in the questionnaire. The panel consisted of 11 allergy and 11 EM specialists affiliated with hospitals from all 7 clusters of the Hong Kong Hospital Authority (HA) and private practices in allergy and EM. The 11 allergy representatives consisted of: the 3 adult allergists who currently practice allergy in Hong Kong and 8 pediatric allergy representatives (3 Steering Committee members, 1 private pediatrician nominated by HKIA, 4 pediatricians nominated by each of the 4 Paediatric Immunology & Infectious Diseases Subspecialty Centres of Hong Kong). The 11 EM representatives consisted of: 2 Steering Committee members and 9 nominees by the HKCEM representing each of the College's subspecialties and subcommittees. Panel members declared their specialty and completed the questionnaire via an online anonymized system. They were not required to answer all questions and could select "no opinion."

In the third and final round of Delphi, the Steering Committee reviewed the aggregated responses of the questionnaires. If further clarification or elaboration on any statements was required, the questionnaire was adapted and sent back to participants with feedback.

Responses were graded as "Strongly Agree," "Tend to Agree," "Neither Agree nor Disagree," "Tend to Disagree," and "Strongly Disagree," scoring +1, +0.5, 0, -0.5, and -1, respectively. Consensus was *a priori* defined as 80% or more responses to "Strongly Agree" or "Tend to Agree." Scores are reported as the mean and standard deviation (scale from +1 to -1). More extreme scores and lower SD therefore indicated stronger consensus. Subgroup analysis was also performed to investigate if there were any differences in responses between allergy and EM representatives. Independent sample *t* test was used to compare between groups and a *p* value of less than 0.05 was considered statistically significant.

Table 1. Summary of consensus statements

Hong Kong Institute of Allergy/Hong Kong College of Emergency Medicine Consensus Statements on Prescription of Adrenaline Autoinjectors

- #1: AAIinj should be used as first-line treatment and prescribed for all patients at risk of anaphylaxis.
- #2: If indicated, AAIinj should be prescribed prior to discharge from the A&E Department and an allergy referral should be triggered immediately.
- #3: The decision for prescribing AAIinj should be based on the severity of previous reactions; including objective signs of respiratory involvement, objective signs of cardiovascular involvement and multiorgan involvement (regardless of severity).
- #4: The decision for prescribing AAIinj should be based on demographics and comorbidities; including history of asthma or chronic obstructive pulmonary disease.
- #5: Patients deemed requiring AAIinj should be offered avoidance advice and prescribed one AAIinj while awaiting allergist review.
- #6: After patients are prescribed AAIinj, demonstration by a healthcare professional or instructional video and return demonstration by the patient are required.
- #7: The long-term decision for the continued need of AAIinj should be reviewed by an allergist.

AAIinj, adrenaline autoinjectors; A&E, Accident & Emergency.

RESULTS

Based on 7 key questions regarding issues on prescribing AAIinj, the Steering Committee generated a total of 13 statements for voting by the expert panel. The expert panel was invited to further elaborate on the details of certain statements that reached consensus. Results after revision following the final round of Delphi were summarized in **Table 1** and were as follows:

Why should AAIinj be prescribed?

Consensus statement #1: AAIinj should be used as first-line treatment and prescribed for all patients at risk of anaphylaxis.

There was an overall 91% agreement (20 of 22 responders; score: 0.67 ± 0.45) with this statement. There was a significant higher score among allergy than EM representatives (score: 0.95 ± 0.15 vs. 0.41 ± 0.49 , $p=0.004$).

Where should be AAIinj be prescribed?

Consensus statement #2: If indicated, AAIinj should be prescribed prior to discharge from the Accident & Emergency (A&E) Department and an allergy referral should be triggered immediately.

There was an overall 82% agreement (18 of 22 responders; score 0.64 ± 0.53) with this statement. There was no significant difference between allergy and EM representatives (score: 0.77 ± 0.47 vs. 0.41 ± 0.54 , $p=0.106$).

When should AAIinj be indicated?

Consensus statement #3: The decision for prescribing AAIinj should be based on the severity of previous reactions; including objective signs of respiratory, objective signs of cardiovascular involvement and multiorgan involvement regardless of severity.

This consensus statement was derived from the stem statement “The decision for prescribing AAIinj should be based on the severity of previous reactions,” with follow-up questions regarding which specific organ manifestations qualified for AAIinj prescription. Outcomes of these questions are shown in **Table 2**.

Table 2. Results of “When should AAIinj be indicated?”

Statement	Overall		Allergy representatives			EM representatives			p value
	Agree (%)	Score	No.	Agree (%)	Score	No.	Agree (%)	Score	
The decision for prescribing AAIinj should be based on the severity of previous reactions	86	0.60±0.58	11	73	0.36±0.71	11	100	0.86±0.23	0.046
Specifically, AAIinj should be prescribed if previous reactions included:									
a. Isolated pruritus or urticaria/rash	0	-0.72±0.35	8	0	-0.75±0.38	11	0	-0.73±0.34	0.893
b. Without respiratory, gastrointestinal or cardiovascular symptoms	21	-0.42±0.64	8	13	-0.56±0.56	11	27	-0.36±0.71	0.521
c. Subjective symptoms of respiratory involvement without objective signs	39	0.03±0.51	8	75	0.38±0.44	10	10	-0.20±0.42	0.013
d. Objective signs of respiratory involvement without desaturation	95	0.61±0.47	8	100	0.88±0.23	11	91	0.45±0.52	0.049
e. Objective signs of respiratory involvement with desaturation	100	0.94±0.16	8	100	1.00±0.00	11	100	0.91±0.20	0.167
f. Isolated nausea without vomiting, diarrhea or abdominal pain	0	-0.61±0.38	8	0	-0.56±0.50	11	0	-0.59±0.30	0.888
g. Vomiting and/or diarrhea	22	-0.32±0.52	7	43	0.00±0.50	11	9	-0.45±0.47	0.069
h. Severe abdominal pain	32	-0.11±0.60	8	50	0.19±0.70	11	18	-0.23±0.47	0.140
i. Subjective symptoms of cardiovascular involvement without objective signs	63	0.25±0.63	8	100	0.69±0.26	11	36	0.00±0.67	0.014
j. Objective signs of cardiovascular involvement	100	0.91±0.19	8	100	1.00±0.00	10	100	0.85±0.24	0.081
k. Multiorgan involvement regardless of severity of each individual organ manifestation	84	0.72±0.38	8	100	0.94±0.18	11	73	0.55±0.42	0.014
The decision for prescribing AAIinj should be based on the ease of reliable allergen avoidance	64	0.21±0.57	11	55	0.14±0.67	11	73	0.23±0.47	0.717

Values are presented as mean±standard deviation.

AAIinj, adrenaline autoinjectors; EM, Emergency Medicine.

Bold indicates statements reaching consensus (overall agreement >80%).

For subjective symptoms and objective signs of respiratory involvement, “feeling short of breath/chest tightness” and “decreased air entry/wheeze” were included as examples in the questionnaire, respectively. For subjective symptoms and objective signs of cardiovascular involvement, examples of “dizziness/blurring of vision/syncope” and “tachycardia/hypotension” were given as examples in the questionnaire.

In subgroup analysis, 100% of allergy representatives agreed that even subjective symptoms of cardiovascular involvement, without objective signs, warranted AAIinj prescription compared to only 36% of EM representatives.

A second statement in this question category: “the decision for prescribing AAIinj should be based on the ease of reliable allergen avoidance” did not reach consensus (Table 2).

What patient circumstances should affect the decision for prescribing AAIinj?

Consensus statement #4: The decision for prescribing AAIinj should be based on demographics and comorbidities; including history of asthma or chronic obstructive pulmonary disease.

This consensus statement was derived from the stem statement “The decision for prescribing AAIinj should be based on demographics and comorbidities,” followed by follow-up questions to investigate which specific factors should influence decision for AAIinj prescription. Outcomes of these questions are shown in Table 3.

In subgroup analysis, 89% of allergy representatives agreed that decision for prescribing AAIinj should be based on history of raised baseline tryptase or mastocytosis, compared to only 14% of voting EM representatives.

Table 3. Results of “What patient circumstances should affect the decision for prescribing AAIinj?”

Statement	Overall		Allergy representatives			EM representatives			p value
	Agree (%)	Score	No.	Agree (%)	Score	No.	Agree (%)	Score	
The decision for prescribing AAIinj should be based on demographics and comorbidities	86	0.5±0.50	11	82	0.45±0.65	10	90	0.55±0.28	0.674
Specifically, the decision should be influenced by:									
a. Patient's age	53	0.22±0.70	9	67	0.33±0.83	8	38	-0.06±0.50	0.259
b. Patient's weight	44	0.03±0.71	9	67	0.44±0.68	9	22	-0.28±0.57	0.026
c. Patient's gender	0	-0.71±0.35	9	0	-0.78±0.36	9	0	-0.67±0.35	0.520
d. History of ischemic heart disease	72	0.47±0.68	9	78	0.50±0.75	9	67	0.28±0.62	0.503
e. History of hypertension	56	0.32±0.65	9	56	0.28±0.71	9	56	0.22±0.62	0.862
f. History of cerebrovascular accident	72	0.47±0.63	9	67	0.39±0.74	9	78	0.39±0.55	1.000
g. History of asthma or COPD	89	0.65±0.33	9	100	0.89±0.22	9	78	0.39±0.22	0.000
h. History of atopic dermatitis	22	-0.24±0.57	9	33	-0.44±0.73	9	11	-0.11±0.33	0.236
i. History of allergic rhinitis	17	-0.32±0.54	9	22	-0.56±0.63	9	11	-0.17±0.35	0.128
j. History of raised baseline tryptase or mastocytosis	56	0.47±0.62	9	89	0.67±0.66	7	14	0.00±0.29	0.027
k. Concomitant medications use (such as ACE-inhibitors, beta-blockers)	72	0.44±0.56	9	78	0.39±0.71	9	67	0.33±0.43	0.842
The decision for prescribing AAIinj should be based on the social context	41	0.00±0.68	11	45	0.00±0.84	11	0.36	-0.05±0.52	0.880

Values are presented as mean±standard deviation.

AAIinj, adrenaline autoinjectors; EM, Emergency Medicine; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme.

Bold indicates statements reaching consensus (overall agreement >80%).

A second statement in this question category: “The decision for prescribing AAIinj should be based on the social context” did not reach consensus (Table 3).

How should AAIinj be prescribed?

Consensus statement #5: Patients deemed requiring AAIinj should be offered avoidance advice and prescribed one AAIinj while awaiting allergist review.

Consensus statement #6: After patients are prescribed AAIinj, demonstration by a healthcare professional or instructional video and return demonstration by the patient are required.

This question category was divided into 2 parts, regarding: (1) the initial number of AAIinj prescribed and (2) education of AAIinj technique. Panel members voted on 3 statements which encompassed different number of AAIinj and levels of education, respectively.

Outcomes of these questions are shown in Table 4.

Table 4. Results of “How should AAIinj be prescribed?”

Statement	Overall		Allergy representatives			EM representatives			p value
	Agree (%)	Score	No.	Agree (%)	Score	No.	Agree (%)	Score	
<i>Patients deemed requiring AAIinj should be offered:</i>									
a. Avoidance advice only and await allergist review for prescribing AAIinj	9	-0.50±0.43	11	9	-0.64±0.45	11	9	-0.87±0.34	0.046
b. Avoidance advice and prescribed one AAIinj while awaiting allergist review	91	0.62±0.42	11	91	0.68±0.46	11	91	0.45±0.35	0.208
c. Avoidance advice and prescribed more than one AAIinj while awaiting allergist review	18	-0.24±0.57	11	36	-0.05±0.72	11	0	-0.50±0.22	0.070
<i>After patients are prescribed an AAIinj:</i>									
a. Reading the product insert and/or written information only is sufficient	0	-0.64±0.32	11	0	-0.77±0.26	11	0	-0.55±0.35	0.100
b. Demonstration by a healthcare professional or instructional video is required	100	0.79±0.25	11	100	0.95±0.15	11	100	0.64±0.23	0.001
c. Return demonstration by patient is required	100	0.67±0.25	11	100	0.86±0.23	11	100	0.50±0.00	0.000

Values are presented as mean±standard deviation.

AAIinj, adrenaline autoinjectors; EM, Emergency Medicine.

Bold indicates statements reaching consensus (overall agreement >80%).

Who should follow-up on the decision for AAIinj

Consensus statement #7: The long-term decision for the continued need of AAIinj should be reviewed by an allergist.

There was 100% agreement for this statement (22 of 22 responders; score: 0.88 ± 0.21) with this statement. There was no significant difference between allergy and EM representatives (score: 0.91 ± 0.20 vs. 0.86 ± 0.23 , $p=0.631$).

DISCUSSION

On behalf of the Hong Kong Anaphylaxis Consortium, we present Hong Kong's first set of consensus statements on the prescription of AAIinj.

In summary:

- (1) AAIinj should be used as first-line treatment and prescribed for all patients at risk of anaphylaxis.
- (2) If indicated, AAIinj should be prescribed prior to discharge from the A&E Department together with an immediate referral to an allergy center.
- (3) The decision for prescribing AAIinj should be based on the severity of previous reactions; including objective signs of respiratory involvement, objective signs of cardiovascular involvement and multiorgan involvement (regardless of severity).
- (4) Patient demographics and comorbidities, specifically history of asthma or chronic obstructive pulmonary disease, should also be considered when deciding on AAIinj prescription.
- (5) Patients deemed eligible for AAIinj should be offered avoidance advice and prescribed one AAIinj while awaiting review by allergists.
- (6) AAIinj technique should be demonstrated by a healthcare professional or instruction video, and a return demonstration by the patient is required.
- (7) The patient should also be counseled that the decision on the continued need of AAIinj prescription in the long-term should be reviewed by an allergist.

This is not an evidence-based treatment guideline, instead, it represents the collective experience and expertise from the specialties of allergy and EM in Hong Kong. Deciding on which patients are “at risk of anaphylaxis” and require AAIinj prescriptions would ultimately be at the discretion of individual clinicians. We advise individual centers to compare their anaphylaxis management plans against these consensus statements until future local evidence-based guidelines are published.

Overall, there was good agreement between the responses by allergy and EM representatives. In the subgroup analysis, only 2 proposed statements reached consensus among allergy but not EM representatives. These statements were “subjective symptoms of cardiovascular involvement (without objective signs)” and “history of raised baseline tryptase or mastocytosis” would affect the decision on prescribing AAIinj. The difference in choosing the “threshold” of cardiovascular involvement may reflect the differences in patients encountered by allergy and EM representatives. Allergists primarily work in the ambulatory care setting and encounter patients who only recall past symptoms of anaphylaxis without presenting the objective signs. On the contrary, EM physicians are often faced with patients presenting acutely with anaphylaxis and often have less time to enquire about symptoms prior to administration of adrenaline or AAIinj. Similarly, mastocytosis is a rare disease primarily managed by allergists/

immunologists or haematologists and less frequently encountered by EM physicians. Because of the increased risk in anaphylaxis due to an increased mast cell population, mastocytosis is included as an indication for AAInj prescription by most national allergy organizations (Table 5); including the American Academy of Allergy, Asthma and Immunology (AAAAI), American College of Allergy, Asthma, and Immunology (ACAAI), Australasian Society of Clinical Immunology and Allergy (ASCI), British Society for Allergy & Clinical Immunology (BSACI), and European Academy of Allergy and Clinical Immunology (EAACI) [8-11].

Table 5. Comparison with other international guidelines on prescription of AAInj

	Hong Kong Anaphylaxis Consortium (Hong Kong) 2020	AAAAI/ACAAI (USA) 2005 [23], 2010 [24], 2015 [25], 2020 [8]	ASCI (Australia) 2019 [9]	BSACI (UK) 2016 [10]	EAACI (Europe) 2014 [11]	WAO 2014 [12]
Prescription of AAInj as first line and to at risk patients	Yes	Yes	Yes	Yes	Yes	Yes
Clinical indications of AAInj prescription	Objective signs of respiratory involvement Objective signs of cardiovascular involvement Multiorgan involvement (regardless of severity)	Patients discharged from A&E department of anaphylaxis should be prescribed AAInj	History of generalized allergic reactions with ≥1 risk factor(s): - Teenage or young adults with food allergy - Peanut, tree nuts and seafood - Generalised urticaria alone without anaphylaxis following insect stings	Significant airway involvement Hypotension as part of an anaphylactic IgE- or non-IgE-mediated reaction	Anaphylaxis with food, latex, aeroallergens or other unavoidable triggers Exercise-induced or Idiopathic anaphylaxis Coexistent unstable or moderate to severe, persistent asthma with food allergy Venom allergy in adults with systemic reactions (unless receiving maintenance VIT) and children with more than systemic cutaneous reactions Underlying mast cell disorder and any previous systemic reaction	Fulfilling the diagnosis of anaphylaxis In resource-limited settings, recommendations for adrenaline injection needs to be provided
Demographics and comorbidities	Asthma or COPD	Comorbidities (e.g., asthma, CVD, mastocytosis) Medications Premenstrual status as a cofactor	Age Occupation Recreational exposure Asthma, CVD, systemic mastocytosis Remote residential locations Prolonged travel abroad	Asthma Raised baseline serum tryptase/ mast cell activation syndrome/ mastocytosis Occupation risk Medications Distance from medical assistance Social context	Age and sex Medications (NSAIDs, ACEI, beta-blockers) Cofactors (e.g., menstrual cycle, psychogenic stress, alcohol, physical exertion) Comorbidities (asthma, IgE-dependent diseases, CVD, mastocytosis, raised baseline tryptase)	Age Comorbidities (e.g., asthma CVD, mastocytosis) Cofactors (e.g., exercise, acute infection, emotional stress, premenstrual status, alcohol, NSAID ingestion)

(continued to the next page)

Table 5. (Continued) Comparison with other international guidelines on prescription of AAIinj

	Hong Kong Anaphylaxis Consortium (Hong Kong) 2020	AAAAI/ACAAI (USA) 2005 [23], 2010 [24], 2015 [25], 2020 [8]	ASCI (Australia) 2019 [9]	BSACI (UK) 2016 [10]	EAACI (Europe) 2014 [11]	WAO 2014 [12]
AED/primary care discharge management plan	AAInj should be prescribed prior to discharge from the AED and immediate allergy referral Avoidance advice Prescribed one AAIinj while awaiting allergist review AAInj prescription decision should be based on the severity of previous reactions	Allergist referral Provide education about anaphylaxis, risk of recurrence, trigger avoidance Prescribe >1 AAIinj Emergency action plan	Referral to clinical immunologist/allergist Routinely 2 AAIinj are recommended (one with the patient or at home for younger children; one at school or childcare center). Two AAIinj for adolescents and adults when: previous hypotensive or near fatal anaphylaxis; need for >1 dose in previous reactions; limited medical access; systemic mastocytosis; high body mass.	Prescription of an AAIinj from AED or primary care Immediate allergy referral Prescribing one AAIinj is the normal practice, except previous life-threatening reaction, requiring two doses within a short period, obesity, geographic location	Specialist referral Prescribe AAIinj Provide discharge advice sheet Provide contact information for patient support groups	Referral to a physician, preferably an allergy/immunology specialist Emergency action plans, medical identification of triggers and comorbidities
How to ensure patients' AAIinj technique?	Demonstration by healthcare professional or instructional video is required Return demonstration by patient is required	Patient discharged from AED should receive instruction in AAIinj proper use	N/A	Patient and carers should be trained Training should be performed Involve pharmacists to undertake the training	AAInj training devices should be available in physician offices or hospitals Immediate referral to allergist if no time for training	N/A
Long-term decision for the continued need of AAIinj	Should be reviewed by an allergist	Consider refer to allergy/immunology specialist for long term management, including evaluation, diagnosis and treatment	Normally yearly review by GP ± specialist review to ascertain if allergy persists or new allergies have developed	Long-term prescription not required if allergens can be avoided; or desensitization has been performed	Yearly review of action plan (decision not restricted to allergist but also other healthcare professionals)	Yearly review of AAIinj use, action plan, management of comorbidities by physicians, preferably allergists/immunologists

AAInj, adrenaline autoinjectors; VIT, venom immunotherapy; AED, Accident & Emergency Department; N/A, not available; NSAIDs, nonsteroidal anti-inflammatory drugs; ACEI, angiotensin-converting enzyme inhibitors; A&E, accident and emergency; CVD, cardiovascular diseases; GP, general practitioner.

In contrast to other guidance documents, indications for AAIinj for specific anaphylaxis phenotypes such as cofactor augmented-, exercise induced-, and idiopathic anaphylaxis were not included in the consensus statements. The clinical presentations and epidemiology of cofactor augmented anaphylaxis may be different from Western populations and underrecognized in Hong Kong [15]. Patients' age and types of allergens are key factors in determining the need for AAIinj in current international guidelines (Table 5). Teenagers and young adults are considered as the high-risk age group; and food allergens like peanuts, tree nuts, and seafood as well as latex and aeroallergens are deemed allergens at high risk of

triggering anaphylaxis. However, our panel did not reach consensus on prescribing AAInj based on the ease of reliable allergen avoidance, reflecting that these important factors may be insufficiently acknowledged. Overall, the Steering Committee omitted specific statements for these conditions, which would hinder its generalisability for both nonallergists and allergists. Similarly, the panel did not agree that the decision for AAInj should be based on social context (e.g., occupation, remoteness from medical care), perhaps due to the proximity of emergency medical care in Hong Kong.

Lastly, these consensus statements serve as a reference with regards to prescription of AAInj in patients presenting to the acute care setting. We emphasize that the long-term decision for continued need for AAInj should be reviewed by an allergist. Upon discharge, an allergy referral should be triggered immediately in order to expedite any allergy investigations and review of the patient's emergency treatment plan. Patients should be informed that the need for AAInj may change following subsequent investigation results or change in clinical condition. The factors governing the final number of AAInj prescribed for each individual patient is beyond the scope of this document but we recommend that only one AAInj should be prescribed prior to review by an allergist. It is critical to highlight the circumstances for AAInj use and to ensure that the medication is correctly administered by observing directly the patient activating the AAInj (into an orange for example) after formal training had been delivered by a health professional. Given the limited number of allergy centers in Hong Kong's public hospital system (only Queen Mary Hospital for adults; Princess Margaret Hospital, Prince of Wales Hospital, Queen Elizabeth Hospital, and Queen Mary Hospital for pediatrics), patients may also need to consider consulting a private allergist. Maintenance of good patient communication at all times is imperative.

The Delphi method is a popular method used for development of consensus statements, given the advantages of anonymity, structured flow of information and opportunity for feedback and revision. However, potential limitations include lower response rates and time taken to complete the questionnaires. The Consortium emphasizes it has not provided a set of evidence-based recommendations, instead they are intended to highlight certain areas which require future research so that any guidance in the future can be evidence-based.

With the advent of more local data and expertise, we hope these statements will be superseded with more robust and specific guidance. Plans for further collaboration with local expertise as well as other specialties (such as general practice, family medicine, and internal medicine) to potentiate these efforts are currently underway. Meanwhile, we hope the present consensus statements will facilitate the pragmatic management and appropriate prescription of AAInj by front-line physicians when treating patients at risk of anaphylaxis in Hong Kong.

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