

Received Date : 31-Aug-2015

Accepted Date : 03-Sep-2015

Article type : Research Letter

Prescription of Adrenaline Auto-Injectors – A *National Survey of UK Allergy Specialists*

Mamidipudi T. Krishna*#, Pia A. J. Huber#, Shuaib M. Nasser#+, Pamela W. Ewan#+, Andrew T. Clark#+

**Department of Allergy and Immunology, Birmingham Heartlands Hospital and Aston University, Birmingham, UK*

#British Society for Allergy and Clinical Immunology, London, UK

+Allergy department, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Key words: *Adrenaline auto-injector, anaphylaxis, mastocytosis, food allergy*

Short title: *UK national survey of prescription of adrenaline autoinjectors*

Corresponding Author

Dr. M. T. Krishna
Department of Allergy and Immunology
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham
B9 5SS
UK
Tel: +44 121 4241807
Fax: +44 121 4243229
Email: mtkrishna@yahoo.com

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/cea.12641

This article is protected by copyright. All rights reserved.

Anaphylaxis is a life-threatening systemic reaction affecting all age groups prompting early administration of adrenaline (1, 2). Most cases of anaphylaxis occur in the community, thus underlining the importance for the provision of adrenaline auto-injector/s (AAIs), appropriate counselling and education for the patient (and carers where relevant) and school staff in children. Whilst foods are the commonest triggers in children, drugs, foods, idiopathic anaphylaxis (IA) and insect stings are common causes in adults (3).

The European Academy of Allergy and Clinical Immunology (EAACI) published a position paper in 2014 listing indications for prescription of AAIs (4). This involves evaluating the risk of accidental exposure to the implicated allergen, severity of previous reaction/s, possibility of recurrent reactions and due consideration for underlying co-morbidities, access to emergency medical care and patient/parental anxiety or preference. The recurrence rate of allergic reactions depends on several factors including ease of avoidance of allergen/trigger, age, compliance with advice, quality of training offered, confidence in the use of AAIs and may be potentially influenced by co-factors such as infection, alcohol, stress and nonsteroidal anti-inflammatory drugs (NSAIDs) particularly in patients with exercise induced anaphylaxis (EIA), food-dependent exercise induced anaphylaxis (FDEIA) and idiopathic anaphylaxis (IA).

Since a multitude of factors influence the decision making process relating to prescription of AAIs, there is likely to be considerable heterogeneity in clinical practice. The main objective of this study was to survey AAI prescribing practices amongst members of the British Society for Allergy and Clinical Immunology (BSACI). This included information on professional background, types of adrenaline devices prescribed, patient selection criteria based on aetiology, severity of reaction/s and co-morbidities, if and what type of education was offered on recognition and treatment of reactions, provision of a written plan and if annual re-training was included in the care plan.

Methods

In September 2014 all BSACI members registered as consultants and general practitioners [GPs] providing allergy care (n=520) were invited to participate *via* email with a web link to the 'Survey Monkey' online questionnaire. The survey was open for 74 days during which five reminders were sent.

The survey questionnaire (Appendix-1) was developed by the authors and reviewed by the BSACI Standards of Care Committee. Data was collated using surveymonkey.com software (Palo Alto, CA, USA). Participants were asked to respond to all the questions if they prescribed AAIs in their clinical practice. For some questions, multiple responses and free text comments were permitted.

Questions relating to severity of reactions were constructed based on the Brown grading system described previously (5).

Results

1. Respondents: The response rate was 42% (n=215 of 517 individuals emailed [3 emails bounced]) of whom 207 (92%) prescribed AAI in their clinical practice. This comprised respondents from 100 different National Health Service (NHS) Trusts/Health Boards in the UK. Four respondents did not specify details of their employer, 1 specified to be working in Ireland, 1 was from the private sector and 2 from community services. 61% (n=130) of respondents were paediatricians, 20% (n=42) were adult physicians and 20% (n=43) involved in adult and paediatric allergy practice. The specialty breakdown of respondents were as follows: paediatric allergist (n=33 [15%]), allergist (n=27 [13%]), general paediatrician with an interest in allergy (n=88 [41%]), clinical immunologist with an interest in allergy (n=28 [13%]), respiratory physician with an interest in allergy (n=10 [5%]), dermatologist with an interest in allergy (n=6 [3%]), general practitioner [GP] (n=15 [7%]) and others (n=8 [4%]).
2. Devices prescribed: The following AAIs were prescribed by respondents: Epipen (91.6%), Jext (48.4%), Emerade (8.4%) and Anapen (0.5%). 32.5% respondents advised patients routinely to carry 1 AAI at all times, 66% two AAIs and 0.5% advised 3, 0.5% 4 and 0.5% >4 AAIs.
3. Patient selection: Details regarding patient selection for AAIs with respect to aetiology and severity of index reaction are summarised in Figure-1 and Table-1. Common food allergies for which respondents (n=192) routinely prescribed AAI were as follows: nut allergy (86%), fruit allergy (12%), oral allergy syndrome (1.6%), fish allergy (41%), shell fish allergy (44%), egg allergy (32%), milk allergy (29%), wheat allergy (20%), seed allergy (37%) and others (24%).
4. Training: This was offered by doctors and nurses of varying experience within the clinical service although in over two thirds of clinics training was carried out by consultants and allergy specialist nurses. 89% of the respondents routinely provided a written document outlining self-management of acute allergic reactions. In addition, respondents also directed patients to other resources regarding self-management of anaphylaxis including video/DVD (54.5%), 'app' (4.8%) and website/s (74.6%). Leaflets provided by the manufacturer and those available *via* charities including Anaphylaxis Campaign, Allergy UK and BSACI were also recommended. 105/152 (69%) of the respondents reviewing patients <16 years liaised with school/community nurse. Annual re-training was provided by only 52% of respondents. Some respondents wrote free text comments. These regarded lack of resource, that their clinic was 'one stop', that they asked the patient's GP to provide re-training or provided patient support group meetings or reviewed less frequently (e.g.: once every 2 years).
5. When to administer AAI: 3.2%, 81% and 76% of respondents advised patients to administer AAI for mild, moderate and severe systemic reactions respectively, as per

grading described by Brown et al (6). The majority (69%) of respondents advised patients to administer the second AAI if symptoms did not improve >5-10 minutes after the first dose. 14.7% and 12.4% advised patients to administer a second dose if symptoms did not improve after 2-5 minutes or >10 minutes respectively. All respondents advised their patients to seek urgent medical attention following administration of AAI.

6. Posture: These data are not presented since this question (Q.15) was regarded in retrospect as being unclear by the authors with respect to not being specific about hypotension.

Discussion

This study highlights the considerable heterogeneity in several important aspects of long term management of anaphylaxis amongst UK allergy specialists including patient selection criteria, types of devices prescribed, number of AAIs patients are asked to carry at all times, provision of written treatment plan and annual retraining/counselling.

Epipen (now replaced by Epipen 2) is the most commonly prescribed AAI in the UK and the likely reason is that it has been available for the longest duration of time possibly leading to greater familiarity amongst health care professionals. Jext was launched in the UK in the last 4-5 years and is the second most commonly prescribed device. Emerade was licensed more recently and may be prescribed more frequently in the future given the option of a larger dose (0.5 mg). Whilst having different devices offers greater choice for patients, it also adds to the complexity of the training process and potentially leads to confusion amongst health care professionals, patients and school staff involved in the care of children with allergy.

Just over two thirds of respondents advise patients to carry two AAIs at all times. There is no evidence from prospective studies that two AAIs are required for treatment of anaphylaxis in the community or indeed that it reduces occurrence of near-fatal or fatal episodes. The EAACI position paper states the circumstances when prescribing an AAI should be considered and suggests indications when prescription of 2 AAIs should be considered (4). These are for patients with severe or uncontrolled asthma, those with a raised baseline serum tryptase or mast cell disorder, previous requirement of ≥ 2 doses to treat an acute episode within a short period during a reaction, those with high body mass index (BMI)/obesity or poor access to emergency medical care (4).

The majority (78-89%) of respondents in this survey routinely consider prescription of AAIs for food allergy, venom allergy, IA, FDEIA and EIA and this is in keeping with EAACI recommendation (4). A smaller proportion of respondents (22%) would also consider prescription of AAI for drug allergy which is difficult to justify given that these are avoidable triggers. Whilst cutaneous and systemic mastocytosis are benign conditions and asymptomatic in most, they are recognised as an independent risk factor of potentially severe, fatal or near-fatal anaphylaxis (6) to bee and wasp stings and only 28% of respondents routinely consider prescription of AAI for this high risk group. A significant majority (86%)

Accepted Article

routinely consider AAIs for patients with nut allergy, a lower proportion would do so for other food allergies including fruits, fish, shellfish, egg, wheat, milk and seeds. There was concordance with respect to consideration of AAIs based on severity of previous reactions with the vast majority prescribing AAIs for those with moderate-severe reactions (87.5-99%) and milder reactions in the presence of co-morbidities (68%) such as asthma, COPD, cardiac disease or elevated baseline serum tryptase/mastocytosis.

All respondents advised their patients to seek urgent medical attention following administration of AAI. The majority (89%) of respondents provided a written plan for self-management of anaphylaxis and directed their patients to other useful resources as well but it is a concern that 11% did not. Furthermore, 31% of respondents involved in the management of children do not liaise with school or community nurses regarding the child's allergy status which is vital to ensure education and training of school staff to allow optimal acute care to be delivered promptly and efficiently in the community.

Previous studies have shown that patients' competence with use of AAIs is sub-optimal despite undergoing training (7) illustrating the importance of refresher sessions and our data suggests that only 52% offered annual re-training. A potential alternative may be to ensure that pharmacists provide training at the time of dispensing and only a device with which the patient or carer is familiar and trained should be prescribed or dispensed. Practice nurses should also provide training when repeat prescriptions are issued. Practical training using a trainer pen should be used at all points of training. Most patients coming to hospital allergy clinics already carry an AAI, and have been 'trained' by being asked to read the leaflet. Electronic resources such as telemedicine, web-based training, provision of 'apps' on smart phones or DVDs may be considered but would need validation in prospective studies. There is some evidence to suggest that a multidimensional and multidisciplinary approach together with provision of printed educational and online material improves knowledge and correct use of AAI and reduces reaction rate in food allergy (8, 9). Factors potentially limiting regular re-training of patients in the UK may be related to geographical inequality of allergy services in the UK NHS, the unmet need (high patient/specialist ratio), restricted funding and lack of standardisation of care and unavailability of national guidelines on this subject (at the time this survey was carried out).

This study has some limitations. First, the response rate was moderate at 42%. However, respondents were from 100 different NHS Trusts of varying professional background, thus likely to provide a fair reflection of current clinical practice in the UK. Second, questions relating to patient selection for AAI should be considered 'generic' or only in broader terms since decision making regarding provision of AAI is ultimately based on several factors that are patient-specific such as dose of allergen triggering 'index reaction', severity of reaction, speed of onset of symptoms, asthma (and other co-morbidities) and its severity, BMI, patient (parent) preference/anxiety and access to emergency medical care. These points add to the complexity and are difficult to capture in an online electronic survey. Third, provision of allergy service in UK is unique in several ways. It is delivered by allergists (adult and paediatric), immunologists, general paediatricians, respiratory physicians, dermatologists and GP's with an interest in allergy with heterogeneity with respect to their training, experience

and infrastructure of their service. Furthermore, lack of national guidelines or consensus to define best practice or bench mark relating to long term management of anaphylaxis may have contributed to the heterogeneity.

In conclusion, there is considerable variation surrounding prescription practice of AAI's amongst UK physicians practising allergy, specifically on issues relating to patient selection, education and training. There is an urgent need for a guideline-based approach to prescribing these AAI's.

Acknowledgement: The authors are grateful to the members of Standards of Care Committee of BSACI for reviewing the study questionnaire. We would also like to thank all BSACI members who have generously given their time to participate in this survey.

Conflicts of Interests: MTK's department has received an educational grant for the PracticAllergy course from MEDA and ALK Abello in recent years.

Contributions: MTK created the questionnaire and wrote the manuscript. PAJH facilitated the survey for BSACI, collated and summarised data and ensured quality assurance was maintained. PAJH, SMN, PWE and ATC provided critiques for the questionnaire and manuscript.

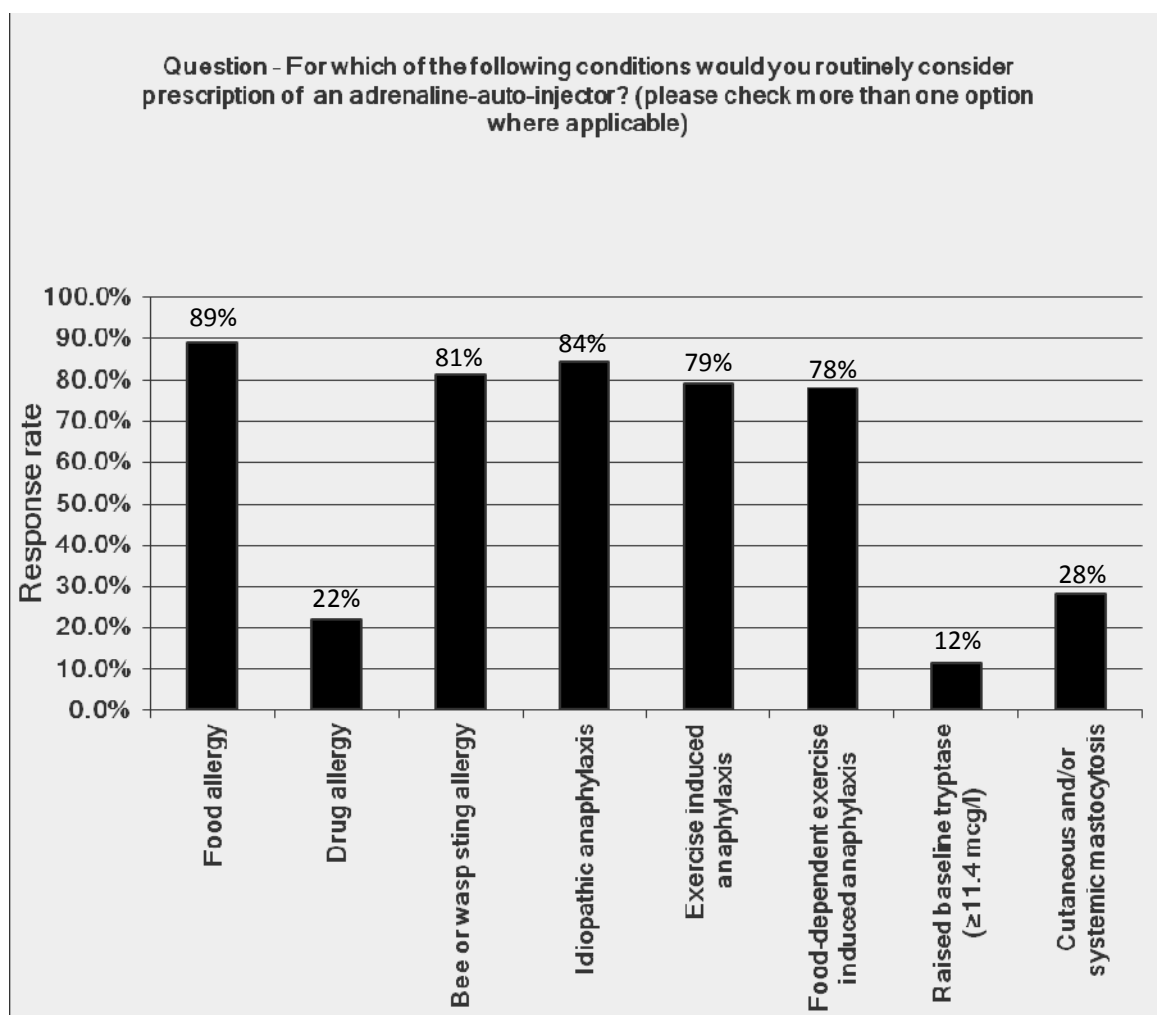


Figure-1: The prescription of AAIs by respondents as per aetiology of anaphylaxis. 192 respondents answered this question and data is shown as % in 'Y' axis.

Table-1

SEVERITY OF REACTION#	‘Yes’ n= (%)	‘No’ n= (%)
Mild (generalised/localised rash, pruritis, flushing, rhinitis/conjunctivitis, angioedema with no cardio-respiratory compromise) without co-morbidities	25 (13%)	167 (87%)
Moderate (as under ‘mild’ with any of the additional features – shortness of breath, wheeze, nausea, vomiting, diarrhoea, GCS* – 15/15) without co-morbidities	168 (87.5%)	24 (12.5%)
Severe (as under ‘moderate’ with any of the additional features - loss of consciousness, syncope, dizziness, light headedness, stridor/laryngeal oedema, hypoperfusion-related seizure or myocardial ischaemia, systolic BP** < 90 mm Hg (adults), GCS* < 15/15) without co-morbidities	190 (99%)	2 (1%)
Mild (with co-morbidities, e.g.: asthma, COPD, cardiac disease, raised baseline tryptase/mastocytosis)	130 (68%)	62 (32%)
Moderate (with co-morbidities, e.g.: asthma, COPD, cardiac disease, raised baseline tryptase/mastocytosis)	183 (95%)	9 (5%)

#number of respondents for this question = 192

Question - Would you consider prescription of an adrenaline auto-injector if the ‘index reaction’ was: (please check more than one option where applicable) [*May not apply in young children; **age-related hypotension –BP:<70mm Hg in children of 1 month -1year, <70mm Hg + (2 x age) in children of 1-10 years, and <90mm Hg in children of 10-17 years.]. Severity of reactions based on Brown grading system(5)

REFERENCES

1. Simons FE, Arduzzo LR, Bilo MB, El-Gamal YM, Ledford DK, Ring J, et al. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol 2011;127(3):587-93 e1-22.
2. McLean-Tooke AP, Bethune CA, Fay AC, Spickett GP. Adrenaline in the treatment of anaphylaxis: what is the evidence? BMJ 2003;327(7427):1332-5.
3. Simons FE, Arduzzo LR, Bilo MB, El-Gamal YM, Ledford DK, Ring J, et al. World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis. World Allergy Organ J 2011;4(2):13-37.
4. Muraro A, Roberts G, Worm M, Bilo MB, Brockow K, Fernandez Rivas M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy 2014;69(8):1026-45.
5. Brown AF, McKinnon D, Chu K. Emergency department anaphylaxis: A review of 142 patients in a single year. J Allergy Clin Immunol 2001;108(5):861-6.
6. Rueff F, Placzek M, Przybilla B. Mastocytosis and Hymenoptera venom allergy. Curr Opin Allergy Clin Immunol 2006;6(4):284-8.

7. Kastner M, Harada L, Waserman S. Gaps in anaphylaxis management at the level of physicians, patients, and the community: a systematic review of the literature. *Allergy* 2010;65(4):435-44.
8. Kapoor S, Roberts G, Bynoe Y, Gaughan M, Habibi P, Lack G. Influence of a multidisciplinary paediatric allergy clinic on parental knowledge and rate of subsequent allergic reactions. *Allergy* 2004;59(2):185-91.
9. Sicherer SH, Vargas PA, Groetch ME, Christie L, Carlisle SK, Noone S, et al. Development and validation of educational materials for food allergy. *J Pediatr* 2012;160(4):651-6.

Appendix-1

Questionnaire

1. Name of NHS Trust you work for
2. Who do you treat in your clinic?
 - a. Both (Adults and Children)
 - b. Adults only
 - c. Children only
3. Which of the following best describes your specialty?
 - a. Allergist
 - b. Clinical Immunologist with an interest in allergy
 - c. Respiratory Physician with an interest in allergy
 - d. Dermatologist with an interest in allergy
 - e. ENT surgeon with an interest in allergy
 - f. Gastroenterologist with an interest in allergy
 - g. Paediatric Allergist
 - h. Paediatrician with an interest in allergy
 - i. GP with an interest in allergy
 - j. Other (please specify)
4. How frequently do you attend the BSACI Annual Meeting?
 - a. Yearly
 - b. Every two years

- c. Occasionally
- d. Other (please specify)

5. Is your main CPD Allergy?

- a. Yes
- b. No

6. Do you prescribe adrenaline auto-injector in your clinical practice?

- Yes
- No

If the answer is 'No', the responder is taken to the end of the questionnaire, otherwise it continues with question 7.

7. For which of the following conditions would you routinely consider prescription of an adrenaline-auto-injector (*please check more than one option where applicable*)?

- Food allergy
- Drug allergy
- Bee or wasp sting allergy
- Idiopathic anaphylaxis
- Exercise induced anaphylaxis
- Food-dependent exercise induced anaphylaxis
- Raised baseline serum tryptase (≥ 11.4 mcg/l)
- Cutaneous and/or systemic mastocytosis

8. Would you consider prescription of an adrenaline auto-injector if the 'index reaction' was: (please check more than one option where applicable) [*May not apply in young children; **age-related hypotension –BP:<70mm Hg in children of 1 month -1year, <70mm Hg + (2xage) in children of 1-10 years, and <90mm Hg in children of 10-17 years.]

- **Mild** (generalised/localised rash, pruritis, flushing, rhinitis/conjunctivitis, angioedema with no cardio-respiratory compromise) without co-morbidities
 - Yes
 - No
- **Moderate** (as under 'mild' with any of the additional features – shortness of breath, wheeze, nausea, vomiting, diarrhoea, GCS* – 15/15) without co-morbidities
 - Yes
 - No
- **Severe** (as under 'moderate' with any of the additional features - loss of consciousness, syncope, dizziness, light headedness, stridor/laryngeal oedema, hypoperfusion-related seizure or myocardial ischaemia, systolic BP** < 90 mm Hg (adults), GCS* < 15/15) without co-morbidities
 - Yes

- No
- **Mild** (with co-morbidities, e.g.: asthma, COPD, cardiac disease, raised baseline tryptase/mastocytosis)
 - Yes
 - No
- **Moderate** (with co-morbidities, e.g.: asthma, COPD, cardiac disease, raised baseline serum tryptase/mastocytosis) – Yes/No
 - Yes
 - No

Please add any comments

9. For which of the following common food allergies would you routinely prescribe an adrenaline auto-injector (*please check more than one option where applicable*)
 - a. Nut allergy
 - b. Fruit allergy
 - c. Oral allergy syndrome
 - d. Fish allergy
 - e. Shell fish allergy
 - f. Egg allergy
 - g. Milk allergy
 - h. Wheat allergy
 - i. Seed allergy
 - j. Other (please specify)

10. How many adrenaline auto-injectors do you routinely advise your patient to carry at all times?
 - a. 1
 - b. 2
 - c. 3
 - d. 4
 - e. >4

11. When would you advise your patient to administer the second dose?
 - a. 2-5 minutes after first dose if symptoms have not improved
 - b. >5-10 minutes after first dose if symptoms have not improved
 - c. > 10 minutes after first dose if symptoms have not improved

12. Do you advise your patient to seek medical attention following administration of adrenaline?
 - a. Yes
 - b. No

13. Which adrenaline auto-injector does your clinic usually prescribe (*please check more than one option where applicable*)?
- Epipen
 - Anapen
 - Emerade
 - JEXT
 - Other (specify)
14. At what stage of the systemic reaction do you advise the administration of adrenaline auto-injector (*Please check more than one option where applicable*)
- Mild symptoms** : generalised/localised rash, pruritis, flushing, rhinitis/conjunctivitis or angioedema with no cardio-respiratory compromise
 - Moderate symptoms**: as under 'mild' with any of the additional features – nausea, vomiting, diarrhoea, shortness of breath, wheeze, throat discomfort, or mild tongue swelling
 - Severe symptoms**: as under 'moderate' with any of the additional features - loss of consciousness, syncope, impending doom, sweating, pallor, dizziness, light headedness, stridor, impaired vision, or floppiness (infants)
 - Other** (Please specify)
15. Do you specifically advise patients to adopt a recovery position during anaphylaxis?
- Yes
 - No
16. Who offers the self-injectable adrenaline auto-injector training in your clinic? (*please check more than one option where applicable*)
- Specialist allergy nurse
 - Junior doctor
 - Consultant
 - Nobody / assume it will be done by GP or pharmacist
 - Other (please specify)
17. Do you routinely offer a written emergency treatment plan to patients who carry self-injectable adrenaline auto-injector ?
- Yes
 - No

Please add any comments

18. Which of the following do you provide or direct the patient to as a supplement to self-management of anaphylaxis (*please check more than one option where applicable*)
- Video/DVD
 - 'App'
 - Refer to website
 - None
 - Other (please specify)
19. For patients who are less than 16 years old, do you liaise with school/community nurses regarding the patients allergy/allergies?
- Yes
 - No
 - I do not review patients <16 years old
20. Does your clinic provide annual re-training/counselling for patients regarding self-management plan for acute allergic reaction or anaphylaxis?
- Yes
 - No
- Please add any comments
21. Who in your clinic provides this annual re-training/counselling for patients regarding self-management plan for acute allergic reaction or anaphylaxis (*please check more than one option where applicable*)

- Specialist allergy nurse
- Junior specialist trainee doctor
- Allergy Consultant
- Others (please specify)