A systematic review of patients', parents' and healthcare professionals' adrenaline auto-injector administration techniques

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Abstract

Introduction

In order to enable fast treatment response to anaphylactic reactions, adrenaline auto-injectors (AAI) have been developed and manufactured. It has been reported in several studies that administration technique is suboptimal. The primary purpose of this study was to review the nature and extent of the deficiencies in administration technique amongst patients, parents/caregivers and healthcare professionals.

Methods

Relevant publications were identified between 1998-2015 using two search methods: a keyword search in Embase, Pubmed, BNI and CINAHL and a search of reference lists of relevant articles.

Results

Twenty three studies met the inclusion criteria. Overall 37% of patients, 32% of parents/caregivers and 21% of healthcare professionals demonstrated correct administration technique. For studies which employed a before and after-training study design, correct technique was achieved in 77% of patients, 79% of caregivers and 65% of healthcare professionals. The most consistently observed error was the failure to hold the device in place for the recommended time. For patients, factors associated with good technique were being aged over 18, trained in AAI administration by an allergist, prescribed an AAI for more than 30 months, having a history of severe anaphylaxis and membership of a support group. For parents/caregivers in addition to those mentioned, being given a training device with which to practice, improved technique.

Discussion

There was wide variation in administration techniques reported. However, studies designed using before and after-training show that even a brief demonstration and educational intervention can improve technique. Further studies are required to design and pilot acceptable and cost-effective educational materials.

What this paper adds?

- Numerous observational studies and anecdotal evidence have suggested that patients and health professionals use of adrenaline auto-injectors (AAIs) is suboptimal
- This review identifies which steps to administration are contributing to this failure and what factors are linked to success
- This review highlights the step to administration most frequently failed (holding the device in place for the recommended time)
- Additionally, this review identifies successful interventions and patient-factors (e.g. severity of allergy, age of AAI-owner) which are shown to improve administration
- The identification of these successful approaches are timely as the European Medicines Agency have released a call for better training tools recommended to support patients who use AAIs

Abbreviations

AAI	Adrenaline auto injector
EAACI	European Academy of Allergy & Clinical Immunology
HCPs	Health Care Professionals
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
MMAT	Mixed Method Appraisal Tool
EMA	European Medicines Agency

Introduction

Adrenaline auto-injectors (AAIs) are first line treatment for anaphylaxis in the community. Prompt injection with adrenaline can be life-saving and abort the progression of the anaphylactic reaction, allowing time to seek formal medical assessment and management. The European Academy of Allergy and Clinical Immunology (EAACI) describes six absolute indications for the prescription of an AAI including food and latex anaphylaxis, exercise-induced anaphylaxis, idiopathic anaphylaxis, moderate to severe persistent asthma with food allergy, venom allergy or underlying mast cell disorder (1). Unlike other allergic conditions, such as rhinitis and eczema, whose prevalence appears to be stabilising over the last decade, anaphylaxis appears to be increasing (2). Rates of hospital admissions in the UK for all causes of anaphylaxis increased seven-fold between 1992-2012 whilst prescriptions for AAIs increased four-fold from 1998-2012 (3). Anaphylaxis is the cause of approximately 20 deaths each year in the UK (4).

AAI is the main emergency treatment for individuals experiencing anaphylaxis, but its effectiveness is largely reliant on correct administration. Over the last few years, studies have assessed healthcare professionals', patients' and parents' administration techniques and skills with respect to the emergency management of anaphylaxis. The primary purpose of this review was to assess the magnitude of the deficit in administration technique and to summarise which stages in the process of administering AAIs are most problematic. Reviewing data from a broad number of studies will help inform the development of AAI design and educational interventions for improving future utilisation.

Methods

Search strategy

A systematic review of literature published between January 1998 to August 2015 was undertaken using four databases (Embase, Pubmed, BNI and CINAHL) (see online supplementary appendix 1). Subsequently a search of the reference lists from relevant papers was performed. No language restrictions were applied.

Inclusion and exclusion criteria

This review focused on studies that included an assessment of AAI technique (either by demonstration or questionnaire) in three populations: patients (paediatric and adult), parents/caregivers of children diagnosed with anaphylaxis and prescribed an AAI device and health care professionals (HCPs). Studies were eligible if they were quantitative in nature including cross-sectional/observational studies, before-and-after studies or randomised controlled trials.

Study selection

Two reviewers (CJ and AT) independently reviewed the titles and then abstracts of articles generated by the electronic bibliographic search, rejecting any articles that clearly did not meet eligibility criteria. There was no disagreement between reviewer's regarding the eligibility of the studies although both reviewers were unsure of inclusion of three studies. These were discussed with a third author (HS) and a consensus reached. The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) (5) flow diagram was used to summarise the systematic review process (Figure 1). Authors of relevant published conference abstracts were contacted to determine if full study details were available.

Data extraction

The process of AAI administration is frequently described by manufacturers and researchers as six component steps (device recognition, removal of safety cap, selection of appropriate injection site, application of correct end of device to body, administration of adrenaline and retaining AAI in

place). We adopted these commonly used steps to prepare a standardised data extraction form and extracted data from the papers on participants' ability relating to each of these steps (Tables 1-3). One reviewer (AeT) extracted the data with a second (CJ) cross-checking 50% to ensure accuracy which was high. In addition we noted any additional skills or knowledge assessed, (i.e. checking expiry date of the AAI), and any factors which were associated with correct administration technique.

Assessment of study quality

All studies included in the systematic review were evaluated for quality using the mixed methods appraisal tool (MMAT) (6). The MMAT has proven to be an effective and practical quality assessment tool for systematic reviews which include different study designs or mixed methods (7). The tool consists of two screening questions followed by four criteria for the appraisal of study quality according to study design. The MMAT enabled all studies included in this review to be assessed within each of the methodological domains used. The MMAT scores range from to 0% (no criterion is met) to 100% (all four criteria are met). Studies were assessed by one reviewer experienced in conducting quality assessments (CJ). 25% of the studies were checked by a second reviewer with any disagreement being resolved by discussion until consensus was reached.

Results

From 1434 studies a total of 23 studies met the inclusion criteria (Figure 1). Eight studies came from the UK (8-15), six from North America (16-21), four from Turkey (22-25), three from Australia (26-28), and two from Israel (29,30) (Tables 1, 2 & 3). Sixteen studies were cross-sectional five were before and after studies, one was a longitudinal survey and one was a randomised controlled trial. Nineteen papers requested participants to demonstrate use of the AAI. Four studies used a questionnaire technique in which the participants responded to true/false questions or described their technique. The papers varied in their focus, four assessed the techniques and skills of patients only, eight focussed on parents/caregivers only and six papers on HCPs only. Five

studies had broader focus; four of which included patients and parents/caregivers, and one study included patients, parents/caregivers and HCPs. The findings of the studies are presented to reflect the three populations of interest; patients (9 studies), parents/caregivers (13 studies), and HCPs (7 studies), with studies reporting multiple populations presented in each of the relevant tables (Tables 1-3). The studies which employed a before and after design or RCT of the effect of instruction on AAI technique were isolated in order to clearly reflect on these findings (Table 4).

Patients

We identified nine studies (550 participants) which documented patient AAI administration technique; all were based in allergy clinic settings (Table 1). Administration assessments varied from five to nine steps. Overall, prior to receiving any instruction or demonstration as part of the study, 37% of patients were able to demonstrate or detail correct administration technique (range 6-74%). This rose to 77% overall for two studies which reported a before and after instruction design (Table 4). The most consistently reported error was the failure to hold the AAI in place for 10 seconds (step 6 Table 1), followed by a failure to apply enough pressure to activate (step 5 Table 1). Six studies reported whether patients had received previous training on how to use AAI, on average 71% patients reported either visual instruction using a trainer device or verbal instruction (range 11-100%). Five studies identified five patient-related factors associated with good AAI technique: being aged over 18, being trained by an allergy specialist, having an AAI for more than 2½ years, membership of a support group and having a history of severe anaphylaxis.

Parent/caregivers

We identified 13 studies documenting parental/caregiver AAI administration technique, ten of which reported the number of parents/caregivers participating (1182 participants). Eleven studies were based in allergy clinics, one study recruited participants from local schools and another from support groups and a private allergy clinic. Out of the 5 studies which reported findings for both patients/caregivers and patients, three did not provide separate results for parents/caregivers and patients and report patients and parents/caregivers results together. Overall, prior to receiving any

instruction or demonstration, 32% of parents/caregivers were able to demonstrate or detail correct administration technique (range 6-57%). This average rose to 79% in the five studies which reported a randomised trial or before and after instruction design in parents/caregivers (Table 4).

Amongst parents or caregivers, the most common errors were the same as those reported for patients; a failure to hold the AAI in place for 10 seconds (step 6), followed by a failure to apply enough pressure to activate (step 5) (Table 2). Nine studies reported whether parents or caregivers had received training or demonstration on how to use AAI, on average 70% said they had received some form of training (range 11-100%). Seven studies reported eight parental/caregiver related factors which were associated with proper AAI administration technique which were having a child with: more serious reactions, an AAI for more than 2½ years, membership to a support group, an AAI prescribed from secondary care, an AAI prescribed by an allergy specialist, insect sting allergy, a training device with a Auvi-Q (audio-prompt) device.

Health care professionals (HCPs)

We identified seven studies which documented HCPs AAI administration technique (923 participants); two were based in primary care, two in paediatric departments and one each in an allergy clinic, community pharmacy and a medical conference (Table 3). Overall, 21% of HCPs were able to demonstrate proper AAI technique prior to receiving any demonstration or instruction. One study reported a before and after instruction study design and showed an increase from 18% to 65% in proper AAI technique amongst community pharmacists (Table 4). The most commonly reported error was the failure to hold the AAI in place for at least 10 seconds (step 6) (Table 3). Accidental digital injection would have occurred in 21% of participants. One study reported the risk of accidental digital injection reduced from 36% to 7% post-education. Three studies reviewed how many HCPs provided training on AAI technique to their patients, which was 28% overall (range 19-51%). In the two studies which looked at factors associated with proper AAI administration technique amongst HCPs, two factors were identified: being a pharmacist and having a more general awareness of anaphylaxis management (specifically asking patients about a management

plan, advising patients to call an ambulance after administration and explaining the side effects of adrenaline).

Quality assessment

Of the 23 studies included in this systematic review, no studies scored 100%, five studies scored 75% (three criteria met), nine scored 50% (two crirteria met), seven scored 25% (one criterion met) and 2 studies scored 0 (Tables 1-3, online supplementary online appendix 2). Shortcomings in study quality were often found in the description of the sampling strategy used and the failure to include a sample size calculation. It was also difficult to ascertain the response rate of studies and any differences between responders and non-responders. Patients were often inadequately described and it was not always clear who the respondents were. Although most studies adequately reported how AAI administration was assessed, this varied significantly between studies.

Discussion

Administration technique and skills in using AAI have been documented to be consistently deficient over the last 17 years across six different countries. Correct administration technique varied widely but overall was 30% for patients, 32% for parents/caregivers and 21% for HCPs. For studies which employed a before and after design of the impact of training, correct technique was achieved in 77% in patients, 79% in caregivers and 65% in HCPs. Approximately 70% of patients and parents/caregivers reported receiving some form of AAI training yet only 28% of HCPs reported providing training. The most consistently observed error common to all three populations was the failure to hold the device in place for the recommended time, and additionally for patients and parents/caregivers, the failure to apply enough pressure to activate.

In addition to observing correct administration technique, 14 studies reported factors related to proper administration technique. For patients, being aged over 18, trained in AAI use by an allergist, prescription of an AAI for more than 30 months, history of severe anaphylaxis and

membership of a support group, were all related to better technique. In addition to those already mentioned, for parents/caregivers, having a training device with which to practice and using an Auvi-Q instead of an EpiPen or Anapen were also correlated with better administration technique. Pharmacists and other HCPs who had a greater general awareness of managing anaphylaxis also demonstrated better administration technique.

This is the first systematic review to explicitly detail the deficiencies in HCPs', patients' and parent/caregivers' AAI administration technique. This review also identified seven studies which used a study design to improve administration technique. Several educational approaches to improving technique were reported varying from a simple two minute demonstration of administration using a training device to a multidisciplinary approach involving an individualised anaphylaxis management plan, followed by education from a clinical nurse specialist and a dietetic assessment to provide families with advice on food avoidance. The time between training and assessment varied from immediate to approximately one year indicating that some of the training techniques were effective at improving administration over a long term period. The identification of these successful approaches are timely as the European Medicines Agency have released a call for better training tools recommended to support patients who use AAIs (31).

There are some limitations to the conclusions drawn from this review. Results in three studies were not separated to reflect administration techniques of the patients and parents/caregivers giving a total score for both which could suggest why overall scores and most common errors were mirrored between these groups. Additionally, the estimates of correct administration technique may be optimistic for three reasons. Firstly, the majority of participants in these studies were self-selected with often no description of differences between responders and non-responders, and may reflect responder bias. However, we know from a recent study involving mothers of non-allergic children with no previous experience of AAIs that only 15% were able to administer the device (32), a figure which falls in the range of correct administration scores by experienced parents/caregivers found in this systematic review (6-57%). Secondly, although the majority of

studies used demonstration to assess administration (82%), self-reported questionnaires were used in the remaining studies indicating that findings may not reflect actual behaviour. Thirdly, it is difficult to capture how the high pressure situation of a “real-life” anaphylaxis emergency would impact AAI administration technique compared to the more controlled scenarios proposed in the research setting.

In relation to the scores used to determine correct technique in studies, these varied from zero to nine steps with some items not directly related or not critical to administration (i.e. awareness of an expiry date) which may underrepresent ability to administer device. The studies included in this systematic review related predominantly, but not exclusively, to one particular device (EpiPen). The introduction of newer AAIs such as the next generation EpiPen, Jext, Emerade and Auvi-Q may impact on future assessments, although the majority of these devices use the same/similar injecting mechanisms. The most recent study in this review compared AAI use between devices and found that when prescribed a new device without receiving specific training, successful administration rates for mothers were higher with Auvi-Q (an audio-prompt AAI) (93%) than other traditional devices (i.e. EpiPen, Anapen, Jext) (49%) (15). It is likely that correct administration rates will increase if audio-prompt devices are made readily available. However, the steps identified as being most likely to be performed incorrectly (e.g. holding the device for the recommended time and applying enough pressure to activate), are common to all AAIs and emphasising the importance of this to patients, parents/caregivers and HCPs during training is essential. Some may argue that the interval between triggering the device and removal of the needle need not be 10 seconds as research has found that for the EpiPen, delivery time is 0.3 seconds (33). However, there are no disadvantages to holding the device in place for a longer period as this discourages rapid removal and is consistent with the majority of manufacturer guidelines (Epi-Pen, Jext, Anapen), although the more recently introduced Auvi-Q recommends 5 seconds. Related to training, we observed a 2.5 fold increase in correct administration technique for patients and parents/caregivers and 3-fold increase in HCPs emphasizing the beneficial effect training can have on technique.

Two non-systematic short-cut reviews conducted in 2013 to determine knowledge of correct AAI use in parents of allergic children and doctors (34,35) failed to identify five key studies. Our more recent, robust and extensive systematic review involving four databases, including papers published in any language identified these five studies plus two more recently published studies. We also present evidence on the most commonly reported mistakes in administration technique, important for the design of future studies which need to move away from documenting poor technique and towards interventions to improve administration technique. Furthermore, our systematic review differentiates between patients, parents/caregivers and HCPs' correct use of auto-injectors and identifies factors related to successful administration technique.

Clinical implications

The lack of correct administration technique among patients and parent/caregivers is worrying, but of greater concern is the variation in techniques observed amongst HCPs. Familiarity with epinephrine as the first-line response in the treatment of anaphylaxis was widespread but fewer were able to detail correct auto-injector technique, suggesting that if prescribing AAI, HCPs could be misinforming or not informing patients how to use the device correctly. The latter is likely given the observation that the majority (70%) of patients and parent/caregivers received training on how to use the device yet only 28% of HCPs included in this review reported providing training. It may be useful to identify those who provide training (if not the HCPs in this review), to ensure that their methods, knowledge and resources are up-to-date. Also, only five studies looked at recognition of symptoms of anaphylaxis or indications for using AAI with wide variation in those which reported results. Indications for AAI use is important to address during patient consultation to avoid either inappropriate use and consequent emergency admissions or more importantly, fatalities from the delayed administration of AAI (36).

Indicators of poor technique and ability were found amongst those patients who were instructed on the use of device or cared for by general practitioners or non-allergy specialists compared to those

cared for by allergy specialists. Those cared for by an allergy specialist were more confident and more likely to carry and have the ability to activate the device. Other significant associations were found. For instance, several studies reported significant positive effects on technique and performance if the patient was a member of an allergy support group. Further work is underway to determine which aspects of support groups are important to patients in terms of knowing how and when to use their AAI but highlights the importance of recommending patients to join support groups. There was no effect on performance in relation to the time interval since training was received. Specifically, two studies showed that correct technique was no more likely to be demonstrated if training had been received in the last six months or over 24 months. This demonstrates the necessity for thorough training in the use of the device at initial consultation.

Future Studies

With this plethora of studies documenting poor administration technique it is time to concentrate on identifying and designing interventions targeting theses areas of poor technique highlighted. Patients and parents/caregivers should be involved in the design of training resources to ensure they are acceptable and understandable in order to address their learning needs. Amongst HCPs, training regarding the use of the device and how to communicate this effectively to patients should be addressed as well as ensuring training devices are available to supply to their patients. Successful educational materials and tools have been identified but further studies should be conducted to determine the cost-effectiveness of these approaches. Further research is required to address other important issues such, poor retention of information (by HCPs and patients/caregivers) after training, the frequency of re-training needed, and how to balance time needed to train versus HCPs' other time constraints.

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Statement of contribution by author:

CJ, HS and CD designed the protocol for the systematic review. CJ and AE conducted separate searches to ensure all eligible studies were identified and included. Data extraction was conducted by CJ and AE before verification by HS and CD. CJ and AE drafted the initial manuscript with substantial involvement from HS and CD.

Conflict of interest:

Dr Aisha El-Turki, Professor Helen E Smith, Dr Carrie D Llewellyn and Dr Christina J Jones declare that they have no conflict of interest.

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Figure1: PRISMA flow diagram for the identification of studies assessing healthcare professionals and patients' administration techniques of adrenaline auto-injectors

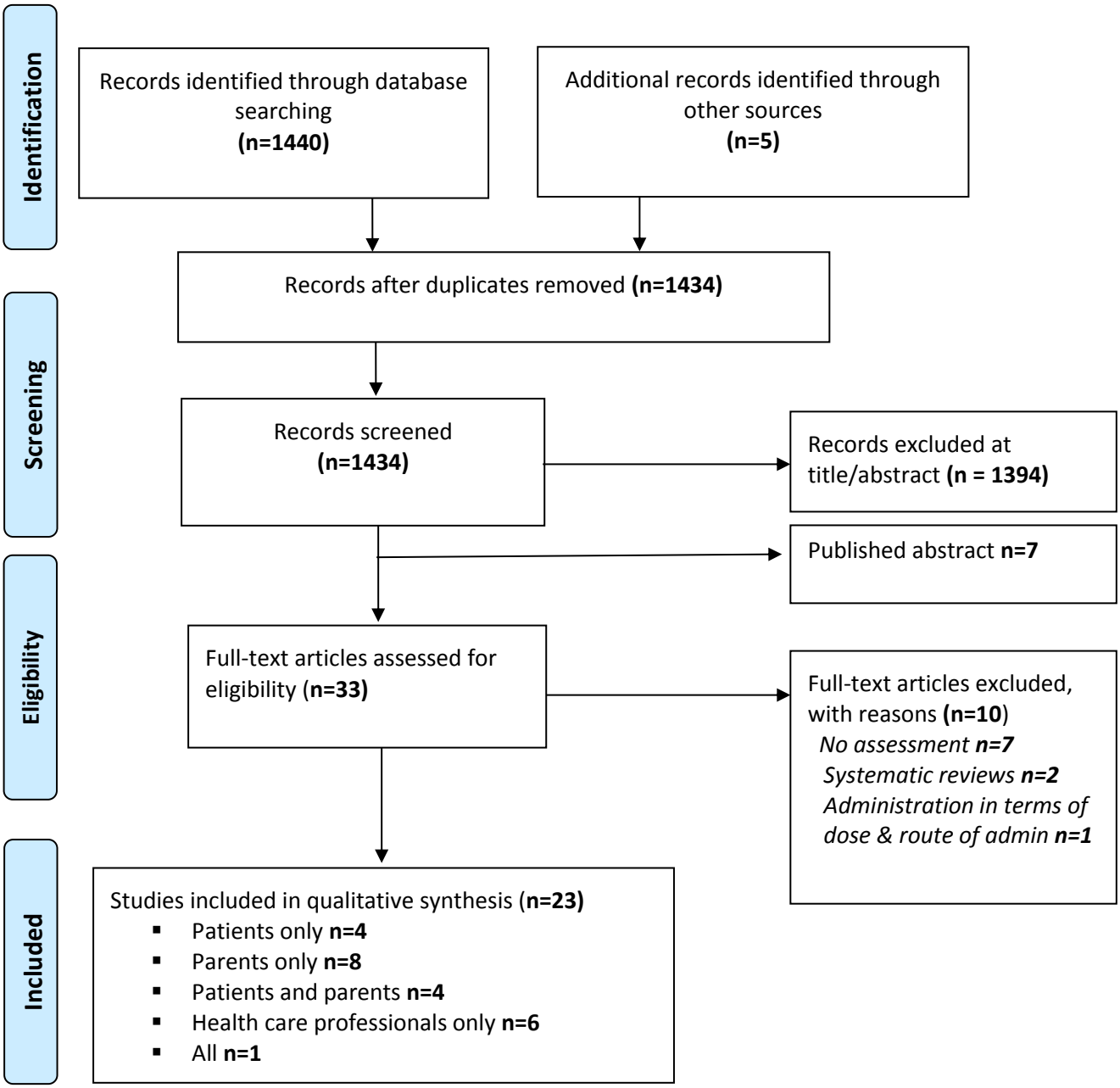

Table 1. Adolescent and adult patients' technique and skills administering an adrenaline auto-injector (Studies are presented in chronological order)

Studies (country, design, method of observation, quality assessment)	**Study population**	**% individuals correctly undertaking key steps of AAI administration (wording used)**						**100% correct**	**Additional observations**
		Device Recognition	**Removal of safety cap**	**Selection of appropriate injection site**	**Application of correct end of AAI to thigh**	**Administration of adrenaline**	**Holding AAI in place**		
Huang, 1998 USA Cross-sectional Assessment by demonstration 50%	98 patients **(83 aged <18y, 15 aged ≥18y)** For <12ys, parents were assessed (exact number not provided)	Not assessed	90% ("Remove the cap")	78% ("Press the Epi-PEN on the lateral thigh")	Not assessed	37% ("Press Epi-PEN until clicking sound is heard")	41% ("Hold Epi-PEN in place for at least 10 seconds")	Not reported	16% knew the circumstances in which the use of AAI is indicated 84% had two devices available 53% knew to use through clothing 97% aware of expiry date but 89% had a valid device with them 11% had previously been trained in how to use AAI (5% by an allergist and 6% by other physician)
Goldberg and Confino-Cohen, 2000 Israel Cross-sectional Assessment by demonstration 75%	**96 patients (n=72 aged <12y)** Children aged ≥12y were assisted in answering questions by parents and results indicate parental response (n=24)	Not assessed	82% ("Pulling out the grey safety tip")	82% ("Holding the device in palm")	82% ("placing the black tip on the outer thigh")	76% ("Pushing in hard until the trainer function is heard")	78% ("Holding it in place for 10 seconds")	36% patients ≥12 y	89% had previously been trained in how to use AAI (46% by an allergist, 12% by a nurse, 10% by a primary physician, 10% by a pharmacist, 1% by emergency department physician and 9% by a non-professional) Mean time since last training received was 2.6 years 18% received instruction with training device Proper injection technique was more common among patients >18years who were trained by an allergist
Sicherer et al., 2000 USA Cross-sectional	101 families of newly referred food allergic children (95	68% approx.* ("Familiar with device"	55% approx.* ("Removes cap")	93% approx.* ("Selects correct end")	93% approx.* ("Selects correct injection site")	59% approx.* ("Presses to activate")	53% approx.*	38% Patient/ Parents	* Approximate values extracted from graphs in published paper

Assessment by demonstration 50%	parents **and 6 children >12y**) & 36 physicians						("Holds in place several seconds")		The data presented in this publication combined findings for patients and parents. No separate results provided for patients; results combined for patients and parents 55% patients had non-expired AAI with them 49% reported previous demonstration of the device by a physician and 80% stated that use was explained verbally 98% said they would seek medical advice after administration Correct use was associated with having had the device >2.5years and membership of a support group
Al-Matar and Sussman, 2001 Canada Before and after study with two minute instruction before immediate re-assessment Assessment by demonstration 25%	**55 patients aged 4-67y (mean age 34y)** (unclear if younger aged participants were assessed directly or responses referred to parents)	Not assessed	64% ("Take the cap off")	64% ("Injection site")	64% ("Injecting with the wrong end" or "not holding the device at the injector end")	Not reported ("Pressing hard enough")	Not assessed	Pre-instruction 13% Post-instruction 100%	Technical errors included failure to activate AAI due to not taking cap off, not injecting hard enough, injecting with the wrong end or not holding the device correctly
Sabroe et al., 2002 UK Cross-sectional Assessment by demonstration 0%	**29 patients** (13y-67y) Only 25 patients completed demonstration	Not assessed	79% ("Removed the cap")	88% ("Inject into the lateral aspect of the thigh")	Not reported	72% ("Press until hearing a click")	68% ("Wait for 10s")	56% (n=14/25) patients were able to complete all steps	12% were unable to perform any step 56% knew to inject through clothing 66% prescribed ≥2 devices

									73% replaced AAI according to expiry date and of these, 53% knew the expiry date 93% trained in how to use device (70% by hospital staff, 30% by a general practitioner and 7% by a pharmacist)
Diwakar et al., 2010 UK Cross-sectional Assessment by questionnaire 25%	**80 patients** (mean age 37y (SD 15y)	Not assessed	Not assessed	% not reported ("draw out area where AAI should be injected (figure provided)")	Not assessed	Not assessed	% not reported ("How long should AAI be held against your skin after injecting?")	Not reported	Other technique items included knowing AAI can be used through clothing, what to do after injecting AAI and symptoms which would precede use (max score 7) 73% previously trained in how to use device (41% by a specliast, 32% by non-specialist) All untrained participants issued AAI by non-specialist Those trained in AAI use by specialist had better AAI administration technique than those untrained (mean=5.86 SD=.83 versus mean=5.05, SD=1.57) No difference between those trained by specialist or non-specialist (mean=5.75, SD=.94)
Segal et al., 2012 Israel Before and after study with average 12 months between instruction and re-assessment Assessment by demonstration 50%	141 (129 parents of patients aged ≤12y and **12 patients age >12y** (total age range 22m-23.4y)	Not assessed	Pre-instruction 52% ("Removing the cap")	Pre-instruction 32% ("Holding the device in first")	Pre-instruction 34% ("Placing against upper outer thigh and pressing")	See previous step	Pre-instruction 26% ("Holding in place for 10 seconds")	6% were able to complete all steps at baseline (n=141) ≤19% were able to complete all steps at first follow up (n=41) ≤53% were able to completed all steps at second follow up (n=41)	77% able to cite at least 2 symptoms of systemic allergic reaction 79% had a valid device 100% trained in how to use device No significant difference between patients and parents demonstration technique
Topal et al., 2013 Turkey	64 (50 caregivers of patients and **14**	74% approx.*	87% approx.*	100%	100%	92% approx.*	36% approx. *	36%	84% knew how to check the expiry date

Cross-sectional Assessment by demonstration 50%	**patients aged ≥12y)**	("Recognise the auto injector")	("Remove the grey safety cap")	("Selecting the outer thigh")	("Applying the black end to the thigh")	("Pressing it until it clicks")	("Holding it in place for at least 10 s")		*Approximate values derived from figure History of severe anaphylaxis was associated with correct use of AAI administration (OR:28.3, 95% CI:2.50-321.38) No difference between parent and child competence in administering device
Jones et al., 2015 UK Cross-sectional Assessment by questionnaire 50%	**188 patients (age 13-19y)**	Not assessed	80% ("Need to remove AAI cap before use")	99% ("Selection of appropriate injection site")	100% ("Identifies needle end of device")	Not assessed	86% ("Length of time to keep needle in muscle")	74% 18% *if additional technique items included	98% recognised symptoms of anaphylaxis 56% knew the correct grip (thumb clear of end of the device) 68% knew to seek medical advice following administration 98% aware that the device has expiry date 93% aware of using the injection through clothing *low % correct reported in paper as the above additional technique items were included in the total technique score

Table 2. Parents' and carer givers' technique and skills administering an adrenaline auto-injector (Studies are presented in chronological order)

Studies (country, design, method of observation, quality assessment)	**Study population**	**% individuals correctly undertaking key steps of AAI administration (wording used)**						**100% correct**	**Additional observations**
		Device Recognition	**Removal of safety cap**	**Selection of appropriate injection site**	**Application of correct end of AAI to thigh**	**Administration of adrenaline**	**Holding AAI in place**		
Huang, 1998 USA Cross-sectional Assessment by demonstration 50%	98 patients (83 aged <18y, 15 aged ≥18y) **For <12ys, parents were assessed (exact number not provided)**	Not assessed	90% ("Remove the cap")	78% ("Press the Epi-PEN on the lateral thigh")	Not assessed	37% ("Press Epi-PEN until clicking sound is heard")	41% ("Hold Epi-PEN in place for at least 10 seconds")	Not reported	16% knew the circumstances in which the use of AAI is indicated 84% had two devices available 53% knew to use through clothing 97% aware of expiry date but 89% had a valid device with them 11% had previously been trained in how to use AAI (5% by an allergist and 6% by other physician)
Gold and Sainsbury, 2000 Australia Cross sectional Assessment by questionnaire 75%	**68 parents** of children with AAI (age 1.5-19y)	Not reported	50% ("Removal of the grey cap")	>80% ("Could describe the site of administration and apply pressure")	Not reported ("Placing the black end on thigh")	Not reported ("Applying pressure until a click was heard")	50% ("holding the auto-injector in place for 10 seconds")	24% parents of patients	5% could not recall any steps for correct use 97% had informed school staff about their child's anaphylaxis 71% did not use their AAI to treat anaphylaxis despite it being available and in date for 69% Greater AAI administration technique was associated with parents whose children had experienced more allergic reactions
Goldberg and Confino-Cohen, 2000 Israel Cross-sectional	96 patients (n=72 aged <12y) **Children aged ≥12y were helped to answer**	Not assessed	82% ("Pulling out the grey safety tip")	82% ("Holding the device in palm")	82% ("placing the black tip on the outer thigh")	76% ("Pushing in hard until the trainer	78% ("Holding it in place for 10 seconds")	42% parents of patients <12y	89% had previously been trained in how to use AAI (46% by an allergist, 12% by a nurse, 10% by a primary physician, 10% by a pharmacist, 1% by emergency

Assessment by demonstration 75%	**questions by their parents. These results indicate parental response (n=24)**					function is heard")			department physician and 9% by a non-professional) Mean time since last training received was 2.6 years 18% received instruction with training device
Sicherer et al., 2000 USA Cross-sectional Assessment by demonstration 50%	101 families of newly referred food allergic children (**95 parents** and 6 children, mean age 6.4y) & 36 physicians	68% approx.* ("Familiar with device"	55% approx.* ("Removes cap")	93% approx.* ("Selects correct end")	93% approx.* ("Selects correct injection site")	59% approx.* ("Presses to activate")	53% approx.* ("Holds in place several seconds")	38% Patient/ Parents	* Approximate values extracted from graphs in published paper The data presented in this publication combined findings for patients and parents. No separate results provided for patients; results combined for patients and parents 55% patients had non-expired AAI with them 49% reported previous demonstration of the device by a physician and 80% stated that use was explained verbally 98% said they would seek medical advice after administration Correct use was associated with having had the device >2.5years and membership of a support group
Blyth and Sundrum, 2002 UK Cross-sectional Assessment by demonstration 0%	**25 parents of children with AAI (aged 4-17y)**	Not reported	64% ("Removing the cap")	Not reported	Not reported	60% ("Pressing on the tip to inject whilst holding the auto-injector against the thigh")	Not reported	24% parents were able to complete all 6 steps	Three children had been prescribed an incorrect dose 64% would call ambulance after administration 72% trained in how to use device
Kapoor et al., 2004 UK	**62 parents of children with AAI (<17 y)**	Not assessed	% not reported	% not reported	Not assessed	% not reported	Not assessed	Pre-education 50% parents able to identify all three	61% previously trained in how to use device

Before-after Assessment by demonstration 75%			("Removal of the grey safety cap")	("Selecting the appropriate site")		("Pressing the EpiPen down until it click")		critical steps (steps, 2, 3 and 5) Post education 96% parents able to identify all three critical steps	Participants referred from secondary care had better technique than those from primary care (38% vs 15% correct AAI technique at baseline)
Kim et al., 2005 USA Cross sectional Assessment by questionnaire 75%	**<u>165 parents of children with AAI (aged 1-19y)</u>**	Not assessed	95% ("Remove grey cap before administration")	92% ("Inject in outside part of thigh")	Not assessed	79% ("Press until clicking sound heard")	70% ("Hold for 10 seconds after injection")	Not reported	93% knew not to remove clothing before injecting 77% knew to call 911 oand 65% knew to go the emergency department following administration 88% knew to replace if the liquid appeared brown 83% trained in how to use device (47% trained by a physician, 36% by a nurse)
Arkwright and Farragher, 2006 UK Cross-sectional Assessment by demonstration 50%	**<u>122 parents of children</u>** (aged 6-13y)	Not assessed	% not reported ("Removed the safety cap")	% not reported ("correct site to inject adrenaline")	Not assessed	% not reported ("Applied enough pressure to trigger the device")	% not reported ("Did not take the needle out of the skin immediately after the device had been triggered")	57% able to trigger device	2 cases with expired date device 81% trained in how to use device Parents given AAIs by allergy specialist were more able to trigger the device, carried the device, had the correct dose and knew when to use the device than those given AAIs by GPs or non-allergy specialists
Huang, 2007 UK Longitudinal survey after auto-injector demonstration (assessment at 3 month intervals) Assessment by demonstration 50%	**<u>224 parents of children with AAI (ages unknown)</u>**	Not assessed	% not reported ("Remove the cap")	% not reported ("Choose the injection site")	% not reported ("Know the orientation of the head and tail (cap) of the device")	% not reported ("Press the device until it clicks")	% not reported ("Press the device steadily for 10 seconds (count to 10)")	22% of parents passed all recorded steps at first visit, 68% at the 2nd visit and 94% at the 3ed visit	At 2nd visit parental pass rate was higher for those whose child had venom allergy compared with food allergy 99 parents receiving a trainer device had a better pass rate at 2nd visit

Segal et al., 2012 Israel Before and after study with average 12 months between instruction and re-assessment Assessment by demonstration 50%	141 (**<u>129 parents of children with AIIs aged ≤12y</u>** and 12 aged >12y (total age range 22m-23.4y)	Not assessed	Pre-instruction 52% ("Removing the cap")	Pre-instruction 32% ("Holding the device in first")	Pre-instruction 34% ("Placing against upper outer thigh and pressing")	Not assessed	Pre-instruction 26% ("Holding in place for 10 seconds")	6% were able to complete all steps at baseline (n=141) ≤19% were able to complete all steps at first follow up (n=41) ≤53% were able to completed all steps at second follow up (n=41)	77% able to cite at least 2 symptoms of systemic allergic reaction 79% had a valid device 100% trained in how to use device No significant difference between patients and parents demonstration technique
Sicherer et al., 2012 USA Longitudinal with before and after Assessment by demonstration immediate post-education and 12-months 25%	**60 families (parent/caregiver of a food allegic child prescribed AAI (aged 6 months to 14y)** 33 completed 12-month assessment	Pre-education 38% approx.* Immediate post-education 100% 12-months post-education 70% ("Recognises device")	Pre-education 78% approx.* Immediate post-education 100% 12-months post-education 96% ("Removes cap")	Pre-education 70% Immediate post-education 100% 12-months post-education 96% ("Correct site")	Pre-education 70% Immediate post-education 100% 12-months post-education 94% ("Correct end")	Pre-education 52% approx.* Immediate post-education 95% approx.* 12-months post-education 94% approx.* ("Press to activate")	Pre-education 28% approx.* Immediate post-education 100% 12-months post-education 89% approx.* ("Hold several seconds")	Pre-education 18% Immediate post-education 95% 12-months post-education not reported	88% pre-education, 98% post-education and 100% 12-month post-education knew the AAI did not require refrigeration 75%, 98% and 98% respectively knew AAI could be used through clothing
Topal et al., 2012 Turkey Cross-sectional Assessment by demonstration 50%	64 (**<u>50 care givers of children with AAI</u>** and 14 patients aged ≥12y)	72% approx.* ("Recognise the autoinjector")	70% approx.* ("Remove the grey safety cap")	98% approx.* ("Selecting the outer thigh")	93% approx.* ("Applying the black end to the thigh")	75% approx.* ("Pressing it until it clicks")	78% approx. * ("Holding it in place for at least 10 s")	40%	84% knew how to check the expiry date *Approximate values derived from figure History of severe anaphylaxis was associated with correct use of AAI administration (OR 28.3, 95% CI:2.50-321.38) No difference between parent and child competence in administering device
Umasunthar et al., 2015 UK	**158 mothers of children (aged 0-18y) with food allergy** (145 completed 6-week assessment, 110 completed	Not assessed	6-weeks post-training Anapen 63%, EpiPen 71% 12-months post-training Anapen 66%, EpiPen 90%	6-weeks post-training Anapen 93%, EpiPen 93% 12-months post-training Anapen	(See previous step)	6-weeks post-training Anapen 100%, EpiPen 82% 12-months post-training Anapen	6-weeks post-training Anapen 86%, EpiPen 82% 12-months post-training Anapen 88%, EpiPen 88%	6-weeks post-training Anapen 42%, EpiPen 43% 12-months post-training Anapen 55%, EpiPen 59%	At 6-weeks post-training, 1% with Anapen and 5% EpiPen injected into the thumb, 56% Anapen and 54% EpiPen massaged site after injection, 68% Anapen and 69% EpiPen called the emergency services

RCT to receive EpiPen or Anapen and training Assessment by demonstration 6 weeks and 1 year after initial training 50%	12-month assessment)		(“Removal of all safety caps”)	100%, EpiPen 83% (“Placement of correct end of the device against the thigh”)		100%, EpiPen 98% (“Activation of device”)	(“Holding the device in place for adrenaline delivery for ≥5s”)		At 12-months, 0% with Anapen and 14% EpiPen injected into the thumb, 80% Anapen and 63% EpiPen massaged site after injection, 86% Anapen and 93% EpiPen called the emergency services After 12-months, 108 participants were given an alternate device with no training. Participants receiving the Auvi-Q had highest administration success rate 93% vs 49% for all other devices

Table 3. Health care professionals' (HCPs) technique and skills administering an adrenaline auto-injector (Studies are presented in chronological order)

Studies (country, design, method of observation, quality assessment)	**Study population**	**% individuals correctly undertaking key steps of AAI administration (wording used)**						100% correct	Additional observations
		Device Recognition	**Removal of safety cap**	**Selection of appropriate injection site**	**Application of correct end of AAI to thigh**	**Administration of adrenaline**	**Holding AAI in place**		
Grouhi et al., 1999 Canada Cross-sectional Assessment by demonstration 50%	122 HCPs (physicians, medical students, pharmacist and nurses) Secondary care	Not assessed	56% approx.* ("Pull out the grey safety cap")	44% approx.* ("Hold the device in the palm with the thumb covering the index finger and the black tip toward the small finger")	27% approx. * ("Place the black tip on the outer thigh. Push hard until you hear the trainer function. Hold in place for 10 seconds")	See previous step	See previous step	25% HCPs	19% had a training device with which to education patients (70% pharmacists) 24% were aware of two available doses Majority of pharmacists performed well (80%) Primary care paediatricians (performed worst (6%) *Approximate values derived from figure
Sicherer et al., 2000 USA Cross-sectional Assessment by demonstration 50%	101 families of newly referred food allergic children (95 parents and 6 children, mean age 6.4y) **& 36 physicians** Secondary care	48% paediatricians 51% paediatric residents approx.* ("Familiar with device"	35% paediatricians 51% paediatric residents approx.* ("Removes cap")	83% paediatricians 90% paediatric residents approx.* ("Selects correct end")	88% paediatricians 99% paediatric residents approx.* ("Selects correct injection site")	59% paediatricians 81% paediatric residents approx.* ("Presses to activate")	48% paediatricians 46% paediatric residents % approx.* ("Holds in place several seconds")	21% Paediatricians 36% Resident Paediatricians	17% HCPs reported training families to use AAI with trainer 24% HCP provided written information on how to use device
Onbasi et al., 2005 Turkey Cross-sectional Assessment by questionnaire	93 physicians Primary care	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	11%	24% knew the correct dose, form and the route of administration

25%									
Mehr, et al., 2007 Australia Cross-sectional Assessment by demonstration 25%	100 physicians Tertiary care	95% ("Recognized EpiPen")	96% ("Removed grey cap")	99% ("Select outer thigh as body part")	84% ("Pressed black end into the thigh")	79% ("Pressed to activate")	43% ("Held pen for >5s")	2% Doctors	45% previously prescribed AAI 51% provided patients with some education information on AAI administration technique and 7% provided a demonstration 16% injected trainer into thumb reported
Arga et al., 2011 Turkey Before-after study Assessment by demonstration assessed 6 months after 25%	196 physicians Secondary care	Not assessed	Pre-education 89% Post-education 97% ("Removed gray cap")	Pre-education 85% Post-education 99% ("Select outer thigh as body part")	Pre-education 66% Post-education 94% ("Placed black end into outer thigh")	Pre-education 60% Post-education 91% ("Pressed to activate")	Pre-education 48% Post-education 82% ("Held pen for > 5s")	23% pre-education 74% post-education	41% knew indications of epinephrine auto-injector Self-injection into thumb (36% pre-education, 7% post-education)
Salter et al., 2014 Australia Cross-sectional simulated patient-study Assessment by demonstration 75%	250 pharmacists Community care	Not assessed	89% ("Remove safety cap")	96% ("Place against thigh")	See next step	73% ("Push and inject")	21% ("Remove and massage injection site for 10 seconds")	18% completed all steps (4 steps) 65% correctly completed 3 steps and	Incorrect positioning of thumb observed in 12% Proper AAI was more likely if pharmacists asked patients if they had an anaphylaxis management plan (OR 16.1, 95% CI:3.86-67.3), advised the patient to call an ambulance after administration (OR 4.00, 95% CI:1.44-11.1) or explained the side effects of epinephrine (OR 4.45, 95% CI:1.48-13.4)
Topal et al., 2014 Turkey Cross-sectional Assessment by demonstration 25%	126 primary care physicians Primary care	Not reported	Not reported	34% ("Knew site for injection")	Not reported	Not reported	Not reported	34% knew how to administer device	30% knew correct adrenaline dose

Table 4. Participants' AAI administration technique for studies including an instruction of AAI administration in design (studies are presented in chronological order)

Studies	Type of instruction	Method of observation	Duration of retest	Correct administration technique
Al-Matar and Sussman, 2001	Two minute instruction of correct administration technique was provided	Demonstration using a trainer device	Immediately following instruction	Pre-instruction 13% Post-instruction 100%
Kapoor et al., 2004	A clinical nurse specialist educated participants on recognition and management of anaphylaxis. A specialist paediatric dietician gave advice regarding food allergen avoidance.	Demonstration using a trainer device	3 months	Pre-instruction 50% Post-instruction 96%
Huang, 2007	A physician observed participants demonstration technique before explaining any steps which needed to be corrected prior to demonstrating correct technique. Participants were then required to repeat the process until they completed all steps correctly.	Observation by physician	No reported (first, second and third visits but duration between not provided)	Pre-instruction (first visit) 22% Post-instruction (second visit) 68% Post-instruction (third visit) 94%
Arga et al., 2011	One-to-one practical session including visual and written prospectus on how to use AAI	Demonstration using a trainer device	6 months	Pre-instruction 23% Post-instruction 74%
Segal et al., 2012	Participants received an individualized written emergency plan and instructions for the use of AAI plus training from one of three physycians	Demonstration using a trainer device	First follow-up visit after 0.04–6.54 years (mean 1.28 years) Second follow-up visit after 1.02 years (range 0.08–2.6 years)	Pre-instructions 6% First follow up ≤19% Second follow up ≤53%
Sicherer et al., 2012	Education materials (written and video) on signs and symptoms of food allergy, labelling and when and how to use AAI	Demonstration using a trainer device	Immediate post-instruction and 12 months	Pre-instruction 18% Immediate post-instruction 95% 12-months post-instruction not reported
Umasunthar et al., 2015	Standardised training including recognition and management of anaphylaxis by researcher who ensured participants were able to demonstrate correct technique before leaving the session plus written manufacturer device specific information	Demonstration using a trainer device	6 weeks and 12 months	6-weeks post-instruction Anapen 42%, EpiPen 43% 12-months post-instruction Anapen 55%, EpiPen 59%