

Anaphylaxis management plans for the acute and long-term management of anaphylaxis: A systematic review

Ulugbek Nurmatov, MD, PhD, Allison Worth, BSc (Hons), PhD, and Aziz Sheikh, MD, FRCP *Edinburgh, United Kingdom*

Background: Anaphylaxis management plans (AMPs) are increasingly advocated to improve outcomes and reduce the risk of recurrence in persons with anaphylaxis. A recent systematic review investigating their effectiveness failed to identify any randomized controlled trial evidence to guide clinical decision making.

Objectives: We sought to identify and describe available AMPs, assess their acceptability and likely effectiveness, and understand potential facilitators and barriers to their use.

Methods: We performed a systematic review of published, unpublished, and ongoing epidemiologic and qualitative studies, searching 13 international databases and contacting an international panel of anaphylaxis experts. Studies were critically appraised using established international criteria and thematically synthesized.

Results: Nineteen of 789 potentially eligible studies identified satisfied our inclusion criteria. A number of AMPs exist, and other than agreement on the central importance of early administration of self-administered epinephrine, there is a range of perspectives on what should be included. AMPs are acceptable to patients/caregivers and might considerably reduce the risk of recurrence. This latter finding needs to be interpreted with caution given the substantial risk of bias in the limited number of intervention studies conducted. Access to specialists, problems with follow-up, and indemnity considerations relating to emergency administration of epinephrine in schools are important structural barriers to their wider use.

Conclusions: There are currently no universally accepted AMPs. The available evidence to support use of self-management plans is encouraging but is, in comparison with other long-term conditions, such as asthma, extremely weak. The effectiveness and cost-effectiveness of AMPs need to be formally evaluated. (*J Allergy Clin Immunol* 2008;122:353-61.)

Key words: *Anaphylaxis, acute management, long-term condition, self-management*

Abbreviations used

AMP: Anaphylaxis management plan

RCT: Randomized controlled trial

UK: United Kingdom

Anaphylaxis is an acute, life-threatening medical emergency with many potential triggers.¹⁻⁶ Because patients with possible anaphylaxis are not always adequately investigated and, furthermore, it is not a reportable condition, the true frequency of anaphylaxis reactions is unknown.^{3,7-10} A recent review of the available epidemiologic evidence, however, estimated that the incidence of anaphylaxis is approximately 50 to 2000 episodes per 100,000 persons, with a lifetime prevalence of 0.05% to 2.0%.¹¹ Anaphylaxis is now responsible for appreciable numbers of consultations with family physicians,¹² emergency department attendances,⁹ and hospitalizations¹³ and, of greatest concern, each year results in approximately 150 deaths in the United States and 20 to 30 reported deaths in the United Kingdom (UK), the majority of which are potentially preventable.¹⁴

Most cases of anaphylaxis occur unpredictably in community settings in the absence of a health care professional.¹⁵ Many of these reactions occur in those with a previous history of anaphylaxis; such individuals are therefore known to be at high risk of subsequent reactions.^{11,15} Anaphylaxis management plans (AMPs) are increasingly being advocated for use in the United States, Europe, and Australasia in an attempt to improve outcomes from acute episodes and also to reduce the risk of repeat reactions.¹⁶⁻²² This is in parallel with moves in other long-term conditions, such as asthma, where there is now good evidence from rigorously conducted trials that self-management plans and regular reviews improve clinical outcomes.²³ Although logical, a recent systematic review found that there is no randomized controlled trial (RCT) evidence to support the routine use of AMPs.²⁴ A limitation of this systematic review (in keeping with most other effectiveness reviews) was that it focused solely on RCT evidence, and therefore it might have overlooked a potentially large body of empiric evidence that has the potential to inform deliberations about the content, acceptability, effectiveness, and possible barriers and facilitators to AMP use.²⁵ We therefore decided to conduct a follow-on review of the broader literature on this subject to answer related questions that might help inform clinical care, help catalyze further research, and inform policy making in relation to the management of anaphylaxis.²⁶

METHODS

We conducted a systematic review of the literature using standard internationally agreed upon approaches for identifying and appraising non-RCT evidence. This involved formulating a clearly described search strategy for

From the Allergy & Respiratory Research Group, Division of Community Health Sciences: General Practice Section, University of Edinburgh.

Supported by the Chief Scientist Office of the Scottish Government Health Department (CZG/2/296).

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

Received for publication April 21, 2008; revised May 15, 2008; accepted for publication May 16, 2008.

Available online June 24, 2008.

Reprint requests: Aziz Sheikh, MD, FRCP, Allergy & Respiratory Research Group, Division of Community Health Sciences: General Practice Section, University of Edinburgh, 20 West Richmond St, Edinburgh EH8 9DX, United Kingdom. E-mail: aziz.sheikh@ed.ac.uk.

0091-6749/\$34.00

© 2008 American Academy of Allergy, Asthma & Immunology

doi:10.1016/j.jaci.2008.05.028

identifying completed and ongoing work and using a standardized approach to assessing study quality, data abstraction, and synthesis that sought to minimize the risk of drawing erroneous conclusions and to maximize transparency.

Inclusion criteria

Methodological criteria for consideration in this review. We included all qualitative, epidemiologic, and intervention studies, with or without control populations, evaluating any aspect of the content, effectiveness, and barriers/facilitators to the use of AMPs in patients with anaphylaxis. Thus any study design, other than isolated case reports, was eligible for inclusion.

Types of participants. Studies of patients of all ages (ie, infants, children, and adults) who had previously experienced anaphylaxis from any cause were eligible for inclusion.

Types of intervention. We included studies that involved any educational intervention that could be considered as a patient/caregiver-oriented management plan for the acute or long-term care of patients at risk of anaphylaxis.

Types of outcome measures. We were interested in any description of the components of these plans, barriers and facilitators to their use, and any insights into their likely clinical effectiveness or acceptability.

Search strategy

We searched the following international databases for published work for the time period from 1996-2007: MEDLINE, EMBASE, Science Citation Index, Cochrane Database of Systematic Reviews, ISI Proceedings, TRIP, LILACS, and CINAHL. Our search terms are available in Table E1 (in the Online Repository at www.jacionline.org). In addition, we sought to identify unpublished work and research in progress by searching key Internet-based databases that list ongoing studies, namely www.clinicaltrials.gov, www.controlledtrials.com, and the UK National Research Register at www.nrr.nhs.uk. To extend our search for published and ongoing studies, we contacted an international panel of 18 anaphylaxis experts and 2 pharmaceutical companies that manufacture self-administered epinephrine (see the Acknowledgments section for a list of names), sending them our list of identified eligible studies and inviting them to add to this body of information. No language restrictions were used in any of these searches.

Study selection, quality assessment, data extraction, and synthesis of findings

One reviewer undertook searches, and the titles and abstracts were then independently scrutinized by a second reviewer; a third reviewer acted as an arbitrator in the case of any disagreement between reviewers. Studies were assessed by using the Critical Appraisal Skills Programme approach,²⁷ drawing on the principles incorporated into the Cochrane Effectiveness and Practice Organisation of Care guidelines for assessing intervention studies²⁸ and the Strengthening the Reporting of Observational Studies in Epidemiology for assessing observational studies.²⁹ Data were extracted onto a customized data extraction sheet by one reviewer, and this process was verified by a second reviewer, with any disagreements again being resolved through discussion or involvement of an arbiter, if necessary. We report our findings using the general approach advocated by the Meta Analysis of Observational Studies in Epidemiology guidelines to reporting systematic reviews and meta-analyses of nonexperimental studies.³⁰

Because of the heterogeneity of the studies identified, formal meta-analysis was neither desirable nor possible. Rather, we summarized key findings from related studies and then qualitatively synthesized the disparate data with a view to, in particular, extracting data on key aspects of care that might inform clinical decision making and future experimental studies of AMPs.

RESULTS

Our database searches revealed a total of 784 potentially eligible studies; 704 of these were excluded on the basis of reviewing titles as clearly not meeting our inclusion criteria. Review of the abstracts of the 80 potentially more relevant articles revealed that

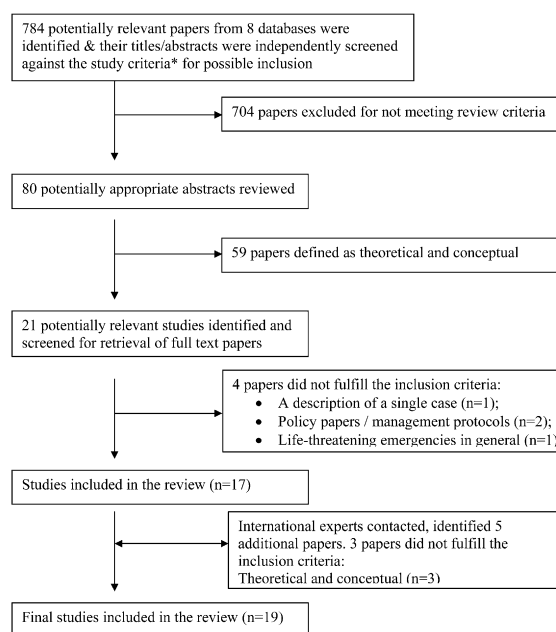


FIG 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. *All qualitative, epidemiologic, and intervention studies, with or without control populations; patients of all ages (ie, infants, children and adults) who had previously experienced anaphylaxis from any cause; and studies that involved any educational intervention that could be considered as a patient/caregiver-oriented management plan for the acute or long-term care of patients at risk of anaphylaxis.

59 of these were theoretic/conceptual/review articles (ie, contained no original data) and were therefore ineligible. A detailed analysis of the full text of the 21 remaining articles identified 17 articles that satisfied our inclusion criteria. The international panel of experts and pharmaceutical companies identified a further 5 articles, 2 of which satisfied the inclusion criteria, thus giving a total of 19 included articles (Fig 1). Our searches revealed no other relevant unpublished work or research in progress.

There was considerable diversity in the aims, populations studied, and methodological approaches used in the studies (Table I).^{17-22,31-43} Most were epidemiologic and qualitative studies describing aspects of the content, use, and accessibility of AMPs.^{19,21,22,31-37,39-43} Although some did seek to assess the effectiveness of AMPs,^{17,18,20,43} none used rigorous experimental designs.²⁶

Contents of AMPs

We identified 12 examples of AMPs (see Table E2 in the Online Repository at www.jacionline.org). There is no overall consensus in the literature on what aspects of care should be included in AMPs. However, all do agree on the need for emergency contact details and advice on recognition of symptoms and treatment of reactions with epinephrine. Some articles also incorporated dimensions of long-term care, these including issues to do with diagnosis, detailed advice on allergen avoidance, and assessment of psychologic effect on patients.

Acceptability and availability of AMPs

Written plans appear acceptable to patients and caregivers and might, when issued together with training, reduce anxiety levels and increase knowledge and self-efficacy among parents and

TABLE I. Summary of studies

Study	Population studied	Age	Country	Setting	Design	Main findings	Quality assessment
Akeson et al, 2007 ³⁶	In-depth interviews with 15 participants: 7 adolescents and 8 of their parents)	Adolescents: 13-16 y	Scotland	Community setting	Exploratory qualitative study	Having a child with anaphylaxis can have a significant long-term psychologic effect on parents, and this anxiety might, in some cases, be transferred from parents onto their children. Parents and adolescents might benefit from tailored information. Limited medical support is available. Transition from childhood to adulthood raised particular issues regarding "letting go."	There were a small number of participants. Robust data collection, clear reporting, and appropriate analysis were performed. The generalizability of the findings to more marginalized groups is, however, questionable.
Blyth and Sundrum, 2002 ³³	Schoolchildren with epinephrine autoinjectors	4-17 y	England	Community study involving schools and parents	Questionnaire to all schools (n = 86) asking them to identify children; interviews with 25 children and their parents	There was inconsistency in prescription and use of autoinjectors, with poor training, absence of written instructions, and lack of follow-up.	There was a high response rate from schools but a low response rate from parents. It was a small geographically localized study. Approach to data generation and analysis was unclear.
Clegg and Ritchie, 2001 ³⁴	Parents (n = 35) and teachers (n = 26) of school-aged children	Adults	Scotland	Community survey	Questionnaire survey	Many parents and schoolteachers did not receive adequate training on use of adrenaline autoinjectors.	It was a small geographically localized survey but had high response rates from both parents and teachers.
Ewan and Clark 2001 ¹⁷	Children and adults (n = 567; 76% ≤17 y)	7 mo-65 y	England	Specialist allergy clinic	Long-term prospective observational study of patients with confirmed nut allergy after participation in an AMP: verbal and written advice, training, and written treatment plan plus follow-up	Only 88 (15%) of 567 patients had a follow-up reaction of reduced severity. Only 3 (0.5%, all adults) patients had severe reactions compared with a baseline rate of 12%.	The study suggests that AMPS including a preventative dimension are associated with large effect sizes, but the lack of randomization and contemporaneous control data raises concerns about the risk of bias.

(continued)

TABLE I. (continued)

Study	Population studied	Age	Country	Setting	Design	Main findings	Quality assessment
Ewan and Clark, 2005 ¹⁸	Children (n = 747); 224 in case-control study	10 mo-15 y	England	Specialist allergy clinic	Longitudinal prospective study and embedded case-control study	AMPs reduced the frequency and severity of further reactions (8-fold reduction in frequency of reactions; 60-fold reduction in frequency of severe reactions).	Analytical study dimension is a strength, but the lack of randomization and independent evaluation raise concerns about the risk of bias.
Gold and Sainsbury, 2000 ¹⁹	94 Children with anaphylaxis and prescribed epinephrine autoinjectors; 68 parents interviewed	1-19 y	Australia	Community survey of parents of children attending hospital allergy clinic	Specialist assessment and verbal and written instruction on use of epinephrine autoinjectors; retrospective telephone questionnaire survey conducted with parents	There were concerns about parental knowledge and school preparedness for dealing with emergencies. Epinephrine autoinjectors were infrequently used in children experiencing episodes of anaphylaxis. When appropriately used, autoinjectors appeared to reduce subsequent morbidity from anaphylaxis.	The report provides few details of the written instructions issued. There was a high response rate, but the lack of randomization, control data, and objective assessment provides little insight into the effectiveness of AMPs in improving outcomes and risk of recurrence.
Grouhi et al, 1999 ³⁵	122 Professionals (emergency physicians, family practitioners, pediatricians, pharmacists, and nurses)	Not given	Canada	General pediatric medical convention	Questionnaire survey and demonstrated ability to use a standard epinephrine autoinjector training pen	There was considerable variation in knowledge and skills between professional groups. Overall, 75% of participants could not demonstrate correct use of epinephrine device, but 80% of pharmacists could. The lack of relevant knowledge among professionals highlighted the need to educate and maintain skills of professionals.	Generalizability of findings is under question given the sampling strategy, but overall conclusions are likely to be sound. The studying of actual simulated use of autoinjectors is a strength of this work.
Hayman and Bansal, 2003 ⁴¹	60 Patients with anaphylaxis diagnosed in primary care; 50 local GPs	14 Adults; 46 children <8 y	England	Community and hospital setting	Review of patients' case notes; evaluation of patients'/parents' knowledge of how and when to use epinephrine; interviews with GPs; GPs asked to demonstrate use of epinephrine autoinjector	Overall, less than a third of patients or parents of affected children had adequate knowledge of the indications and how to use the device. One of 50 GPs knew how to use because of his personal history.	This was a very short report, which lacks details of important methodological issues. Nonetheless, concerns about professional and patient knowledge and skills are likely to be valid. The geographically localized study makes assessment of external validity of findings difficult.

Hannaway et al, 2005 ⁴⁰	School nurses in 3 Massachusetts school district in 44 schools enrolling 21,875 students	Not given	United States	School settings	A postal survey of school nurses; semistructured questionnaire	A total of 181 students in all 3 districts were dispensed epinephrine autoinjectors. White subjects were nearly 5 times more likely to be dispensed injectable epinephrine than nonwhite subjects.	This is the most robust study on differences in race, ethnicity, and socioeconomic status in schoolchildren dispensed injectable epinephrine. Reporting quality was high.
Kapoor et al, 2004 ²⁰	62 Children with food allergy attending allergy clinic and parents	<17 y	England	Allergy clinic	Before-after design evaluating effectiveness of multidisciplinary consultation with pediatric allergist, nurse, and dietician; formulation of individualized AMP and epinephrine training	Families had poor knowledge of allergen avoidance and managing reactions. After intervention, there was a significant increase in knowledge of allergen avoidance measures, managing reactions, and use of epinephrine autoinjectors.	There was high reporting quality, robust data collection, and data analysis. Control group was considered unethical, and this raises concerns about the validity of the findings, as does the lack of independent assessment of outcomes.
Kim et al, 2005 ³⁷	Parents of children with physician-diagnosed food allergy and prescribed epinephrine autoinjectors	Parents aged 29-55 y of children aged 1-19 y	United States	A local suburban food allergy support group and a private pediatric allergist's practice	Survey of "comfort" in using epinephrine autoinjector, as measured by using a visual analog scale	Prior administration of epinephrine and empowerment directly correlated with increased comfort with epinephrine use, but knowledge did not.	This was the first study to identify psychologic factors that influence epinephrine administration by parents to their children with food allergy. There was robust data analysis. The lack of representative sampling and low response rates, however, raise concerns about the overall validity of findings.
Litarowsky et al, 2004 ³²	Adult unlicensed assistive personnel (n = 53)	25-64 y	United States	High school	Pre-experimental design evaluating the effect of a theoretically based training program on knowledge and self-efficacy of dealing with anaphylaxis emergencies	Training program can significantly increase the knowledge and self-efficacy of unlicensed assistive personnel	The lack of a control group and the use of 2 new or revised instruments raise concerns about the internal validity of the study; the small localized study raises additional concerns regarding the external validity of findings.

(continued)

TABLE I. (continued)

Study	Population studied	Age	Country	Setting	Design	Main findings	Quality assessment
Moneret-Vautrin et al, 2001 ⁴³	45 Families with children with a history of anaphylaxis	4-20 y	France	Allergy clinic	Telephone survey to retrospectively evaluate the effectiveness of AMPs a mean of 25 mo after implementation	The majority (87%) of AMPs were implemented, and use was associated with a greatly reduced risk of further reaction.	This was a small study. The retrospective design and lack of control raise important concerns about possible bias. Details about the actual AMPs used are poorly described.
Murphy et al, 2006 ²¹	99 Students, in 78 Omaha public schools, parents, and teachers	All ages from elementary to high school	United States	Schools	Descriptive evaluation of an innovative school-based emergency protocol for the management of life-threatening asthma or anaphylaxis	There was improvement in emergency management of asthma and anaphylaxis in schools and improved awareness among parents, teachers, and physicians of need for an emergency plan. Parents reported satisfaction and decreased anxiety. The protocol was adopted statewide.	This study focuses more on asthma than anaphylaxis: only 5 students had anaphylaxis. The descriptive evaluative approach used needs to be extended through use of more rigorous designs to assess the effectiveness of this approach. Parental perceptions were not formally enquired about and are therefore likely to be impressionistic.
Patel et al, 2006 ³¹	39 Childcare centers	Children aged 1-6 y	United States	Schools	Allergy seminar for staff and repeat surveying of staff knowledge at 1, 6, and 12 months after the seminar	Initially, the intervention significantly increased the ability of staff to recognize, evaluate, and treat anaphylaxis, but knowledge diminished gradually at 6-mo and 1-y follow-ups compared with the 1-mo postintervention evaluation. This indicates the need for regular anaphylaxis education among childcare providers.	There was a good overall response rate, and the serial evaluation of the same sites using the same instrument is a strength. There was no description of the statistical techniques used. Knowledge is only a surrogate marker for actual decision making/ actions.
Powers et al, 2007 ⁴²	School nurses (n = 250) attending a conference	Not given	United States	School settings	Postal survey comparing food allergy plans used for children compared with the Food Allergy and Anaphylaxis Network's (FAAN) Food Allergy Action Plan	Of 250 nurses, 94 (38%) returned the surveys. Eighty-four percent of children with food allergies have a reaction in school, and 25% of first food reactions occur in schools. Only 15% used the current FAAN Food Allergy Action Plan.	Opportunistic sampling strategy and low response rate (38%) puts the study validity and generalizability under doubt. Nonetheless, this study points to the need for an agreed and professionally agreed upon standard approach.

Rae et al, 2007 ³⁸	Parents (n = 10): 8 with the child's mother, 2 with both parents	Children aged 3-17 y	Scotland	Community setting	Exploratory qualitative study	Prescribed epinephrine might have initially increased parental anxiety, but when combined with training and education, it reduced feelings of helplessness and provided reassurance.	There was an appropriate qualitative approach to data generation and analysis. The small sample with the resulting risk of not reaching saturation and the failure to explore the perspectives of children are important limitations.
Rankin and Sheikh, 2006 ³⁹	250 Schools	4-17 y	Scotland	Schools	National postal survey; semistructured questionnaire on emergency and long-term management	The majority of schools with at-risk children had AMPs in place and trained staff; 59% of respondents did not, however, feel confident in their school's ability to respond in an emergency situation. The majority of schools with at-risk children had poorly developed strategies for preventing food-triggered anaphylaxis reactions.	Stratified random sampling was a strength, but the suboptimal response rate (60%) and the lack of direct independent verification of stated responses raise important concerns about possible bias.
Vickers et al, 1997 ²²	56 Children with potential anaphylaxis to foods	Not specified	England	Community setting working with parents and nursery/school staff	Description of development of a good practice model for acute and long-term management considerations and some evaluation of this	The training package and sessions (60 min) appear to have been well received by all stakeholders and might have reduced anxiety of nursery/school staff and parents. The authors were unable to say whether it reduced reactions.	The lack of formal evaluation makes it difficult to assess the effectiveness of this approach. Nonetheless, it is a useful piece of developmental work.

GP, General practitioner.

school staff in managing anaphylactic emergencies.^{21,22,32,37,38} However, the majority of persons with anaphylaxis currently do not appear to have any written AMPs.

Likely effectiveness

Four studies^{17,18,20,43} suggest that AMPs encompassing training for patients, parents, and school staff might greatly reduce the frequency and severity of further reactions (ie, an up to 8-fold reduction in frequency of reactions and 60-fold reduction in frequency of severe reactions). These are encouraging data; however, the lack of control groups and potential for observational and selection biases means that these findings need to be interpreted with caution. The allergy clinic–based study²⁰ involving a multidisciplinary team (pediatric allergist, dietician, and clinical nurse specialist) assessment found that a training package prepared and delivered by a clinical nurse specialist and multidisciplinary consultation also resulted in improvements in relevant process measures: increased knowledge of food avoidance techniques (27%), managing reactions (185%), and use of epinephrine autoinjectors (83%). An additional study found that a single educational intervention possibly improved families' abilities to manage anaphylaxis and reduced parental/staff anxiety.²²

Facilitators and barriers to the use of AMPs

Although these are, to an extent, context specific, lack of knowledge and skills among parents, schools, and professionals in recognizing symptoms, administering epinephrine, and long-term management were recurrent themes in the literature.^{20,33,34,36,40,41} Training and education have been identified as effective but only with regular reinforcement.^{19,22,31} There also appears to be a lack of national guidelines for schools and concerns about indemnity issues in both school and work settings.^{33,34,39} Lack of follow-up is common,^{18,33,34} and although specialist diagnosis, management, and follow-up are recommended,¹⁷ this does not appear to be widely available. Although complex and multifaceted, these barriers to use might be overcome through dedicated local initiatives.^{17,18}

DISCUSSION

This systematic review has demonstrated the lack of professional agreement on what needs to be covered when formulating AMPs, the focus of many existing AMPs on emergency situations at the expense of longer-term management considerations (including preventative measures), and the current only very weak evidence in support of their use. However, our work does suggest that AMPs are likely to prove acceptable to patients/caregivers and professionals and might well improve clinical outcomes and that many of the multifaceted barriers that are currently mitigating their use are potentially surmountable.

Strengths and limitations of this review

This work is probably the most comprehensive review ever undertaken on the subject of AMPs and as such should represent a valid and up-to-date summary of the existing international literature on this subject. Despite our extensive searches for published and unpublished work, it is nonetheless possible that we might have failed to identify some relevant completed/ongoing studies. Another potential limitation of this work is that we have been involved in conducting some of the studies included in this review.

The relative paucity of the evidence base uncovered is a further limitation and underscores the pressing need for further work.

Implications for practice, policy, and research

AMPs have the potential to greatly improve outcomes in persons with anaphylaxis. However, there are currently no universally accepted AMPs, and in the absence of an agreed upon evidence-based approach, developing professional/academic consensus on the dimensions to incorporate into these AMPs would seem to be a logical next step. We are currently involved in such a venture in the UK, and given the importance of contextual considerations on whether such a development can meaningfully take place internationally or should initially be undertaken nationally remains an as-yet open question.

The available evidence to support the use of AMPs is potentially very encouraging, as demonstrated by several studies,¹⁷⁻²⁰ but is, in comparison with asthma, for example, extremely weak in that it is not based on rigorous RCT evidence.^{23,24,44} In addition to the potential of benefit, interventions run the risk of introducing harms, many of which might be unexpected.⁴⁵ In the context of anaphylaxis, the major known risks of harm are the possible unnecessary disruption to the lives of large numbers of persons associated with possibly overstringent allergen avoidance measures in some persons, anxiety and stress in both patients and caregivers, the inconvenience of regular reviews, and the risks associated with inappropriate epinephrine use.^{14,24,46} There are, in addition, important cost implications for health providers, both in relation to the regular reviews and the additional prescriptions for epinephrine that will invariably ensue. The effectiveness and cost-effectiveness of AMPs therefore needs to be formally evaluated by using the most methodologically robust design that is considered ethical to use. Despite the concerns expressed by several authors, we believe that a formal RCT comparing AMPs and regular reviews with standard models of care for patients likely to experience recurrence^{10,44} might be ethical and necessary before any universal recommendation about their clinical value can be made given the weak evidence base and the need to identify benefits, costs, and possible harms from interventions. Although the exact form in which such trials can be conducted will need to be shaped, in part, by local contextual considerations, in summary, these trials should ideally take place in areas where new services are due to be implemented, thereby allowing a standard care-control arm; will in most cases need to be cluster RCTs; and should, if found to be successful, offer the intervention to those in the control arm. Given the relative infrequency of key clinical end points, such trials, if focusing on these key parameters, will inevitably need to be large and multicentered, which in turn will need a shared professionally agreed upon regional/national understanding of what constitutes an appropriate AMP. We have recently completed such an exercise in the UK (unpublished data). Careful consideration also needs to be given to the range of outcome measures important to study, including process measures (knowledge and satisfaction), measures of reduced morbidity (quality of life, recurrence, and severity of reactions), health care use, and, although inevitably underpowered for definitive findings, mortality. Given the increasing numbers of persons now affected by anaphylaxis, such a study is also likely to prove methodologically feasible.^{12,13} None of the plans thus far developed have investigated the use of technology-based interventions for use in those with severe drug allergy.⁴⁷

We thank Marshall Dozier for librarian support with the systematic review. We also thank the international panel of anaphylaxis experts and pharmaceutical companies for their time and helpful contribution to the study, namely Dr A. Bock (United States), Dr A. F. Brown (Australia), Dr C. Camargo (United States), Dr S. Clark (United States), Professor P. Ewan (UK), Professor M. Fisher (Australia), Dr D. Golden (United States), Dr A. Helbling (Switzerland), Dr S. Kemp (United States), Professor P. L. Lieberman (United States), Dr R. Lockey (United States), Ms L. McInnes (Allerbio LTD–Ana-pen; France), Dr D. A. Moneret-Vautrin (France), Professor U. Muller (Switzerland), Dr J. M. Negro-Alvares (Spain), Dr R. Pumphrey (UK), Professor J. Ring (Germany), Professor L. Robert (United States), Professor H. A. Sampson (United States), and Mr R. Travers (ALK-Abelló Ltd–Epi-pen; UK).

Key messages

- AMPs have the potential to greatly reduce the risk of recurrence and improve outcomes in persons with anaphylaxis, but the empiric evidence in support of their use is currently very weak.
- There is no agreement on the key components of AMPs.
- There is a need for consensus on the key components of AMPs, both in relation to acute and long-term management considerations and the subsequent evaluation of AMPs using robust methodological approaches.

REFERENCES

- Brown SGA, Mullins RJ, Gold MS. Anaphylaxis: diagnosis and management. *Med J Australia* 2006;185:283-9.
- Kemp AS. EpiPen epidemic: suggestions for rational prescribing in childhood food allergy. *J Paed Child Health* 2003;39:372-5.
- Lieberman P, Decker W, Camargo CA, O'Connor R, Oppenheimer J, Simons FE. SAFE: a multidisciplinary approach to anaphylaxis education in the emergency department. *Ann Allergy Asthma Immunol* 2007;98:519-23.
- Muraro A, Roberts G, Clark A, Eigenmann PA, Halken S, Lack G, et al. The management of anaphylaxis in childhood: position paper of the European Academy of Allergology and Clinical Immunology. *Allergy* 2007;62:857-71.
- Sampson HA. Anaphylaxis and emergency treatment. *Pediatrics* 2003;111:1601-8.
- Sicherer SH, Simons FE, Williams PV, Bahna SL, Chipps BE, Fasano MB, et al. Self-injectable epinephrine for first-aid management of anaphylaxis. *Pediatrics* 2007;119:638-46.
- Neugut AI, Ghatak AT, Miller RL. Anaphylaxis in the United States: an investigation into its epidemiology. *Arch Intern Med* 2001;161:15-21.
- Peng MM, Jick H. A population-based study of the incidence, cause, and severity of anaphylaxis in the United Kingdom. *Arch Intern Med* 2004;164:317-9.
- Ross MP, Ferguson M, Street D, Klontz K, Schroeder T, Luccioli S. Analysis of food-allergic and anaphylactic events in the National Electronic Injury Surveillance System. *J Allergy Clin Immunol* 2008;121:166-71.
- Simons FE, Frew AJ, Ansoategui IJ, Bochner BS, Golden DB, Finkelman FD, et al. Risk assessment in anaphylaxis: current and future approaches. *J Allergy Clin Immunol* 2007;120(suppl):S2-24.
- Lieberman P, Camargo CA, Bohlke K, Jick H, Miller PL, Sheikh A, et al. Epidemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. *Ann Allergy Asthma Immunol* 2006;97:596-602.
- Sheikh A, Hippisley-Cox J, Newton J, Fenty J. Trends in national incidence, lifetime prevalence and adrenaline prescribing for anaphylaxis in England. *J R Soc Med* 2008;101:139-43.
- Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007;62:91-6.
- Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy* 2000;30:1144-50.
- Simons FE. Anaphylaxis: evidence-based long-term risk reduction in the community. *Immunol Allergy Clin North Am* 2007;27:231-48.
- Antoine LC. Management of children with a food allergy and the individualized reception plan [in French]. *Allerg Immunol* 2001;33:357-62.
- Ewan PW, Clark AT. Long-term prospective observational study of patients with peanut and nut allergy after participation in a management plan. *Lancet* 2001;357:111-5.
- Ewan PW, Clark AT. Efficacy of a management plan based on severity assessment in longitudinal and case-controlled studies of 747 children with nut allergy: proposal for good practice. *Clin Exp Allergy* 2005;35:751-6.
- Gold MS, Sainsbury R. First aid anaphylaxis management in children who were prescribed an epinephrine auto injector device (EpiPen). *J Allergy Clin Immunol* 2000;106:171-6.
- 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;59:185-91.
- Murphy KR, Hopp RJ, Kittelson EB, Hansen G, Windle ML, Walburn JN. Life-threatening asthma and anaphylaxis in schools: a treatment model for school-based programs. *Ann Allergy Asthma Immunol* 2006;96:398-405.
- Vickers DW, Maynard L, Ewan PW. Management of children with potential anaphylactic reactions in the community: a training package and proposal for good practice. *Clin Exp Allergy* 1997;27:898-903.
- Gibson PG, Powell H, Coughlan J, Wilson AJ, Abramson M, Haywood P, et al. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev* 2003;1:CD001117.
- Choo K, Sheikh A. Action plans for the long-term management of anaphylaxis: systematic review of effectiveness. *Clin Exp Allergy* 2007;37:1090-4.
- Hourihane JO, Beirne P. Evidence of effectiveness of anaphylaxis management plans: are we waiting for Godot? *Clin Exp Allergy* 2007;37:967-9.
- Simons FER, Sheikh A. Evidence-based management of anaphylaxis. *Allergy* 2007;62:827-9.
- Critical Appraisal Skills Programme (CASP). Appraisal tools. Available at: <http://www.phru.nhs.uk/Pages/PHD/resources.htm>. Accessed April 16, 2008.
- Cochrane Effective Practice and Organisation of Care Group. Methods papers. Available at: <http://www.epoc.cochrane.org/en/handsearchers.html>. Accessed February 3, 2008.
- Vandenbroucke JP, Elm Eric von, Altman DG, Gotzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med* 2007;4:1628-54.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology. *JAMA* 2000;283:2008-12.
- Patel BM, Bansal PJ, Tobin MC. Management of anaphylaxis in child care centers: evaluation 6 and 12 months after an intervention program. *Ann Allergy Asthma Immunol* 2006;7:813-5.
- Litarowsky JA, Murphy SO, Canham DL. Evaluation of an anaphylaxis training program for unlicensed assistive personnel. *J Sch Nurs* 2004;20:279-84.
- Blyth TP, Sundrum R. Adrenaline autoinjectors and schoolchildren: a community based study. *Arch Dis Child* 2002;86:26-7.
- Clegg SK, Ritchie JM. "EpiPen" training: a survey of the provision for parents and teachers in West Lothian. *Ambulatory Child Health* 2001;7:169-75.
- Grouhi M, Alshehri M, Hummel D, Roifman CM. Anaphylaxis and epinephrine auto-injector training: Who will teach the teachers? *J Allergy Clin Immunol* 1999;104:190-3.
- Akeson N, Worth A, Sheikh A. The psychological impact of anaphylaxis on young people and their parents. *Clin Exp Allergy* 2007;37:1213-20.
- Kim JS, Sinacore JM, Pongracic JA. Parental use of EpiPen for children with food allergies. *J Allergy Clin Immunol* 2005;116:164-8.
- Rae J, Worth A, Sheikh A. Does prescribing adrenaline to children with allergy increase parental anxiety? An exploratory qualitative study. Edinburgh: University of Edinburgh; 2007.
- Rankin KE, Sheikh A. Serious shortcomings in the management of children with anaphylaxis in Scottish schools. *PLoS Med* 2006;3:1429-33.
- Hannaway PJ, Connelly ME, Cobbett RM, Dobrow PJ. Differences in race, ethnicity and socioeconomic status in schoolchildren dispensed injectable epinephrine in 3 Massachusetts school districts. *Ann Allergy Asthma Immunol* 2005;95:143-8.
- Hayman GR, Bansal AS. Knowledge about using auto-injectable adrenaline: review of patients' case notes and interviews with general practitioners. *BMJ* 2003;327:1328.
- Powers J, Berggren MD, Finnegan L. Comparison of school food allergy emergency plans to the Food Allergy and Anaphylaxis Network's standard plan. *J Sch Nurs* 2007;23:252-8.
- Moneret-Vautrin DA, Kanny G, Morisset M, Flabbee J, Guenard L, Beaudouin E, et al. Food anaphylaxis in schools: evaluation of the management plan and the efficiency of the emergency kit. *Allergy* 2001;56:1071-6.
- Summers CW, Pumphrey RS, Woods CN, McDowell G, Pemberton PW, Arkwright PD. Factors predicting anaphylaxis to peanuts and tree nuts in patients referred to a specialist center. *J Allergy Clin Immunol* 2008;121:632-8.
- Cochrane AL. Effectiveness and efficiency. Random reflections on health services. London: RSM; 2004.
- Colver A. Are the dangers of childhood food allergy exaggerated? *BMJ* 2006;333:494-6.
- Cresswell K, Sheikh A. Information technology-based approaches to reducing repeat drug exposure in patients with known drug allergies. *J Allergy Clin Immunol* 2008;121:1112-7.

TABLE E1. MEDLINE and EMBASE search strategy

Search term
1 ANAPHYLAXIS/
2 anaphylaxis react\$.mp.
3 anaphylactic react\$.mp.
4 anaphylactic shock\$.mp.
5 anaphylactoid syndrome\$.mp.
6 anaphylactoid react\$.mp.
7 anaphylactic syndrome\$.mp.
8 anaphylactoid shock\$.mp.
9 acute systemic allergic react\$.mp.
10 idiopathic anaphylaxis.mp.
11 systemic anaphylaxis.mp.
12 or/1-11
13 guideline\$.mp.
14 training\$.mp.
15 training protocol\$.mp.
16 chronic diseas\$ management.mp.
17 long term plan\$.mp.
18 action plan\$.mp.
19 EDUCATION/
20 Self management.mp.
21 Or/13-21
22 12 and 21

For TRIP and LILACS databases, we used the terminology (anaphyla* or acute systemic allergic react*) and (guideline* or training* or chronic diseas* management or long term plan* or action plan* or education or self management). Other databases were searched for title, abstracts, and key words of articles that contain the term *anaphylaxis*.

TABLE E2. Examples of AMPs

	Name of AMP	Country, author, year	Design	Implementation site
1	Management of anaphylaxis at school, food allergy action plan	Australia, Australian Family Physician, 2002 ^{E1}	Emergency management plan	Schools
2	Action plan for anaphylaxis: emergency response plan	Australia, Australian Society of Clinical Immunology and Allergy (ASCIA), 2003 ^{E2}	Emergency management and preventive strategies, EpiPen visual instructions	Schools
3	Anaphylaxis emergency treatment plan	Australia, Australian Capital Territory Education and Training, 2003 ^{E3}	Emergency management, EpiPen visual instructions	Schools and preschools
4	Long-term anaphylaxis management plan	Canada, Simons, 2006 ^{E4}	Anaphylaxis emergency action plan and long-term management	Community
5	Personalized care project in schools	France, Moneret-Vautrin et al, 2001 ^{E5}	Emergency management	Schools
6	Individualized reception plan for anaphylaxis	France, Antoine, 2001 ^{E6}	Emergency management	Schools
7	Food anaphylaxis management plan for children and adults	United Kingdom, Ewan and Clark, 2001 ^{E7}	Emergency and preventive strategies	Community
8	School management of severe allergies (anaphylaxis)	United Kingdom, Lothian school nurses, 2007 (unpublished data)	Emergency management	Schools
9	Emergency health care plan	United States, Sicherer, 1999 ^{E8}	Emergency management	Schools
10	Anaphylaxis management plan	United States, Fogg and Pawlowski, 2003 ^{E9}	Emergency care and directions for use of Epi-Pen	Schools
11	Extreme allergy management and emergency plan	United States, New Brunswick Schools, 2004 ^{E10}	Emergency management	Schools
12	Food allergy action plan	United States, The Food Allergy and Anaphylaxis Network, 2006 ^{E11}	Emergency management with Epi-Pen directions	Schools

REFERENCES

- E1. Management of anaphylaxis at school. *Australian Family Physician* 2002;31:810.
- E2. Australian Society of Clinical Immunology (ASCI) 2003. Action Plan for anaphylaxis. Available at: http://www.allergy.org.au/images/stories/anaphylaxis/Action_Plan_anaphylaxis_personal.pdf. Accessed June 11, 2008.
- E3. Australian Capital Territory Education and Training. Anaphylaxis emergency treatment plan. 2003. Available at: http://www.det.act.gov.au/_data/assets/pdf_file/0017/18332/firstaid.pdf. Accessed June 11, 2008.
- E4. Simons E. Anaphylaxis, killer allergy: Long-term management in the community. *J Allergy Clin Immunol* 2006;117:367-77.
- E5. Moneret-Vautrin DA, Kanny G, Morrisset M, Flabbee J, Guenard L, Beaudoin E, et al. Food anaphylaxis in schools: evaluation of the management plan and the efficiency of the emergency kit. *Allergy* 2001;56:1071-6.
- E6. Antoine LC. Management of children with a food allergy and the individualized reception plan. *Allergie et Immunologie* 2001;33:357-62.
- E7. Ewan PW, Clark AT. Long-term prospective observational study of patients with peanut and nut allergy after participation in a management plan. *Lancet* 2001;357:111-5.
- E8. Sicherer S. Manifestations of food allergy: evaluation and management. *American Family Physician*, 1999. Available at: <http://www.aafp.org/afp/990115ap/415.html>. Accessed June 11, 2008.
- E9. Fogg MI, Pawlowski NA. Anaphylaxis. *Pediatric Case Reviews* 2003;3:75-82.
- E10. New Brunswick Department of Education. Extreme allergy management and emergency plan. New Brunswick Department of Education 2004. Available at: <http://www.gnb.ca/0000/pol/e/704AD.pdf>. Accessed June 11, 2008.
- E11. The Food Allergy and Anaphylaxis Network (FAAN). Food allergy action plan. The Food Allergy and Anaphylaxis Network 2006. Available at: <http://www.foodallergy.org/actionplan.pdf>. Accessed June 11, 2008.