National Institute for Health and Clinical Excellence

Anaphylaxis
Scope Consultation Table
1 – 29 September 2010

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Anaphylaxis Campaign, The	15.00	General	The Anaphylaxis Campaign would like to see the scope of the guideline extended to include all those who have experienced an anaphylactic episode but did not translate into an emergency admission at the time. These patients usually present to their GP at a later date.	We have not restricted the setting where the emergency treatment may have occurred, so we anticipate that any person who has needed emergency treatment, including by self-administration, who then presents at any setting, including primary care would be covered in this guideline. No change to the guideline scope is therefore needed.
SH	Anaphylaxis Campaign, The	15.01	General	It is crucial that referral is included as part of the guidance .Following an admission for anaphylaxis referral to an allergy specialist is essential but is not currently uniformly carried out.	We accept that this is important and this is specified in 4.3.1d – when, where, and to whom to refer after assessment. No change was considered to be needed to the guideline Scope.
SH	Anaphylaxis Campaign, The	15.02	General	It is essential that emergency medication is prescribed. The provision of a trainer autoinjector with each autoinjector prescribed would represent a significant step forward.	To address your concerns, education for patients on the appropriate use of adrenaline auto-injectors pre-referral is specified as being covered in the guideline (section 4.3.1e). The format and content of this education will be part of the guideline development. We have added in 'training' to 4.3.1 to cover this issue specifically.
SH	Anaphylaxis Campaign, The	15.03	General	Management advice should be available to each patient on discharge. This should include information regarding patient support groups (the Anaphylaxis Campaign) so that the appropriate websites and helplines can be accessed.	Information and support for patients in the period after the post emergency treatment assessment is part of this guideline and is specified in 4.3.1e. The format and content of this information and support will be part of the guideline development. No change was considered to be needed to the guideline Scope.
SH	Anaphylaxis Campaign, The	15.04	General	It is vital that the guideline makes clear that the emergency admission is often the first stage of the allergic persons journey and needs to pave the way	This guideline focuses on the specific period post emergency treatment; however, as you note, this is only part of the care pathway. We consider that this

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				to a robust pathway giving appropriate specialist care.	is clear in the guideline Scope and no change was considered necessary.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.00	3 f	Statement misleading. It is not 'initial assessment of' but should read 'management after recovery from acute episode'. There is guidance on initial assessment and acute treatment. That is not the purpose of this guideline	We have now changed the use of initial throughout the Scope (including removal where appropriate), to address this concern.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.01	2	Same point as above, it is not 'the initial assessment' – but is the further assessment after the attack – which should involve identifying aetiology and providing avoidance advice and medical management to prevent or treat further attacks (and might take care in primary or secondary care after recovery from the acute episode). This requires specific action and often includes decision to make a referral. Suggest rewording of 'initial assessment' and clarification of remit	This is the remit as received from the DH. No changes to the remit can be made. However, we have changed the guideline title to reflect more clearly the intent of the guideline.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.02	4.4 a	Further attacks is a key outcome. This will be dependent on accurate diagnosis of aetiology of the anaphylaxis and the quality of management. This will depend on 4.3 c and d – which are not being considered. Suggest important they are included.	This section describes those outcomes which will be searched for in the evidence base to underpin recommendations. So although we will not be making recommendations on prophylaxis or management of associated co-morbidities, we will be examining the impact of an intervention, for example referral or not, on the rate of further attacks. No change was considered to be needed to the guideline Scope in response to this comment.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.03	4.4.c	Physical examination in the recovered patient is unlikely to be relevant in the majority of patients – who are well between attacks. This is therefore not an important or useful outcome measure	However, we will be looking for evidence to determine the usefulness of a physical examination, and it may prove that there is no evidence to support the recommendation of a physical examination. No change was considered to be needed to the guideline Scope in response to this comment.

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SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.04	4.5	Health economics. The important measure is prevention of further anaphylaxis which reduces cost by avoiding admissions and A&E attendances; a secondary measure is medical management to reduce severity (depends on the aetiology) and ability to self treat and intervene early should further episodes occur (also costs saving). Adrenaline auto-injectors should be made available to the patient ie are needed but if management is of high quality should rarely be required ie used (eg if trigger is diagnosed and avoidance advice of high quality there will be no further episodes yet it is appropriate to carry adrenaline). It will be difficult to use them (particularly numbers used but also numbers prescribed) as an indicator of cost effectiveness. This point needs to be made.	In the assessment of the cost effectiveness of specialist clinics and the prescription of adrenaline auto-injectors the issues raised will need to be considered in any health economic analyses.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes) & British Society for Allergy & Clinical Immunology (BSACI)	16.05	5.1	These examples are not related	We have removed these examples.
SH	College of Emergency Medicine	11.00	3.1a,b,c	Although a precise definition is not important in the emergency management of anaphylaxis, clearer definition of what constitutes a "systemic hypersensitivity reaction" may be needed. It is well recognised that patients may be diagnosed with other conditions or may be treated inappropriately for anaphylaxis. Although this will not necessarily affect their emergency treatment, it will be particularly relevant in determining who gets diagnosed and thus referred with an anaphylactic reaction.	Thank you for this point, and we anticipate that this will be part of the guideline development process, specifically around confirmation of the anaphylactic episode and who should be referred. No change to the guideline Scope was considered necessary.
SH	College of Emergency Medicine	11.01	3.2a	Increasingly, Emergency Departments (ED) are utilising Clinical Decision Units (CDU) to manage patients after emergency treatment. This model is used in many UK EDs for anaphylactic reactions,	Thank you for this information and this is an issue that will become very relevant when the Implementation support is developed.

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				and allows consistent, streamlined diagnostics, management and referral on discharge. There exists an opportunity to formalise this model within the care pathway for patients with Anaphylaxis presenting to EDs.	
SH	College of Emergency Medicine	11.02	4.3.1a	See comment 1. above. Presumably, this will focus on assessment in the outpatient setting, but some criteria for identification (as this is where most diagnostic uncertainty arises) of appropriate patients would be useful.	We have been asked by the DH to produce a short guideline after emergency treatment. The criteria therefore that we have used to define the guideline population is those who have received emergency treatment for anaphylaxis. If the issue is how these patients are identified in practice, this would be part of the Implementation support provided when the guideline is published. No change was considered to be needed to the guideline Scope in response to this comment.
SH	College of Emergency Medicine	11.03	4.3.1c,e	Clear guidance as to which specific groups of patients are given auto-injectors would be welcome, bearing in mind the safety issues with inappropriate use. In addition, specifying where the responsibility for prescribing and training patients on their use rests would be useful.	Both provision and education for adrenaline auto-injectors pre-referral are specified as being covered in the guideline (section 4.3.1 c and e). And we anticipate that both the responsibility for prescribing and education will be part of the guideline development. This has been clarified in section 4.3.1.
SH	College of Emergency Medicine	11.04	4.3.2a,b	Presumably, Resuscitation Council (UK) guidance on emergency management on anaphylaxis should continue to be followed.	As emergency management is outside the Scope of this guideline, we would expect that current practice would remain unchanged, whichever guidelines or protocols are in use.
SH	Department of Health	12.00	General	This organisation responded and said they had no comments to make.	Thank you
SH	Lincoln Medical Ltd	3.00	4.3.1	Where adrenaline auto-injectors are provided the pack should contain a dummy Trainer device with clear instructions on how to use the real device. The Trainers should be included free of charge. There is a significant amount of published data showing that both health care professionals and patients and carers are not taught properly how to use a device, forget how to use it and immediate family and friends	To address your concerns, education for patients on the appropriate use of adrenaline auto-injectors pre-referral is specified as being covered in the guideline (section 4.3.1e). The format and content of this education will be part of the guideline development. We have added in 'training' in 4.3.1 to cover this specific point.

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				and colleagues have frequently no idea what to do in an emergency. Mandatory Trainer device provision would go some way to helping to solve a growing problem	
SH	NHS Direct	6.00	General	NHS Direct welcome the guidance and have no comment on its content.	Thank you
SH	Nottingham Support Group for Carers of Children with Eczema	4.00	4.1.1	What constitutes "emergency"? It seems to me unacceptable if the implication that someone has to get to the point where their life is in the balance before those "at high risk of anaphylactic episodes" can be set upon an agreed pathway. My experience was that my youngest reacted to the aerosol effect of bags of peanuts being opened in the same room as him. At that stage he became severely asthmatic but treatable with his medication for that: so he was not an "emergency" but equally "at high risk of anaphylactic episodes".	We have been asked by the DH to produce a short clinical guideline on 'the initial assessment and the decision to refer following emergency treatment for anaphylactic episode', which would exclude the other groups, such as your example, where the cause of the reaction was known. The Scope has therefore not been changed. We agree that people should not have to experience an emergency before appropriate care is given. It is however, not the focus of this guideline.
SH	Nottingham Support Group for Carers of Children with Eczema	4.01	4.3.2	What relationship do associated co morbidities have with the anaphylaxis? If poor control of a co morbidity has an implication on the vulnerability of the patient to anaphylaxis, this must have a bearing on the treatment and information provided to the patient before referral.	However, this may form part of the history taking (in that people may be asked if, for example, their asthma is well controlled), but we will not be making recommendations on the optimal management of co-morbidities (hence the exclusion). No change was considered to be needed to the guideline Scope in response to this comment.
SH	Queen Anne St Medical Centre	9.00	General	This organisation responded and said they had no comments to make.	Thank you
SH	RCPCH Allergy Care Pathways Project	17.00	General	The current process makes if very difficult to attend all the planned days for the GDG meetings. Having alternate days for attendance makes it difficult for consultants who provide clinics to attend. The key issue is that NICE will not get those with the best clinical and research experience because of their clinical and research commitments within their institutions. There needs to be far greater opportunity for adjusting scheduling based on the	Whilst every effort is made to let prospective GDG members know the dates of the GDG meetings as far in advance as possible, we accept that there may be occasions when someone is unable to join the GDG due to prior commitments. Our experience of holding 2 day GDG meetings is generally very positive. As we only have a total number of 6 days with which to develop each short clinical guideline, it is essential the group form, and function well

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				people selected to serve on the committee. Surely the priority should, in the first instance, be to get the most skilled people with the appropriate expertise rather than setting limits in relation to the timing of meetings first.	together as quickly as possible. The feedback we have received from previous GDG members suggests that by holding 2 day GDG meetings, this enables the group to function well together, in a short space of time.
SH	RCPCH Allergy Care Pathways Project	17.01	General	It will be important to determine the severity of a reaction to be covered by the scope and how this is defined as there may be "potential life threatening reactions" which were reduced in severity by antihistamine treatment or similar (perhaps even adrenaline) before arrival at a and e. (It will sometimes be difficult to determine if the adrenaline had for example been given too soon and whether the reaction was truly life threatening so this will have to be considered.) This is similar to determining those at potential future risk – what may have been a mild / aborted reaction first time may endanger life more quickly on subsequent exposure. The word "suspected" anaphylaxis will need defining well.	We anticipate that the severity of reaction will be part of any history to confirm an episode of anaphylaxis. However, the population covered in this guideline is those who receive emergency treatment for anaphylaxis. Regarding the definition of 'suspected'; this is something that will be agreed early in development with the Guideline Development Group.
SH	RCPCH Allergy Care Pathways Project	17.02	General	The introduction refers to non Ige mediated anaphylaxis – does this mean severe GI symptoms needing resuscitation with fluids – is this to be included? Should it just cover any " life threatening reaction caused by an allergenic trigger" or IgE mediated allergic reactions alone??	The definition that we have used does not cover this population, so this group are excluded. No change to the guideline Scope was considered necessary.
SH	RCPCH Allergy Care Pathways Project	17.03	4.1.1	This section indicates what will actually be covered by the review which is those patients who have received emergency treatment for suspected anaphylaxis or are at high risk of anaphylaxis. It is the latter section which is very unclear and appears to conflict with statements in future sections. Thus for instance in 4.1.2 excluded will be those conditions other than suspected anaphylaxis. This would appear to exclude patients with acute asthma who may or may not have had an anapylactic reaction triggering their asthma attack and likewise	We have been asked by the DH to produce a short clinical guideline on 'the initial assessment and the decision to refer following emergency treatment for anaphylactic episode'. This would therefore exclude the emergency management of the episode and also the identification of those in whom an anaphylactic episode has occurred but where anaphylaxis was not suspected; so this guideline only starts in those treated for a suspected anaphylactic episode.

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				urticaria and angioedema which is not in itself life threatening but may be a marker of an allergy with potential to be life threatening in the future. By excluding such cases they are probably excluding the vast majority of individuals who have actually subsequently died of anaphylaxis. This again is in the exclusions section in 4.3.2 which suggests that the only consideration will be those people who have already received emergency treatment for an anaphylactic episode with a very rigid description of a full blown life threatening reaction. However, the vast majority of people who have the potential for anaphylactic reactions will in the first instance present with a milder acute reaction such as urticaria, angioedema or perhaps a somewhat more severe but less likely to be detected as anaphylaxis exacerbation of asthma. The imperative is to include all such patients in the initial risk assessment to decide on the need for appropriate rescue treatment and avoidance advice. I would therefore make a plea to include people who, before they received emergency treatment, have the potential for having a future anaphylactic episode.	
SH	RCPCH Allergy Care Pathways Project	17.04	4.1.2 a	The statement in relation to exclusion is obvious. Perhaps you could clarify why it is written and if you mean or indicate something else	Noted, however, it is there for clarity.
SH	RCPCH Allergy Care Pathways Project	17.05	4.3.2	Perhaps the key is in the clinical history to assess a dose response relationship. Thus an individual who has merely had skin contact with an allergen or perhaps even more remotely has been in an environment where the allergen is present, and has mild urticaria and angioedema has a very high risk of anaphylaxis if the product is ingested or injected in the future.	We anticipate that such detail will form part of the evidence review and discussions when drafting recommendations on the clinical history.
SH	RCPCH Allergy Care Pathways Project	17.06	4.5	As has been discussed between RCPCH and NICE previously, the formula for QALYS is based on adult	Thank you for your comment. The issue is not the calculation of the QALY, but the values that are used

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				practice. There is an imperative for the use of a different formula when applied to children. In relation to potential anaphylaxis this is particularly important as there are major impacts on schooling, the parents and indeed siblings in the family. The costs in terms of food purchasing for the family are increased in those where there is food allergy. There are major psychological impacts on the child and family which can affect schooling, educational attainments and socialisations. Children with food allergy often find themselves excluded from parties, school trips and need to have their lunches in isolation from their peers.	in the calculation. The values that used in the analysis should have been obtained from children using the public's valuation. NICE understands the technical and methodological difficulties in doing this. Therefore, the cost effectiveness analysis and guideline development group will explicitly consider this.
SH	RCPCH Allergy Care Pathways Project	17.07	6	Other guidelines or standards of care documents should be cross referenced, including the RCPCH anaphylaxis allergy care pathway which should be helpful for those who wish to elaborate. Other guidelines should include: ▪ The Resuscitation Council UK (Resus UK) guideline on the emergency medical treatment of anaphylactic reactions ▪ The European Academy of Allergy and Clinical Immunology (EAACI) guideline on the management of anaphylaxis in childhood ▪ The Guidelines in Emergency Medicine Network (GEMNet) guideline for the management of acute allergic reaction	We have added brief reference to these other guidelines in section 3.2b.
SH	Resuscitation Council (UK)	5.00	General	The Resuscitation Council (UK) [RCUK] supports NICE in the development of this Guidance. The Resuscitation Council (UK) has produced guidelines for the Emergency Treatment of Anaphylaxis since 1999 with the most recent update in 2008 (http://www.resus.org.uk/pages/reaction.pdf.) The next update is due in 2013. It is important that the NICE guidance sticks to its scope of dealing with	Thank you. Our pathway will begin after initial emergency treatment has been given.

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				issues after the initial emergency treatment and avoids introducing any inconsistencies between the Current RCUK guidance and the NICE guidance. It is important that new NICE guidance does not cause confusion by addressing initial emergency treatment issues. On the whole the RCUK is pleased with the topic scope.	
SH	Resuscitation Council (UK)	5.01	1.	The title should actually refer to the fact that the guidance is 'following emergency treatment for suspected anaphylaxis. The term suspected anaphylaxis would better convey that these patients may need specialist investigation to confirm the diagnosis.	We have changed the title as suggested.
SH	Resuscitation Council (UK)	5.02	3.1	This whole section is mainly taken from the RCUK 2008 anaphylaxis guideline. It would be nice if this were acknowledged.	We acknowledge that the 2008 guideline was a key source of background information. However, references are not cited in NICE guideline Scopes.
SH	Resuscitation Council (UK)	5.03	3.1.a	This definition is the RCUK modification of the EAACI guideline.	This has been clarified in the text.
SH	Resuscitation Council (UK)	5.04	General	Anaphylaxis is the severe end of the spectrum of allergy related disorders – not all reactions that present to emergency departments are life threatening. Widening the scope to include other groups – severe allergic rashes, angio-oedema that may benefit from referral to an allergy specialist may be useful.	We agree that anaphylaxis is a spectrum, but we have been asked by the DH to produce a short clinical guideline on 'the initial assessment and the decision to refer following emergency treatment for anaphylactic episode', which would exclude the other groups. The Scope has therefore not been widened.
SH	Resuscitation Council (UK)	5.05	4.3.1a	A schedule for measurement of tryptase currently exists in the RCUK guidelines and in guidelines from the Association of Anaesthetists for anaphylaxis associated with anaesthesia(http://www.aagbi.org/publications/guidelines/docs/anaphylaxis_2009.pdf) The current guidance should not be changed unless there is new evidence.	We are aware of the current guidance, however this was considered by attendees of the Scoping Workshop to be a relevant and important question for this guideline. And as you note, any recommendations will be based on the reviewed evidence. No change was considered to be needed to the guideline Scope in response to this comment.
SH	Royal College of General Practitioners	18.00	4.3.2 (a)	It would be very helpful if the review could cover the diagnosis and recognition of anaphylaxis. Many clinicians are not clear about this. Formal reference	We recognise the importance of correct diagnosis and recognition; however, we were asked by the DH to produce a short clinical guideline on 'the initial

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				to the EAACI definition would be OK. If the Guideline is to give advice on structure about what to do after an epidode of anaphylaxis then it must define what we are talking about.	assessment and the decision to refer following emergency treatment for anaphylactic episode'.
SH	Royal College of General Practitioners	18.01	4.3.1 (e)	Should specifically mention training on Epinephrine injectors	This has been added.
SH	Royal College of General Practitioners	18.02	4.4 (b)	Specifically address the fact that there is a tendency for 'middle class' patients to be referred – social inclusion	We anticipate that where there is evidence on different referral rates, this will form part of the discussions and recommendations, where appropriate. We have also added socioeconomic groups as needing special consideration in section 4.1.1b
SH	Royal College of Nursing	14.00	General	The Royal College of Nursing welcomes proposals to develop this guideline. The draft scope seems comprehensive.	Thank you
SH	Royal College of Nursing	14.01	General	The study is timely. Having been involved in training on anaphylaxis with Gps/practice nurses, district nurses, school nurses, we are aware that there are positive and negative concerns regarding the use/requirements for epipen/anapen.	Thank you
SH	Royal College of Nursing	14.02	4.3.1 (a)	We are pleased to see in bullet point3 of this section that the measurement of serum mast cell tryptase will be key in the clinical assessment.	Thank you
SH	Royal College of Nursing	14.03	4.3.1 (a)	We assume that under the first bullet point, this will include the Swedish work on molecular allergology?	We will look for relevant evidence as agreed with the Guideline Development Group. However, we will not be looking for evidence on how the possible cause should be confirmed through allergy testing, but whether the clinical history can identify possible causes before referral for further assessment if required. No change was considered to be needed to the guideline Scope in response to this comment.
SH	Royal College of Paediatrics and Child Health	13.00	General	The College thinks this guidelines is timely and welcome.	Thank you
SH	Royal College of Paediatrics and Child Health	13.01	General	We note the decision to refer will be more helpful where division between referral from a primary care	We have not restricted the setting where emergency treatment may have occurred, so we anticipate that

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				setting is considered vs. referral from an Emergency Department.	any recommended referral strategies will cover both examples. No further clarification was considered needed in the guideline Scope.
SH	Royal College of Paediatrics and Child Health	13.02	General	Clear definitions of what emergency treatment covers will be needed.	The definition of emergency treatment is outside the Scope of this guideline, but we would expect any patients to be treated in line with recognised protocols and guidelines as applicable to their setting and location. No definitions have been added to the guideline Scope.
SH	Royal College of Paediatrics and Child Health	13.03	General	Anecdotally, we note the frequent question that arises in the outpatient allergy consultation is whether an adrenaline device should have been prescribed prior to referral, with full assessment and education about how and when to use it. Anecdotal experience demonstrates that full education around such devices happens more within the secondary allergy clinic setting than in primary care. GPS and families are often uncertain about this issue.	Both provision and education for adrenaline auto-injectors pre-referral are specified as being covered in the guideline (section 4.3.1 c and e).
SH	Royal College of Paediatrics and Child Health	13.04	3.1 (g)	We would like clarification on whether IgE involvement is part of the definition of anaphylaxis. Reactions that result in direct mast cell degranulation that can look like anaphylaxis (pseudoanaphylaxis) usually result from drugs only likely to be given in hospital – morphine, x-ray contrast media and muscle relaxants. We think this distinction could be made more clearly.	We will be considering both IgE and non-IgE mediated anaphylaxis (as these are not differentiated between in the definition we have used), through the recommendation of strategies to confirm 'true' anaphyalaxis. No change to the guideline Scope was considered necessary.
SH	Royal College of Paediatrics and Child Health	13.05	3.1 (h) / (i)	There has been an apparent seven-fold increase in hospital treatment for anaphylaxis. Clearly then it is a diagnosis which is recognised and coded and extractable for epidemiological studies. This does not seem to be reflected in any measurable increase in mortality. The statement that the mortality of 20 per year "may be a substantial under-estimate" should be put into context. Whether it is an under-estimate or not, there has been no increase in mortality, despite a seven-fold increase in hospital	We accept your concerns about the potential for increased and unnecessary anxiety. However, there is a risk of death associated with anaphylaxis which may be higher in specific groups. To address your concerns, education for patients on the appropriate use of adrenaline auto-injectors pre-referral is specified as being covered in the guideline (section 4.3.1 c and e). We also anticipate that we will be considering which patients should receive auto-injectors, with the possible outcome

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				treatment. This suggests that the majority of the events do not fulfil the definition of anaphylaxis given at the start of the paper as a "severe life-threatening reaction". Is this the definition really applied to the startling figure that 1 in 1333 people in the UK will have an anaphylactic reaction in their lifetime? Low and stable anaphylaxis mortality rates are not unique to the UK – they are similar in the US and in Australia. For example a paper published in 2009 (Liew WK, Williamson E, Tang M. Anaphylaxis fatalities and admissions in Australia. J Allergy Clin Immunol, 123,2: pp 434-442) found anaphylaxis deaths at 12 per year (0.64 deaths per million population per year), which would equate to around 40 deaths per year in the UK. Of these deaths 60% were definitely or probably caused by drug reactions and only 6% to foods. We do not wish to diminish the importance of properly recognising severe allergic responses and providing correct advice and treatment. We do think it is important, however, not to create additional anxiety by the suggestion that these interventions will save lives. This is particularly relevant to the provision of adrenaline autoinjectors, which are a significant source of anxiety to those to whom they are given, and are perceived as a life saving treatment that must be carried at all times. The evidence base for their widespread use appears to be very weak.	that such devices should not be prescribed for all patients who have experienced an anaphylactic episode.
SH	Royal College of Paediatrics and Child Health	13.06	3.1 (h) / (i)	It would be helpful to have the epidemiological data broken down by age group. In the Australian study there were 10 deaths in children (1.1 per year) of which four were related to food allergy.	This section is a general review of the epidemiology and we do not consider that any further break down is required. However, we accept that there may be differences in the risk of recurrence and death in different age groups, and such considerations will be

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					key to the development of appropriate referral strategies.
SH	Royal College of Paediatrics and Child Health	13.07	4.3.1 (c)	We suggest this is re-worded to "Provision of adrenaline auto-injectors and by whom".	Thank you and we have revised as suggested.
SH	Royal College of Paediatrics and Child Health	13.08	4.4	We suggest this section includes an outcome measure about appropriate and inappropriate prescription of adrenaline auto-injectors: this could be total prescriptions of such injectors after release of guideline compared to historic data, and could be area by area variations in such prescriptions. Anecdotal experience suggests that, in children, adrenaline auto-injectors are probably over prescribed from pressure by parents or by comments to parents by school nurses.	This section describes those outcomes which will be searched for in the evidence base to underpin recommendations. The outcomes measures you describe are more relevant to the assessment of the guideline implementation. So although are important, such outcomes would not be directly relevant to the development of this guideline. No change was considered to be needed to the guideline Scope in response to this comment.
SH	Royal College of Pathologists	8.00	3.1b)	Suggest re-phrasing of paragraph as follows: 'Many people with anaphylaxis do not currently benefit from a robust or optimal post-acute process for definitive diagnosis and continuing management of anaphylaxis. The reasons for this include failure to a) recognise the clinical scenario of anaphylaxis, b) differentiate anaphylaxis from other, less severe histamine-releasing reactions, c) differentiate anaphylaxis from other conditions which may mimic some or all of its clinical features, d) refer, or refer appropriately, for specialist opinion after the acute episode. This may give rise to potential difficulties for the affected individual (anxiety, incorrect diagnosis, lack of or inappropriate management, recurrent episodes) or the NHS (burden of acute care requirements, avoidable costs).' The presumption in the scoping document that allergy is an inevitable and identifiable cause underlying a clinical diagnosis of anaphylaxis is incorrect.	Thank you for the suggested wording. It now reads as follows: "After an acute episode of anaphylaxis, many people do not currently go through an optimal post acute process. The reasons for this include anaphylaxis not being recognised, or not being differentiated from less severe histamine-releasing reactions or from other conditions that mimic some or all of its clinical features. Also, people may not be referred, or be referred appropriately, to a specialist. This can affect the likelihood of the person receiving a definitive diagnosis and can lead to anxiety, inappropriate management and recurrent episodes. It can also give rise to avoidable costs for the NHS and increase the need for acute care." Minor changes may have been made in editing for the final version.
SH	Royal College of Pathologists	8.01	3.1c)	Suggest addition to end of existing paragraph as follows: 'There is significant variation across clinicians as to the definition and clinical application	We have not added this, as we consider that the clinician variation has been covered in 3.1a) & 3.1b), which would include both definition and application.

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				of the term anaphylaxis.'	
SH	Royal College of Pathologists	8.02	3.1e), paragraph 1	Suggest addition to end of existing paragraph as follows: 'This figure may be significantly influenced by factors outlined in c) above.'	We have added in the term 'estimate' to indicate that this figure may not be a true representation as indicated.
SH	Royal College of Pathologists	8.03	3.1g), paragraph 1, lines 1-3	Suggest existing text in lines 1-3 may be altered, for clarity. To 'Anaphylaxis may be allergic (i.e. immunologically mediated via IgE or other immune mechanisms) or non-allergic. Foods, insect venoms, latex and some drugs are common precipitants of IgE-mediated allergic anaphylaxis. Many drugs can also act through non-allergic mechanisms. A significant proportion of anaphylaxis is also classified as idiopathic, where there are significant clinical effects arising from histamine release but neither the precipitant nor the preceding inflammatory mechanisms (allergic, non-allergic) can be defined with certainty'.	Thank you for the suggested wording. It now reads as follows: "Anaphylaxis may be an allergic response (that is, immunologically mediated via IgE or other immune mechanisms) or a non-allergic response. Foods, insect venoms, latex and some drugs are common precipitants of IgE-mediated allergic anaphylaxis. Many drugs can also act through non-allergic mechanisms. A significant proportion of anaphylaxis is also classified as idiopathic, where there are significant clinical effects arising from histamine release but neither the precipitant nor the preceding inflammatory mechanisms (allergic, non-allergic) can be identified with certainty." Minor changes may have been made in editing for the final version.
SH	Royal College of Pathologists	8.04	3.2b), lines 4-7	Suggest change to '….trusts do not specifically or overtly commission specialist allergy services. There is a common (but incorrect) assumption that allergic disease can be adequately managed in the context of a number of clinical disciplines even where the majority of physicians working within these disciplines do not have the training, experience or expertise to provide informed and optimal care at a specialist level'	This section has been considerably shortened, and in the process, this paragraph was removed.
SH	Royal College of Pathologists	8.05	3.2c), sentence 2	Suggest re-phrase text to: 'Surveys of GP experience and understanding of allergy in the UK have shown widespread inadequacies in knowledge, training, experience and confidence to effectively manage conditions such as food allergy, multisystem	This section has been considerably shortened, and in the process, this paragraph was removed.

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				allergic disease and anaphylaxis'.	
SH	Royal College of Pathologists	8.06	3.2e)	More recent patient survey data may be available from the Anaphylaxis campaign as a result of their involvement in the 2010 RCP/RCPath Working Group Report on progress with implementing the 2007 House of Lords Science & Technology Committee recommendations.	We have checked this report and there is no reference to any more recent patient surveys, so we have retained the original wording.
SH	Royal College of Pathologists	8.07	3.2	Consider addition of sub-section g) to existing text a)-f): g) There have been a number of publications in recent years from the Royal Colleges, Her Majesty's Government and the House of Lords which have identified significant long-term structural and operational deficiencies in the care of people with allergic disease, including anaphylaxis, in the NHS. A national care pathway for anaphylaxis in childhood is currently under development.	We consider the 'Current Practice' section to adequately explain the need for this guideline. As such, no changes have been made in response to this comment.
SH	Royal College of Pathologists	8.08	4.1.2a)	Consider additional sentence as follows: 'It is recognised that there is overlap between anaphylaxis, other histamine-mediated conditions of lesser severity and a range of other disorders which may present acutely. Variable usage, definition and application of the term anaphylaxis are additional contributory factors which may complicate accurate disease classification'.	This has not been added. We consider that these issues are recognised in section 3. This section specifically refers to the population that will be covered in the guideline; that is, those people who have been treated for suspected anaphylaxis. The guideline will then make recommendations on how this suspicion should be confirmed or refuted, and any appropriate referral strategies.
SH	Royal College of Pathologists	8.09	4.3.1a)	Add 4th bullet point: undertake selected, initial, specific-IgE testing based on clinical history	This has not been added, as we consider that such testing would be part of the investigations made when referred, as relates to confirmation of the cause, rather than the episode of anaphylaxis.
SH	Royal College of Pathologists	8.10	4.3.1b)	Re-phrase to: 'Timing of assessment and confirmatory tests at the time of and after the presenting episode.'	This has been added.
SH	Royal College of Pathologists	8.11	4.3.1	Consider additional subsection g) to existing text a)-f): g) Conditions which may clinically mimic anaphylaxis.	We have not added this as we consider the Scope to be clear that we are considering the confirmation of 'true' anaphylaxis. And although we will be excluding alternative diagnoses, we will not be making recommendations on the confirmation of

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					other conditions which mimic anaphylaxis.
SH	Royal College of Pathologists	8.12	5.1	Indicated published guidance materials x3 have no direct or significant relevance to anaphylaxis.	We have removed these examples.
SH	Royal College of Pathologists	8.13	General	The guideline scope may usefully link to the updated Specialised Services National Definitions Set No. 17 (Allergy, all ages).	We anticipate that we will refer to such definitions during the development of the guideline, particularly when considering any service issues and implementation, but we do not consider that any link is required in the guideline Scope (so this has not been added).
SH	Royal College of Physicians London	7.00	General	The Royal College of Physicians is grateful for the opportunity to respond to this draft scope consultation. We consider this to be an important topic and would like to make the following comments.	Thank you. Please see responses below to your specific comments.
SH	Royal College of Physicians London	7.01	General and 4.3.2 (a)	We are very concerned that the diagnosis of anaphylaxis during the initial presentation in an emergency setting is not within the scope of the guideline. If the diagnosis is not suspected and accurately made in A&E then appropriate referrals to allergy services will not take place. Our experts (who attending the scoping meeting) were surprised to find that the draft scope would not be dealing with diagnosis and raised the above point strongly at that meeting. It was explained that anaphylaxis is often misdiagnosed/incorrectly diagnosed and that without dealing with this, our starting point for referrals would be incorrect. This included discussion of the data. We would therefore strongly recommend that NICE reconsider this aspect of the scope.	The correct diagnosis of anaphylaxis is important as you note; however, we have been asked by the DH to produce a short guideline after emergency treatment. However, as the guideline population is defined as people who have received emergency treatment for anaphylaxis we will identify those people in whom the working diagnosis is anaphylaxis but who did not have a 'true' anaphylactic episode. No change was considered to be needed to the guideline Scope in response to this comment.
SH	Royal College of Physicians London	7.02	4.5	This section should make it clear that it is the cost effectiveness of specialist allergy clinics in the diagnosis of the <u>cause</u> of anaphylaxis (as oppose to the acute event) that is the key point. We would recommend that the text is amended to include the following:	This guideline will not explicitly examine the cost effectiveness of diagnosing the cause of anaphylaxis but the issues around management, prevention and reduction in mortality and morbidity will be considered in evaluating the cost effectiveness of specialist clinics. Therefore, the wording has been rephrased to:

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				'The prevention of future episodes and the reduction in overall morbidity and mortality from future episodes '	The key health economic questions for this guideline appear to be the cost effectiveness of specialist allergy clinics for the diagnosis of anaphylaxis (as opposed to the acute event) and the prevention of future episodes and the reduction in overall morbidity and mortality from future episodes.
SH	Royal College of Physicians London	7.03	General	While we can understand that the management of anaphylaxis in an emergency setting is not part of the scope as this has been the subject of other guidelines we are concerned that the diagnosis of anaphylaxis during the initial presentation in an emergency setting is not within the scope of the guideline. If the diagnosis is not suspected and accurately made in A&E then appropriate referrals to allergy services will not take place.	We have been asked by the DH to produce a short clinical guideline on 'the initial assessment and the decision to refer following emergency treatment for anaphylactic episode'. This would therefore exclude the emergency management of the episode and also the identification of those in whom an anaphylactic episode has occurred but where anaphylaxis was not suspected; so this guideline only starts with those treated for a suspected anaphylactic episode.
SH	Royal College of Physicians London	7.04	General	In terms of economic aspects it needs to be made clear that it is the cost effectiveness of specialist allergy clinics in the diagnosis of the CAUSE of anaphylaxis (as oppose to the acute event), THE PREVENTION OF FUTURE EPISODES AND THE REDUCTION IN OVERALL MORBIDITY AND MOR TALITY FROM FUTURE EPISODES (text in capital s to be added).	This guideline will not explicitly examine the cost effectiveness of diagnosing the cause of anaphylaxis but the issues around management, prevention and reduction in mortality and morbidity will be considered in evaluating the cost effectiveness of specialist clinics. Therefore, the wording has been rephrased to: The key health economic questions for this guideline appear to be the cost effectiveness of specialist allergy clinics for the diagnosis of anaphylaxis (as opposed to the acute event) and the prevention of future episodes and the reduction in overall morbidity and mortality from future episodes.
SH	Royal Pharmaceutical Society	10.00	General	The RPS welcomes these proposed guidelines and does not have any comments to add to the scope.	Thank you
SH	UK Ophthalmic Pharmacy Group	2.00	3.1.c and General	In ophthalmology intravenous fluorescein is given for fundus angiography. The only injection available to UK hospitals is an unlicensed product. Until there us a licensed option we do not have a baseline level for acceptable level of reaction/ anaphylaxis to the intravenous dye. Licensed consistent quality	And we note that there are many reasons why such baseline figures may not be available or a true estimate. However, we do not consider that any change is required to the guideline Scope.

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				products help to reduce the incidence of adverse reactions including potentially anaphylaxis.	
SH	UK Ophthalmic Pharmacy Group	2.01	General	The MHRA Yellowcard data base for adverse drug reactions does not identify which formulation of fluorescein is given so an entry of an event could relate to the injection, ophthalmic diagnostic strip or preservative free eye drop. Including formulation/ product details on this data base would give a more accurate indication of the level of anaphylaxis to a specific fluorescein product.	Although this may be important additional information that would be useful in tracking the level of anaphylaxis, the scope of this guideline is focussed on the confirmation of an anaphylactic episode and the appropriate referral.

These organisations were approached but did not respond:

Airedale Acute Trust
Alder Hey Children's NHS Foundation Trust
ALK Abello
Allergy UK
Association of Anaesthetists of Great Britain & Ireland
Association of Paediatric Anaesthetists of Great Britain and Ireland
Association of Paediatric Emergency Medicine
BMJ
BOC Healthcare
British National Formulary (BNF)
British Paediatric Allergy, Immunity & Infection Group
British Society of Interventional Radiology
Care Quality Commission (CQC)
Citizens Commission on Human Rights
Commission for Social Care Inspection
Connecting for Health
Dental Practitioners Association
Department for Communities and Local Government
Department for Education
Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)
Dorset Cancer Network
Education for Health

Faculty of Dental Surgery
Faculty of General Dental Practice
Gloucestershire Hospitals NHS Trust
Humber Mental Health Teaching NHS Trust
Intensive Care Society
Interhealth Canada
JBOL Ltd
Lambeth Community Health
Leeds PCT
Liverpool Community Health
Lothian University Hospitals Trust
Luton & Dunstable Hospital NHS Foundation Trust
Medicines and Healthcare Products Regulatory Agency (MHRA)
Ministry of Defence (MoD)
National Allergy Strategy Group
National Day Nurseries Association
National Patient Safety Agency (NPSA)
National Public Health Service for Wales
National Treatment Agency for Substance Misuse
NETSCC, Health Technology Assessment
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Plus
NHS Quality Improvement Scotland
NHS Sheffield
NHS Western Cheshire
North West Allergy and Clinical Immunology Network
Northumberland Hills Hospital, Ontario
Paediatric Intensive Care Society
PERIGON Healthcare Ltd
Phadia Ltd
Poole and Bournemouth PCT
RCPCH Allergy Care Pathways Project
Royal Brompton & Harefield NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales

Royal College of Obstetricians and Gynaecologists

Royal College of Radiologists
Royal Free Hospital NHS Trust
Royal Society of Medicine
Royal United Hospital
Salford Royal Hospitals Foundation NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield Children's NHS Foundation Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence (SCIE)
Society for Acute Medicine
Society of Chiropodists & Podiatrists
South Tees Hospitals NHS Trust
UK NEQAS for Immunology and Immunochemistry
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
Western Health and Social Care Trust
Wirral University Teaching Hospital NHS Foundation Trust
York NHS Foundation Trust