

Appendix C Guideline scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode.

1.1 *Short title*

Anaphylaxis

2 The remit

The Department of Health has asked NICE: 'to produce a short clinical guideline on the initial assessment and the decision to refer following emergency treatment for anaphylactic episode'.

3 Clinical need for the guideline

3.1 *Epidemiology*

A broad definition of anaphylaxis was proposed by the European Academy of Allergy and Clinical Immunology Nomenclature Committee and adapted by the UK Resuscitation Council. The current definition is a severe, life-threatening, generalised or systemic hypersensitivity reaction, characterised by rapidly developing life-threatening airway, breathing and/or circulation problems, usually associated with skin and mucosal changes.

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.

There is no overall figure for the frequency of anaphylaxis from all causes in the UK. Because anaphylaxis presents mainly in accident and emergency departments and outpatient settings, few counts of prevalence are available from NHS sources. Anaphylaxis may not be recorded, or may be mislabelled as something else, for example, asthma; it may also be recorded by cause, such as food allergy, rather than as an anaphylactic episode.

The American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis working group summarised the findings from a number of important international epidemiological studies and concluded that the overall frequency of anaphylaxis lies between 30 and 950 episodes per 100,000 persons per year.

The same group provided data indicating a lifetime prevalence of between 50 and 2000 episodes per 100,000 persons, or 0.05–2.0%. More recent UK primary care estimates indicate a lifetime age-standardised prevalence of a recorded diagnosis of anaphylaxis of 75.5 per 100,000 in 2005. Calculations based on these data indicate that approximately 1 in 1333 of the population of England have experienced anaphylaxis at some point in their lives.

A retrospective study of accident and emergency department attendances in the UK, identifying only the most severe cases and relating this number to the population served, estimated that approximately 1 in 3500 people had an episode of anaphylaxis during the study period 1993 to 1994.

Anaphylaxis may be an allergic response (that is, immunologically mediated by immunoglobulin E or other immune mechanisms) or a non-allergic response. Foods, insect venoms, latex and some drugs are common precipitants of immunoglobulin E (IgE)-mediated allergic anaphylaxis. Many

drugs can also act through non-allergic mechanisms. A significant proportion of anaphylaxis is classified as idiopathic, in which there are significant clinical effects arising from histamine release but neither the precipitant nor the preceding inflammatory mechanisms (allergic or non-allergic) can be identified with certainty. The relative likelihood of the reaction being allergic, non-allergic or idiopathic varies considerably with age.

Food is a particularly common trigger in children and medicinal products are much more common triggers in older people. Worldwide there are 1 million cases of venom anaphylaxis and 0.4 million cases of nut anaphylaxis each year in people younger than 45.

Data indicate a dramatic increase in the rate of hospital admissions for anaphylaxis. Between 1990 and 2004 they went from 0.5 admissions per 100,000 to 3.6 per 100,000; an increase of 700%.

There are approximately 20 anaphylaxis deaths reported each year in the UK, although this may be a substantial underestimate. Risk of death from an anaphylactic episode is increased in people with pre-existing asthma, particularly if the asthma is poorly controlled, and in asthmatics who do not use, or delay treatment with, adrenaline.

3.2 Current practice

There is considerable geographic variation in both practice and service provision, specifically in reviews after emergency treatment for anaphylaxis and decisions about when and where to refer.

There are professional guidelines on the emergency treatment and management of anaphylaxis, but there is currently no relevant national guidance for England and Wales on assessment after the event to confirm an anaphylactic episode or on the decision to refer after emergency treatment.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 *Population*

4.1.1 Groups that will be covered

Adults, young people and children who receive emergency treatment for suspected anaphylaxis.

Within this population, people who are at high risk of anaphylactic episodes, or for whom further anaphylactic episodes would have significant impact, have been identified as needing special consideration.

Consideration will also be given to ensuring equity for all socioeconomic groups if the evidence shows that socioeconomic status affects access to services.

4.1.2 Groups that will not be covered

Adults and children who have received emergency treatment for conditions other than suspected anaphylaxis.

4.2 *Healthcare setting*

Primary, secondary and tertiary settings.

4.3 *Clinical management*

4.3.1 Key clinical issues that will be covered

Clinical assessment after emergency treatment. This will include:

- history, including signs and symptoms, and identification of the possible cause
- physical examination

- measurement of serum mast cell tryptase levels to confirm the diagnosis.

Timing of assessment and confirmatory tests at the time of and after the episode.

Provision of adrenaline auto-injectors, including by whom.

When, where and to whom to refer after assessment.

Information and support needs for patients and carers up to the point of referral, including information and training on the use of adrenaline auto-injectors if prescribed.

Assessment of risk for future episodes up to the point of referral.

4.3.2 Clinical issues that will not be covered

Initial assessment and diagnosis of anaphylactic episode before emergency treatment.

Emergency treatment.

Investigations (specifically IgE and non-IgE testing) to confirm the suspected cause of the anaphylactic reaction, as identified in the history.

Prophylaxis after referral.

Management of associated comorbidities.

Identification and management of complications arising from testing or management.

4.4 Main outcomes

Further or repeat anaphylactic episodes.

Rate of referral between healthcare settings.

Measure of diagnostic utility of physical examination, history taking, serum mast tryptase measurement.

Admission rate for further anaphylactic episodes.

Mortality resulting from further anaphylactic episodes.

Health related quality of life.

Resource use and costs.

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

The key health economic questions for this guideline appear to be firstly the cost effectiveness of referral to specialist allergy clinics for the diagnosis of anaphylaxis (as opposed to for the acute event) and for the prevention of future episodes and the reduction in morbidity and mortality from future episodes. The second issue is the cost effectiveness of adrenaline auto-injectors for the treatment of anaphylaxis this includes the cost implications of training in the use of the auto-injectors. Further cost effectiveness analysis will be considered if any further questions are identified during guideline development.

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline recommendations will begin in December 2010.

5 Related NICE guidance

NICE is currently developing the following related guidance (details available from the NICE website):

- Food allergy in children and young people. NICE clinical guideline. Publication expected January 2011.

6 Further information

Information on the guideline development process is provided in:

- ‘How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS’
- ‘The guidelines manual’.

These are available from the NICE website

(www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

Appendix D How this guideline was developed

This guideline was developed in accordance with the process for short clinical guidelines set out in 'The guidelines manual' (2009) (see www.nice.org.uk/GuidelinesManual). There is more information about how NICE clinical guidelines are developed on the NICE website (www.nice.org.uk/HowWeWork). A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1739).

A systematic review of clinical effectiveness (sections 3.1.2, 3.2.2, 3.4.2 and 3.5.2) was completed by NICE. A technical assessment report, which comprised of a systematic review of clinical and cost effectiveness with additional health-economic modelling (sections 3.3.2 and 3.3.4) was commissioned by NICE from Kleijnen Systematic Reviews Ltd, based in York, England. For full details of the technical assessment report, see appendices F and G Search strategies

The evidence reviews used to develop the guideline recommendations were underpinned by systematic literature searches, following the methods described in 'The guidelines manual' (2009). The aim of the systematic searches was to comprehensively identify the published evidence to answer the review questions developed by the Guideline Development Group and Short Clinical Guidelines Technical Team.

The search strategies for the review questions were developed by the Information Services Team with advice from the Short Clinical Guidelines Technical Team. Structured questions were developed using the PICO (population, intervention, comparison, outcome) model and translated into search strategies using subject heading and free text terms. The strategies

were run across a number of databases with no date restrictions imposed on the searches.

The NHS Economic Evaluation Database (NHS EED) and the Health Economic Evaluations Database (HEED) were searched for economic evaluations. Search filters for economic evaluations and quality of life studies were used on bibliographic databases. There were no date restrictions imposed on the searches.

Guideline Development Group members were also asked to alert the Short Clinical Guidelines Technical Team to any additional evidence, published, unpublished or in press, that met the inclusion criteria.

The searches were undertaken between November 2010 and May 2011.

Scoping searches

Scoping searches were undertaken in August 2010 using the following websites and databases (listed in alphabetical order); browsing or simple search strategies were employed. The search results were used to provide information for scope development and project planning.

Main searches

The following sources were searched for the topics presented in the sections below.

- Clinical Trials.gov
- Current Controlled Trials
- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (CRD)
- Health Technology Assessment Database – HTA (CRD)
- CINAHL (EBSCO)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

- National Research Register Archive
- UK Clinical Research Network

[Specific review question] search

Question 1: Mast Cell Tryptase Test (searched August 2010)

Database: Ovid MEDLINE(R) <1950 to August Week 3 2010> & : Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 31, 2010>

Search Strategy:

- 1 Anaphylaxis/
- 2 Anaphyla*.tw.
- 3 or/1-2
- 4 Tryptases/
- 5 Tryptase*.tw.
- 6 ((Serum* or Mastcell*or Mast-cell* or Mast Cell*) adj3 (Test* or Biops* or Assay* or Exam*)).tw.
- 7 or/4-6
- 8 3 and 7
- 9 Animals/ not Humans/
- 10 8 not 9
- 11 limit 10 to english language

Database: EMBASE <1980 to 2010 Week 34> via Ovid

Search Strategy:

- 1 ANAPHYLAXIS/
- 2 ANAPHYLACTIC SHOCK/
- 3 Anaphyla*.tw.
- 4 or/1-3
- 5 tryptase/
- 6 Tryptase*.tw.
- 7 ((Serum* or Mastcell*or Mast-cell* or Mast Cell*) adj3 (Test* or Biops* or Assay* or Exam*)).tw.
- 8 or/5-7
- 9 4 and 8
- 10 Nonhuman/ not Human/
- 11 9 not 10
- 12 limit 11 to english language

Database: Cochrane Database of Systematic Reviews (CDSR) Issue 8 of 12, Aug 2010. & Cochrane Central Database of Controlled Trials (CENTRAL) Issue 3 of 4, Jul 2010 via Wiley.

Search Strategy:

#1 MeSH descriptor Anaphylaxis explode all trees

- #2 Anaphyla*
- #3 (#1 OR #2)
- #4 MeSH descriptor Tryptases explode all trees
- #5 Tryptase*
- #6 ((Serum* or Mastcell* or Mast-cell* or Mast Cell*) near/3 (Test* or Biops* or Assay* or Exam*))
- #7 (#4 OR #5 OR #6)
- #8 (#3 AND #7)

Database: Database of Abstracts of Reviews of Effects (DARE) & Health Technology Assessments (HTA) via Centre for Reviews and Dissemination

Search Strategy:

- #1 MeSH Anaphylaxis EXPLODE 1
- #2 Anaphyla*
- #3 #1 or #2
- #4 MeSH Tryptases EXPLODE 1
- #5 Tryptase*
- #6 Serum* NEAR Test*
- #7 Serum* NEAR Biops*

- #8 Serum* NEAR Assay*
- #9 Serum* NEAR Exam*
- #10 Mastcell* NEAR Test*
- #11 Mastcell* NEAR Biops*
- #12 Mastcell* NEAR Assay*
- #13 Mastcell* NEAR Exam*
- #14 Mast-cell* NEAR Test*
- #15 Mast-cell* NEAR Biops*
- #16 Mast-cell* NEAR Assay*
- #17 Mast-cell* NEAR Exam*
- #18 Mast NEAR Cell* NEAR Test*
- #19 Mast NEAR Cell* NEAR Biops*
- #20 Mast NEAR Cell* NEAR Assay*
- #21 Mast NEAR Cell* NEAR Exam*
- #22 #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
- #23 #3 and #22

Database: Cumulative Index to Nursing and Allied Health Literature (CINAHL)
1981 to Present via NHS Evidence

Search Strategy:

-
1. ANAPHYLAXIS/
 2. Anaphyla*.ti,ab;
 3. 1 OR 2;
 4. Tryptase*.ti,ab;
 5. (Serum* adj3 Test*).ti,ab;
 6. (Serum* adj3 Biops*).ti,ab;
 7. (Serum* adj3 Assay*).ti,ab;
 8. (Serum* adj3 Exam*).ti,ab;
 9. (Mastcell* adj3 Test*).ti,ab;
 10. (Mastcell* adj3 Biops*).ti,ab;
 11. (Mastcell* adj3 Assay*).ti,ab;
 12. (Mastcell* adj3 Exam*).ti,ab;
 13. (Mast-cell* adj3 Test*).ti,ab;
 14. (Mast-cell* adj3 Biops*).ti,ab;
 15. (Mast-cell* adj3 Assay*).ti,ab;
 16. (Mast-cell* adj3 Exam*).ti,ab;
 17. ((Mast adj1 cell*) adj3 Test*).ti,ab;
 18. ((Mast adj1 cell*) adj3 Biops*).ti,ab;
 19. ((Mast adj1 cell*) adj3 Assay*).ti,ab;
 20. ((Mast adj1 cell*) adj3 Exam*).ti,ab;

21. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15
OR 16 OR 17 OR 18 OR 19 OR 20;

22. 3 AND 21;

24. 22 [Limit to: (Language English)];

Question 2: Biphasic reaction (searched May 2011)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
<2nd Quarter 2011>, EBM Reviews - Cochrane Database of Systematic
Reviews <2005 to April 2011>, Embase <1980 to 2011 Week 18>, Ovid
MEDLINE(R) <1948 to April Week 4 2011>, Ovid MEDLINE(R) In-Process &
Other Non-Indexed Citations <May 09, 2011> All searched via Ovid.

Search Strategy:

-
- 1 Anaphylaxis/ use mesz
 - 2 ANAPHYLAXIS/ use emez
 - 3 anaphylactic shock/ use emez
 - 4 Anaphylaxis/ use cctr
 - 5 Anaphylaxis.kw. use coch
 - 6 Anaphyla*.tw.
 - 7 Anaphyla*.ti,ab,hw. use cctr
 - 8 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).tw.
 - 9 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).ti,ab,hw. use cctr

- 10 or/1-9
- 11 (biphasic* or bi-phasic* or bi phasic*).tw.
- 12 (biphasic* or bi-phasic* or bi phasic*).ti,ab,hw. use cctr
- 13 ((Second* or post* or further* or repeat* or more*) adj3 (react* or episode* or observ*)).tw.
- 14 ((Second* or post* or further* or repeat* or more*) adj3 (react* or episode* or observ*)).tw. use cctr
- 15 or/11-14
- 16 10 and 15
- 17 animals/ use mesz not humans/ use mesz
- 18 nonhuman/ use emez not human/ use emez
- 19 or/17-18
- 20 16 not 19 (1702)

Database: Database of Abstracts of Reviews of Effects (DARE) & Health
Technology Assessments (HTA) via Centre for Reviews and Dissemination

Search Strategy:

- 1 MeSH DESCRIPTOR Anaphylaxis EXPLODE ALL TREES
- 2 Anaphyla*
- 3 (Severe*) NEAR (allerg*)
- 4 (Severe*) NEAR (hypersensitiv*)

- 5 (Immediat*) NEAR (allerg*)
- 6 (Immediat*) NEAR (hypersensitiv*)
- 7 (Acute* NEAR allerg*)
- 8 (Acute* NEAR hypersensitiv*)
- 9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
- 10 (biphasic* OR bi-phasic* OR bi AND phasic*)
- 11 (Second* NEAR react*)
- 12 (Second* NEAR episode*)
- 13 (Second* NEAR observ*)
- 14 (Post* NEAR react*)
- 15 (Post* NEAR episode*)
- 16 (Post* NEAR observ*)
- 17 (further* NEAR react*)
- 18 (further* NEAR episode*)
- 19 (further* NEAR observ*)
- 20 (repeat* NEAR react*)
- 21 (repeat* NEAR episode*)
- 22 (repeat* NEAR observ*)
- 23 (more* NEAR react*)
- 24 (more* NEAR episode*)
- 25 (more* NEAR observ*)

26 #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25

27 #9 AND #26

Database: Cumulative Index to Nursing and Allied Health Literature (CINAHL)
1981 to Present via NHS Evidence

Search Strategy:

-
- 1, ANAPHYLAXIS/
 - 2 Anaphyla*.ti,ab
 - 3 (Severe* adj3 allerg*).ti,ab
 - 4 (Severe* adj3 hypersensitiv*).ti,ab
 - 5 (Immediat* adj3 allerg*).ti,ab
 - 6 (Immediat* adj3 hypersensitiv*).ti,ab
 - 7 (Acute* adj3 allerg*).ti,ab
 - 8 (Acute* adj3 hypersensitiv*).ti,ab
 - 9 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8
 - 10 (biphasic* OR bi-phasic* OR bi AND phasic*).ti,ab
 - 11 (Second* adj3 react*).ti,ab
 - 12 (Second* adj3 episode*).ti,ab
 - 13 (Second* adj3 observ*).ti,ab
 - 14 (Post* adj3 react*).ti,ab
 - 15 (Post* adj3 episode*).ti,ab
 - 16 (Post* adj3 observ*).ti,ab
 - 17 (further* adj3 react*).ti,ab
 - 18 (further* adj3 episode*).ti,ab
 - 19 (further* adj3 observ*).ti,ab
 - 20 (repeat* adj3 react*).ti,ab

- 21 (repeat* adj3 episode*).ti,ab
- 22 (repeat* adj3 observ*).ti,ab
- 23 (more* adj3 react*).ti,ab
- 24 (more* adj3 episode*).ti,ab
- 25 (more* adj3 observ*).ti,ab
- 26 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19
OR 20 OR 21 OR 22 OR 23 OR 24 OR 25
- 27 9 AND 26

Question 4: Patient Information (searched April 2011)

Database: Ovid MEDLINE(R) <1948 to April Week 1 2011> & Ovid
MEDLINE(R) In-Process & Other Non-Indexed Citations <April 15, 2011>

Search Strategy:

- 1 Anaphylaxis/
- 2 Anaphyla*.tw.
- 3 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).tw.
- 4 or/1-3
- 5 Qualitative Research/
- 6 Nursing Methodology Research/
- 7 exp Interviews as topic/
- 8 Questionnaires/

- 9 Narration/
- 10 Health Care Surveys/
- 11 (qualitative\$ or interview\$ or focus group\$ or questionnaire\$ or narrative\$ or narration\$ or survey\$).tw.
- 12 (ethno\$ or emic or etic or phenomenolog\$ or grounded theory or constant compar\$ or (thematic\$ adj3 analys\$) or theoretical sampl\$ or purposive sampl\$).tw.
- 13 (hermeneutic\$ or heidegger\$ or husserl\$ or colaizzi\$ or van kaam\$ or van manen\$ or giorgi\$ or glaser\$ or strauss\$ or ricoeur\$ or spiegelberg\$ or merleau\$).tw.
- 14 (metasynthes\$ or meta-synthes\$ or metasummar\$ or meta-summar\$ or metastud\$ or meta-stud\$ or metathem\$ or meta-them\$).tw.
- 15 or/5-14
- 16 exp Patients/px
- 17 exp Family/px
- 18 Caregivers/px
- 19 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$) adj5 (experience\$ or belief\$ or stress\$ or emotion\$ or anx\$ or fear\$ or concern\$ or uncertain\$ or unsure or thought\$ or feeling\$ or felt\$ or view\$ or opinion\$ or perception\$ or perspective\$ or attitud\$ or satisfact\$ or know\$ or understand\$ or aware\$)).ti.
- 20 Stress, Psychological/
- 21 Adaptation, psychological/
- 22 Emotions/

- 23 Anxiety/
- 24 Fear/
- 25 exp Consumer Satisfaction/
- 26 or/16-25
- 27 exp Patients/
- 28 exp Family/
- 29 Caregivers/
- 30 (patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$).ti.
- 31 or/27-30
- 32 Pamphlets/
- 33 Needs Assessment/
- 34 Information Centers/
- 35 Information Services/
- 36 Health Education/
- 37 Information Dissemination/
- 38 Counseling/
- 39 Social Support/
- 40 Self-Help Groups/
- 41 Self Care/
- 42 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5

(educat\$ or informat\$ or communicat\$ or pamphlet\$ or handout\$ or hand-out\$ or hand out\$ or booklet\$ or leaflet\$ or support\$ or need\$ or advice\$ or advis\$)).ti.

43 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5 (counsel\$ or selfhelp\$ or self-help\$ or self help\$ or selfcar\$ or self-car\$ or self car\$)).ti.

44 Patient Education as Topic/

45 Patient Education Handout/

46 Consumer Health Information/

47 patient* diar*.tw.

48 or/32-47

49 31 and 48

50 15 or 26 or 49

51 4 and 50

52 limit 51 to english language

Database: EMBASE <1980 to 2011 Week 15> via Ovid

Search Strategy:

1 *ANAPHYLAXIS/

- 2 *anaphylactic shock/
- 3 Anaphyla*.ti.
- 4 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).ti.
- 5 or/1-4
- 6 Qualitative Research/
- 7 exp Interview/
- 8 exp Questionnaire/
- 9 exp Observational Method/
- 10 Narrative/
- 11 (qualitative\$ or interview\$ or focus group\$ or questionnaire\$ or narrative\$ or narration\$ or survey\$).tw.
- 12 (ethno\$ or emic or etic or phenomenolog\$ or grounded theory or constant compar\$ or (thematic\$ adj3 analys\$) or theoretical sampl\$ or purposive sampl\$).tw.
- 13 (hermeneutic\$ or heidegger\$ or husser\$ or colaizzi\$ or van kaam\$ or van manen\$ or giorgi\$ or glaser\$ or strauss\$ or ricoeur\$ or spiegelberg\$ or merleau\$).tw.
- 14 (metasynthes\$ or meta-synthes\$ or metasummar\$ or meta-summar\$ or metastud\$ or meta-stud\$ or metathem\$ or meta-them\$).tw.
- 15 or/6-14
- 16 exp parent/
- 17 exp family/
- 18 caregiver/
- 19 exp Patient/

20 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or inpatient\$ or in-patient\$ or spouse\$ or husband\$ or wife\$ or wives\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$) adj5 (experience\$ or belief\$ or stress\$ or emotion\$ or anx\$ or fear\$ or concern\$ or uncertain\$ or unsure or thought\$ or feeling\$ or felt\$ or view\$ or opinion\$ or perception\$ or perspective\$ or attitud\$ or satisfact\$ or know\$ or understand\$ or aware\$)).tw.

21 exp Patient Attitude/

22 EMOTION/

23 FEAR/

24 Anxiety/

25 exp family attitude/

26 Mental Stress/

27 Adaptive Behavior/

28 Consumer/

29 or/16-28

30 exp parent/

31 exp family/

32 caregiver/

33 exp Patient/

34 (patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or inpatient\$ or in-patient\$ or spouse\$ or husband\$ or wife\$ or wives\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$).tw.

35 or/30-34

- 36 publication/
- 37 needs assessment/
- 38 information center/
- 39 information service/
- 40 health education/
- 41 information dissemination/
- 42 exp counseling/
- 43 social support/
- 44 self help/
- 45 self care/
- 46 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5 (educat\$ or informat\$ or communicat\$ or pamphlet\$ or handout\$ or hand-out\$ or hand out\$ or booklet\$ or leaflet\$ or support\$ or need\$ or advice\$ or advis\$)).ti.
- 47 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5 (counsel\$ or selfhelp\$ or self-help\$ or self help\$ or selfcar\$ or self-car\$ or self car\$)).ti.
- 48 patient education/
- 49 consumer health information/
- 50 patient* diar*.tw.
- 51 or/36-50
- 52 35 and 51

- 53 15 or 29 or 52
- 54 5 and 53
- 55 limit 54 to english language

Database: PsycINFO <1806 to April Week 2 2011> via Ovid

Search Strategy:

- 1 anaphylactic shock/
- 2 Anaphyla*.tw.
- 3 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).tw.
- 4 or/1-3
- 5 limit 4 to english language

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to March 2011> via Ovid

Search Strategy:

- 1 Anaphylaxis.kw.
- 2 Anaphylaxis.tw.

3 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).tw.

4 or/1-3

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
<1st Quarter 2011> via Ovid

Search Strategy:

1 Anaphylaxis/

2 Anaphyla*.tw.

3 ((Severe* or Immediat* or Acute*) adj3 (allerg* or hypersensitiv*)).tw.

4 or/1-3

5 Qualitative Research/

6 Nursing Methodology Research/

7 exp Interviews as topic/

8 Questionnaires/

9 Narration/

10 Health Care Surveys/

11 (qualitative\$ or interview\$ or focus group\$ or questionnaire\$ or
narrative\$ or narration\$ or survey\$).tw.

12 (ethno\$ or emic or etic or phenomenolog\$ or grounded theory or
constant compar\$ or (thematic\$ adj3 analys\$) or theoretical sampl\$ or
purposive sampl\$).tw.

13 (hermeneutic\$ or heidegger\$ or husserl\$ or colaizzi\$ or van kaam\$ or van manen\$ or giorgi\$ or glaser\$ or strauss\$ or ricoeur\$ or spiegelberg\$ or merleau\$).tw.

14 (metasynthes\$ or meta-synthes\$ or metasummar\$ or meta-summar\$ or metastud\$ or meta-stud\$ or metathem\$ or meta-them\$).tw.

15 or/5-14

16 exp Patients/px

17 exp Family/px

18 Caregivers/px

19 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$) adj5 (experience\$ or belief\$ or stress\$ or emotion\$ or anx\$ or fear\$ or concern\$ or uncertain\$ or unsure or thought\$ or feeling\$ or felt\$ or view\$ or opinion\$ or perception\$ or perspective\$ or attitud\$ or satisfact\$ or know\$ or understand\$ or aware\$)).ti.

20 Stress, Psychological/

21 Adaptation, psychological/

22 Emotions/

23 Anxiety/

24 Fear/

25 exp Consumer Satisfaction/

26 or/16-25

27 exp Patients/

28 exp Family/

29 Caregivers/

30 (patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$ or mother\$ or father\$ or sibling\$ or sister\$ or brother\$).ti.

31 or/27-30

32 Pamphlets/

33 Needs Assessment/

34 Information Centers/

35 Information Services/

36 Health Education/

37 Information Dissemination/

38 Counseling/

39 Social Support/

40 Self-Help Groups/

41 Self Care/

42 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5 (educat\$ or informat\$ or communicat\$ or pamphlet\$ or handout\$ or hand-out\$ or hand out\$ or booklet\$ or leaflet\$ or support\$ or need\$ or advice\$ or advis\$)).ti.

43 ((patient\$ or parent\$ or famil\$ or relative\$ or carer\$ or caregiver\$ or care-giver\$ or spous\$ or husband\$ or wife\$ or wive\$ or partner\$) adj5 (counsel\$ or selfhelp\$ or self-help\$ or self help\$ or selfcar\$ or self-car\$ or self car\$)).ti.

44 Patient Education as Topic/

- 45 Patient Education Handout/
- 46 Consumer Health Information/
- 47 patient* diar*.tw.
- 48 or/32-47
- 49 31 and 48
- 50 15 or 26 or 49
- 51 4 and 50

Database: Database of Abstracts of Reviews of Effects (DARE) & Health Technology Assessments (HTA) via Centre for Reviews and Dissemination

Search Strategy:

-
- 1 MeSH DESCRIPTOR Anaphylaxis EXPLODE ALL TREES
 - 2 (Anaphyla*)
 - 3 (Severe*) NEAR (allerg*)
 - 4 (Severe*) NEAR (hypersensitiv*)
 - 5 (Immediat*) NEAR (allerg*)
 - 6 (Immediat*) NEAR (hypersensitiv*)
 - 7 (Acute*) NEAR (allerg*)
 - 8 (Acute*) NEAR (hypersensitiv*)
 - 9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

Database: Cumulative Index to Nursing and Allied Health Literature (CINAHL)
1981 to Present via NHS Evidence

Search Strategy:

-
- 1 ANAPHYLAXIS/
 - 2 Anaphyla*.ti,ab
 - 3 (Severe* adj3 allerg*).ti,ab
 - 4 (Severe* adj3 hypersensitiv*).ti,ab
 - 5 (Immediat* adj3 allerg*).ti,ab
 - 6 (Immediat* adj3 hypersensitiv*).ti,ab
 - 7 1 OR 2 OR 3 OR 4 OR 5 OR 6
 - 8 7 [Limit to: (Language English)]
 - 9 QUALITATIVE STUDIES/
 - 10 METHODOLOGICAL RESEARCH/
 - 11 INTERVIEWS/
 - 12 QUESTIONNAIRES/
 - 13 NARRATIVES/
 - 14 (qualitative* OR interview* OR focus AND group* OR questionnaire*
OR narrative* OR narration* OR survey*).ti,ab
 - 15 (ethno* OR emic OR etic OR phenomenolog* OR grounded AND
theory OR constant AND compar* OR theoretical AND sampl* OR purposive

AND sampl*).ti,ab

16 (thematic* adj3 analys*).ti,ab

17 (hermeneutic* OR heidegger* OR husserl* OR colaizzi* OR van AND
kaam* OR van AND manen* OR giorgi* OR glaser* OR strauss* OR ricoeur*
OR spiegelberg* OR merleau*).ti,ab

18 (metasynthes* OR meta-synthes* OR metasummar* OR meta-
summar* OR metastud* OR meta-stud* OR metathem* OR meta-them*).ti,ab

19 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR

20 PATIENTS/

21 FAMILY/

22 CAREGIVERS/

23 (patient* OR parent* OR famil* OR relative* OR carer* OR caregiver*
OR care-giver* OR spous* OR husband* OR wife* OR wive* OR partner* OR
mother* OR father* OR sibling* OR sister* OR brother* adj5 experience* OR
belief* OR stress* OR emotion* OR anx* OR fear* OR concern* OR
uncertain* OR unsure* OR thought* OR feeling* OR felt* OR view* OR
opinion* OR perception* OR perspective* OR attitud* OR satisfact* OR know*
OR understand* OR aware*).ti,ab

24 STRESS, PSYCHOLOGICAL/

25 ADAPTATION, PSYCHOLOGICAL/

26 EMOTIONS/

27 ANXIETY/

28 FEAR/

29 CONSUMER SATISFACTION/

30 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29

31 PATIENTS/

- 32 FAMILY/
- 33 CAREGIVERS/
- 34 (patient* OR parent* OR famil* OR relative* OR carer* OR caregiver* OR care-giver* OR spous* OR husband* OR wife* OR wive* OR partner* OR mother* OR father* OR sibling* OR sister* OR brother*).ti
- 35 31 OR 32 OR 33 OR 34
- 36 PAMPHLETS/
- 37 NEEDS ASSESSMENT/
- 38 INFORMATION CENTERS/
- 39 INFORMATION SERVICES/
- 40 HEALTH EDUCATION/
- 41 SELECTIVE DISSEMINATION OF INFORMATION/
- 42 COUNSELING/
- 43 SOCIAL SUPPORT INDEX/
- 44 SUPPORT GROUPS/
- 45 SELF CARE/
- 46 (patient* OR parent* OR famil* OR relative* OR carer* OR caregiver* OR care-giver* OR spous* OR husband* OR wife* OR wive* OR partner* adj5 educat* OR informat* OR communicat* OR pamphlet* OR handout* OR hand-out* OR hand AND out* OR booklet* OR leaflet* OR support* OR need* OR advice* OR advis*).ti,ab
- 47 (patient* OR parent* OR famil* OR relative* OR carer* OR caregiver* OR care-giver* OR spous* OR husband* OR wife* OR wive* OR partner* adj5 counsel* OR selfhelp* OR self-help* OR self AND help* OR selfcar* OR self-car* OR self AND car*).ti,ab
- 48 PATIENT EDUCATION/

49 CONSUMER HEALTH INFORMATION/
50 (patient* AND diar*).ti,ab

51 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45
OR 46 OR 47 OR 48 OR 49 OR 50

52 35 AND 51
53 19 OR 30 OR 52

54 (Acute* adj3 allerg*).ti,ab
55 (Acute* adj3 hypersensitiv*).ti,ab
56 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 54 OR 55

57 AND 56 [Limit to: (Language English) and (Language English)]

Question 7: Care pathways (searched September 2010)

Database: Ovid MEDLINE(R) <1950 to August Week 5 2010> & Ovid
MEDLINE(R) In-Process & Other Non-Indexed Citations <September 08,
2010>

Search Strategy:

-
- 1 Anaphylaxis/
 - 2 Anaphyla*.tw.
 - 3 or/1-2
 - 4 Critical Pathways/
 - 5 Patient Care Team/

- 6 "Delivery of Health Care, Integrated"/
- 7 Aftercare/
- 8 Follow-Up Studies/
- 9 Clinical Protocols/
- 10 ((Care* or Clinical* or Critical* or Integrate* or Multidisciplin* or Interdisciplin* or Healthcare* or Health-care* or Health Care* or Aftercare* or After-care* or After Care* or Post* or Followup* or Follow-up* or Follow up) adj3 (Path* or Plan* or Protocol* or Procedure* or Program* or Manag* or Process* or Outline* or Map* or Schedul* or Team* or Treat* or Stud* or React*)).ti,ab.
- 11 ((Post* or Followup* or Follow-up* or Follow up) adj3 (Care* or Path* or Plan* or Procedure* or Program* or Team* or Treat* or Stud* or React*)).ti,ab.
- 12 "Referral and Consultation"/
- 13 Patient Readmission/
- 14 Patient Admission/
- 15 (Referral* or Readmis* or Readmit* or Admit* or Admis*).tw.
- 16 "Delivery of Health Care"/
- 17 Models, Organizational/
- 18 ((Deliver* or model*) adj3 (Care* or Healthcare* or Health-care* or Health Care*)).tw.
- 19 (Service* adj3 Deliver*).tw.
- 20 ((Organisat* or Organizat*) adj3 (Care* or Model*)).tw.
- 21 or/4-20
- 22 3 and 21

- 23 Animals/ not Humans/
- 24 22 not 23
- 25 limit 24 to english language

Database: EMBASE <1980 to 2010 Week 36>

Search Strategy:

-
- 1 ANAPHYLAXIS/
 - 2 ANAPHYLACTIC SHOCK/
 - 3 Anaphyla*.tw.
 - 4 or/1-3
 - 5 clinical pathway/
 - 6 patient care/
 - 7 integrated health care system/
 - 8 AFTERCARE/
 - 9 follow up/
 - 10 clinical protocol/
 - 11 ((Care* or Clinical* or Critical* or Integrate* or Multidisciplin* or Interdisciplin* or Healthcare* or Health-care* or Health Care* or Aftercare* or After-care* or After Care* or Post* or Followup* or Follow-up* or Follow up) adj3 (Path* or Plan* or Protocol* or Procedure* or Program* or Manag* or

Process* or Outline* or Map* or Schedul* or Team* or Treat* or Stud* or React*)).ti,ab.

12 ((Post* or Followup* or Follow-up* or Follow up) adj3 (Care* or Path* or Plan* or Procedure* or Program* or Team* or Treat* or Stud* or React*)).ti,ab.

13 patient referral/

14 hospital readmission/

15 hospital admission/

16 (Referral* or Readmis* or Readmit* or Admit* or Admis*).tw.

17 health care delivery/

18 nonbiological model/

19 ((Deliver* or model*) adj3 (Care* or Healthcare* or Health-care* or Health Care*)).tw.

20 (Service* adj3 Deliver*).tw.

21 ((Organisat* or Organizat*) adj3 (Care* or Model*)).tw.

22 or/5-21

23 4 and 22

24 Nonhuman/ not Human/

25 23 not 24

26 limit 25 to english language

Database: Cochrane Database of Systematic Reviews (CDSR) Issue 9 of 12, Sept 2010. & Cochrane Central Database of Controlled Trials (CENTRAL) Issue 3 of 4, Jul 2010 via Wiley.

Search Strategy:

-
- #1 MeSH descriptor Anaphylaxis explode all trees
 - #2 Anaphyla*
 - #3 (#1 OR #2)
 - #4 MeSH descriptor Critical Pathways explode all trees
 - #5 MeSH descriptor Patient Care Team explode all trees
 - #6 MeSH descriptor Delivery of Health Care, Integrated explode all trees
 - #7 MeSH descriptor Aftercare explode all trees
 - #8 MeSH descriptor Follow-Up Studies explode all trees
 - #9 MeSH descriptor Clinical Protocols explode all trees
 - #10 ((Care* or Clinical* or Critical* or Integrate* or Multidisciplin* or Interdisciplin* or Healthcare* or Health-care* or Health Care* or Aftercare* or After-care* or After Care* or Post* or Followup* or Follow-up* or Follow up) NEAR (Path* or Plan* or Protocol* or Procedure* or Program* or Manag* or Process* or Outline* or Map* or Schedul* or Team* or Treat* or Stud* or React*))
 - #11 ((Post* or Followup* or Follow-up* or Follow up) NEAR (Care* or Path* or Plan* or Procedure* or Program* or Team* or Treat* or Stud* or React*))
 - #12 MeSH descriptor Referral and Consultation explode all trees
 - #13 MeSH descriptor Patient Readmission explode all trees

- #14 MeSH descriptor Patient Admission explode all trees
- #15 (Referral* or Readmis* or Readmit* or Admit* or Admis*)
- #16 MeSH descriptor Delivery of Health Care explode all trees
- #17 MeSH descriptor Models, Organizational explode all trees
- #18 ((Deliver* or model*) NEAR (Care* or Healthcare* or Health-care* or Health Care*))
- #19 (Service* NEAR Deliver*)
- #20 ((Organisat* or Organizat*) NEAR (Care* or Model*))
- #21 (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)
- #22 (#3 AND #21)

Database: Database of Abstracts of Reviews of Effects (DARE) & Health Technology Assessments (HTA) via Centre for Reviews and Dissemination

Search Strategy:

- #1 MeSH Anaphylaxis EXPLODE 1
- #2 Anaphyla*
- #3 #1 OR #2
- #4 MeSH Critical Pathways EXPLODE 1 2
- #5 MeSH Patient Care Team EXPLODE 1
- #6 MeSH Delivery of Health Care, Integrated EXPLODE 1 2

- #7 MeSH Aftercare EXPLODE 1 2
- #8 MeSH Follow-Up Studies EXPLODE 1 2 3
- #9 MeSH Clinical Protocols EXPLODE 1 2
- #10 Care* OR Clinical* OR Critical* OR Integrate* OR Multidisciplin* OR Interdisciplin* OR Healthcare* OR Health-care* OR Aftercare* OR After-care* OR Post* OR Followup* OR Follow-up*
- #11 Health NEAR Care*
- #12 After NEAR Care*
- #13 Follow NEAR up
- #14 MeSH Referral and Consultation EXPLODE 1
- #15 MeSH Patient Readmission EXPLODE 1 2
- #16 MeSH Patient Admission EXPLODE 1 2
- #17 Referral* OR Readmis* OR Readmit* OR Admit* OR Admis*
- #18 MeSH Delivery of Health Care EXPLODE 1 2
- #19 MeSH Models, Organizational EXPLODE 1 2
- #20 Service* NEAR Deliver*
- #21 Organisat* NEAR Model*
- #22 Organizat* NEAR Model*
- #23 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
- #24 #3 and #23

Database: Cumulative Index to Nursing and Allied Health Literature (CINAHL)
1981 to Present via NHS Evidence

Search Strategy:

-
1. ANAPHYLAXIS/;
 2. Anaphyla* .ti,ab;
 3. 1 OR 2;
 4. CRITICAL PATH/;
 5. PATIENT CARE/;
 6. HEALTH CARE DELIVERY, INTEGRATED/;
 7. AFTER CARE/;
 8. (Care* OR Clinical* OR Critical* OR Integrate* OR Multidisciplin* OR Interdisciplin* OR Healthcare* OR Health-care* OR Aftercare* OR After-care* OR Post* OR Followup* OR Follow-up*).ti,ab;
 9. (Health ADJ Care*).ti,ab;.
 10. (After ADJ Care*).ti,ab;
 11. (Follow ADJ up).ti,ab;
 12. REFERRAL AND CONSULTATION/;
 13. READMISSION/;
 14. PATIENT ADMISSION/;
 15. (Referral* OR Readmis* OR Readmit* OR Admit* OR Admis*).ti,ab; 40198 results.

16. HEALTH CARE DELIVERY/;
17. (Service* adj3 Deliver*).ti,ab;
18. (Organisat* ADJ Model*).ti,ab;
19. (Organizat* ADJ Model*).ti,ab;
20. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19;
21. 3 AND 20;
22. 21 [Limit to: (Language English)];

Health Economics searches: (searched June 2010)

Database: Ovid MEDLINE(R) <1950 to May Week 4 2010> & Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 07, 2010>

Search Strategy:

-
- 1 Anaphylaxis/
 - 2 Anaphyl*.tw.
 - 3 or/1-2
 - 4 Economics/
 - 5 exp "Costs and Cost Analysis"/
 - 6 Economics, Dental/
 - 7 exp Economics, Hospital/
 - 8 exp Economics, Medical/
 - 9 Economics, Nursing/

- 10 Economics, Pharmaceutical/
- 11 Budgets/
- 12 exp Models, Economic/
- 13 Markov Chains/
- 14 Monte Carlo Method/
- 15 Decision Trees/
- 16 econom\$.tw.
- 17 cba.tw.
- 18 cea.tw.
- 19 cua.tw.
- 20 markov\$.tw.
- 21 (monte adj carlo).tw.
- 22 (decision adj2 (tree\$ or analys\$)).tw.
- 23 (cost or costs or costing\$ or costly or costed).tw.
- 24 (price\$ or pricing\$).tw.
- 25 budget\$.tw.
- 26 expenditure\$.tw.
- 27 (value adj2 (money or monetary)).tw.
- 28 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw.
- 29 or/4-28
- 30 "Quality of Life"/

- 31 quality of life.tw.
- 32 "Value of Life"/)
- 33 Quality-Adjusted Life Years/
- 34 quality adjusted life.tw.
- 35 (qaly\$ or qald\$ or qale\$ or qtime\$).tw.
- 36 disability adjusted life.tw.
- 37 daly\$.tw.
- 38 Health Status Indicators/
- 39 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
- 40 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
- 41 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
- 42 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
- 43 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
- 44 (euroqol or euro qol or eq5d or eq 5d).tw.
- 45 (qol or hqol or hqol or hrqol).tw.
- 46 (hye or hyes).tw.
- 47 health\$ year\$ equivalent\$.tw.
- 48 utilit\$.tw.

- 49 (hui or hui1 or hui2 or hui3).tw.
- 50 disutili\$.tw.
- 51 rosser.tw.
- 52 quality of wellbeing.tw.
- 53 quality of well-being.tw.
- 54 qwb.tw.
- 55 willingness to pay.tw.
- 56 standard gamble\$.tw.
- 57 time trade off.tw.
- 58 time tradeoff.tw.
- 59 tto.tw.
- 60 or/30-59
- 61 29 or 60
- 62 3 and 61
- 63 limit 62 to english language

Database: EMBASE <1980 to 2010 Week 22> via Ovid

Search Strategy:

1 *anaphylaxis/

- 2 Anaphyl*.tw.
- 3 or/1-2
- 4 exp Health Economics/
- 5 exp "Health Care Cost"/
- 6 exp Pharmacoeconomics/
- 7 Monte Carlo Method/
- 8 Decision Tree/
- 9 econom\$.tw.
- 10 cba.tw.
- 11 cea.tw.
- 12 cua.tw.
- 13 markov\$.tw.
- 14 (monte adj carlo).tw.
- 15 (decision adj2 (tree\$ or analys\$)).tw
- 16 (cost or costs or costing\$ or costly or costed).tw.
- 17 (price\$ or pricing\$).tw.
- 18 budget\$.tw.
- 19 expenditure\$.tw.
- 20 (value adj2 (money or monetary)).tw.
- 21 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw.
- 22 or/4-21

- 23 "Quality of Life"/
- 24 Quality Adjusted Life Year/
- 25 Quality of Life Index/
- 26 Short Form 36/
- 27 Health Status/
- 28 quality of life.tw.
- 29 quality adjusted life.tw.
- 30 (qaly\$ or qald\$ or qale\$ or qtime\$).tw.
- 31 disability adjusted life.tw
- 32 daly\$.tw.
- 33 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
- 34 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
- 35 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
- 36 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
- 37 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
- 38 (euroqol or euro qol or eq5d or eq 5d).tw.
- 39 (qol or hql or hqol or hrqol).tw.
- 40 (hye or hyes).tw.

- 41 health\$ year\$ equivalent\$.tw.
- 42 utilit\$.tw.
- 43 (hui or hui1 or hui2 or hui3).tw.
- 44 disutili\$.tw.
- 45 rosser.tw.
- 46 quality of wellbeing.tw.
- 47 quality of well-being.tw.
- 48 qwb.tw.
- 49 willingness to pay.tw.
- 50 standard gamble\$.tw.
- 51 time trade off.tw.
- 52 time tradeoff.tw.
- 53 tto.tw.
- 54 or/23-53
- 55 22 or 54
- 56 3 and 55
- 57 limit 56 to english language

Database: NHS Economic Evaluation Database (searched via Wiley & Centre for Reviews and Dissemination)

Search Strategy:

#1 MeSH Anaphylaxis EXPLODE

#2 Anaphyl*

#3 #1 or #2

Review questions and review protocols

Review questions

Review question 1: Should the mast cell tryptase test be performed in patients with suspected anaphylaxis? And if so, what is the optimal timing for testing?

Review question 2: Should people be observed post anaphylactic reaction? And if so, for how long?

Review question 3: What should be part of the review post reaction to confirm a diagnosis of anaphylaxis and to guide referral? (Please see Assessment Group Searches and Protocols)

Review question 4: What information do people need after an anaphylactic reaction, and before referral?

Review question 5: Who should be referred, when and to where or whom? (Please see Assessment Group Searches and Protocols)

Review question 6: Who should be given an emergency treatment plan and when should that include an adrenaline injector? (Please see Assessment Group Searches and Protocols)

Review question 7: What model or organisation of care should be adopted to improve the diagnosis of anaphylaxis post reaction?

Review Protocol

Review	Should the mast cell tryptase test be performed
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question 1	in patients with suspected anaphylaxis? And if so, what is the optimal timing for testing?
Objectives	To identify accuracy of mast cell tryptase test to detect anaphylaxis, when it is appropriate to be used, and optimal timing for use of the test after suspected anaphylaxis.
Language	English only
Study design	Cross-sectional studies, case-control studies, RCTs, Cohort studies
Status	Published papers (full papers only)
Population & Healthcare setting	Inclusion: Adults and children who have received emergency treatment for suspected anaphylaxis. Setting: Primary, secondary and tertiary care
Intervention	Mast cell tryptase test
Comparisons	N/A
Outcomes	Clinical utility or diagnostic test accuracy (if available) including: test validity such as Face validity, Content validity, Construct validity, Concurrent validity, Criterion validity; test reliability such as Internal reliability/consistency, Test-retest reliability,

	<p>Inter-rater reliability.</p> <p>sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, diagnostic odds ratio and area under the ROC analyses.</p> <p>Appropriate timing</p>
<p>Other criteria for inclusion/exclusion of studies</p>	<p>Exclusion:</p> <p>Measure of serum mast tryptase to guide initial treatment and diagnosis of anaphylactic episode (prior to emergency treatment).</p> <p>Identification and management of complications arising from testing.</p> <p>Measurement of mast cell tryptase post-mortem to confirm anaphylaxis.</p> <p>Case reports.</p> <p>Studies comparing mast cell tryptase with levels of histamine, IgE, or intradermal tests without clinical assessment.</p> <p>Measurement of mast cell tryptase to test baseline serum levels in order to diagnose systematic mastocytosis.</p>
<p>Search strategies</p>	<p>Please see above</p>
<p>Review strategies</p>	<p>The NICE Methodology Checklist (QUADAS) will be used as a guide to appraise the quality</p>

	<p>of individual studies.</p> <p>Data on all included studies will be extracted into evidence tables.</p> <p>Where statistically possible, a meta-analytic approach will be used to give an overall summary effect.</p> <p>All key outcomes from evidence will be presented in GRADE profiles, or modified evidence profiles, and further summarised in evidence statements.</p>
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	Details
Review question 2	Should people be observed post anaphylactic reaction? And if so, for how long?
Objectives	To identify how long people should be observed after an anaphylactic reaction. This is particularly important to detect the risk of a second reaction if they have a biphasic pattern. This is also important to determine if there are particular subgroups that require special observation after treatment for anaphylaxis, for example, if they are at a particular risk of a biphasic reaction.
Language	English only.

Study design	Cross-sectional studies, RCTs, non-randomised comparative studies, Cohort studies, case series, case reports
Status	Published papers (full papers only)
Population & Healthcare setting	<p>Inclusion:</p> <p>Adults and children who have received suspected emergency treatment for anaphylaxis who require special observation after anaphylaxis, such as those at risk for a biphasic reaction.</p> <p>Setting:</p> <p>Primary, secondary and tertiary care</p>
Intervention	Observation of patients after an anaphylactic reaction.
Comparisons	No observation
Outcomes	<p>Further or repeat of anaphylactic episodes</p> <p>Rate of referral between healthcare settings</p> <p>Measure of diagnostic utility of physical examination, history taking, serum mast tryptase measurement.</p> <p>Admission rate for further anaphylactic episodes</p> <p>Mortality</p> <p>Health related quality of life (QoL)</p>

	Complications
Other criteria for inclusion/exclusion of studies	<p>Exclusion:</p> <p>Studies evaluating:</p> <p>Initial assessment and diagnosis of anaphylactic episode (prior to emergency treatment).</p> <p>Emergency management of anaphylaxis from either preliminary or any subsequent biphasic reactions.</p> <p>Prophylaxis for anaphylaxis after referral.</p> <p>Studies covering management of associated co morbidities.</p> <p>Case reports</p>
Search strategies	Please see above
Review strategies	<p>Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.</p> <p>Data on all included studies will be extracted into evidence tables.</p> <p>All key outcomes from evidence will be presented in GRADE profiles, or modified evidence profiles, and further summarised in evidence statements.</p>

	Details
Review question 4	What information do people need after an anaphylactic reaction, and before referral?
Objectives	To determine what advice should be provided to people before referral to an allergy service
Language	English only.
Study design	No restrictions on study design
Status	Published papers (full papers only)
Population & Healthcare setting	Inclusion: Adults and children who have received suspected emergency treatment for anaphylaxis. Setting: Primary, secondary and tertiary care
Intervention	
Comparisons	
Outcomes	Patient and carer information and support needs Health related quality of life Further or repeat of anaphylactic episodes

	Admission rate for further anaphylactic episodes
Other criteria for inclusion/exclusion of studies	<p>INCLUSION</p> <p>Any information and/or advice for adults, and children, young people, and their parents or carers</p> <p>People with first or subsequent episodes of anaphylaxis or severe allergic reactions</p>
Search strategies	Please see above
Review strategies	<p>Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.</p> <p>Data on all included studies will be extracted into evidence tables.</p> <p>All key outcomes from evidence will be presented in GRADE profiles, or modified evidence profiles, and further summarised in evidence statements.</p>

	Details
Review	What model or organisation of care should be adopted to improve the diagnosis of

question 7	anaphylaxis post reaction?
Objectives	To identify best care pathway(s) for referral after treatment for anaphylaxis to improve patient care.
Language	English only.
Study design	RCTs, controlled clinical trials, interrupted time series
Status	Published papers (full papers only)
Population & Healthcare setting	Inclusion: Adults and children who have received suspected emergency treatment for anaphylaxis. Setting: Primary, secondary and tertiary care
Intervention	Key components of care pathway after treatment for anaphylaxis
Comparisons	Any relevant comparator (either as contemporaneous control or before-and-after control)
Outcomes	Further or repeat of anaphylactic episodes Rate of referral between healthcare settings Admission rate for further anaphylactic episodes Mortality

	<p>Health related quality of life (QoL)</p> <p>Complications</p>
Other criteria for inclusion/exclusion of studies	<p>Exclusion:</p> <p>Studies evaluating models/organisation of care for the</p> <p>Initial assessment and diagnosis of anaphylactic episode (prior to emergency treatment).</p> <p>Emergency management of anaphylaxis.</p> <p>Prophylaxis for anaphylaxis after referral.</p> <p>Studies covering management of associated co morbidities.</p> <p>Identification and management of complications arising from testing.</p>
Search strategies	Please see above
Review strategies	<p>Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.</p> <p>Data on all included studies will be extracted into evidence tables.</p> <p>Where statistically possible, a meta-analytic approach will be used to give an overall summary effect.</p> <p>All key outcomes from evidence will be</p>

	presented in GRADE profiles, or modified evidence profiles, and further summarised in evidence statements.
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Assessment Group Search Strategy and Protocol

Scoping searches were undertaken in January 2011 using the following websites and databases (listed in alphabetical order); browsing or simple search strategies were employed. The search results were used to provide information for scope development and project planning.

Guidance/guidelines	Systematic reviews/ economic evaluations
Cochrane Central Register of Controlled Trials – CENTRAL	International Guidelines Network - GIN
Cochrane Database of Systematic Reviews - CDSR	National Guidelines Clearinghouse
Database of Abstracts of Reviews of Effects - DARE	
Health Technology Assessment Database – HTA	
NHS Economic Evaluation Database – NHS EED	

Table 1: sources of guidance/guidelines

Main searches

The following sources were searched for the topics presented in the sections below.

Cochrane Database of Systematic Reviews – CDSR (Wiley)

Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)

Database of Abstracts of Reviews of Effects – DARE (CRD)

Health Technology Assessment Database – HTA (CRD)

NHS Economic Evaluation Database – NHS EED (CRD)

Science Citation Index – SCI (Web of Science)

CINAHL (EBSCO)

EMBASE (Ovid)

MEDLINE (Ovid)

MEDLINE In-Process (Ovid)

Inclusion and exclusion criteria

Participants

Adults, young people and children who receive emergency treatment for suspected anaphylaxis or severe allergic reactions (that may have developed into anaphylaxis without treatment).

Setting

Relevant settings are primary, secondary or tertiary care.

Interventions / diagnostic assessments

History taking

Physical examination

Provision of adrenaline auto-injectors

Referral to specialist allergy clinics

Comparators

Elements of history taking compared with each other and with not considering those elements

Elements of physical examination compared with each other and compared with not considering these elements

Provision of auto-injectors by different health care professionals

No provision of adrenaline auto-injectors

Referral to other specialists

No referral

Outcomes

Any or all of the following outcomes will be considered:

Impact of testing/predictors on clinical outcome, (e.g. subsequent episodes, morbidity, mortality), correlations between tests and clinical outcomes.

Impact of adrenaline auto-injectors on clinical outcome, (e.g. subsequent episodes, morbidity, mortality)

Impact of referral on clinical outcome, (e.g. subsequent episodes, morbidity, mortality)

Indeterminacy (test failure rate)

Impact of testing/predictors on treatment plan (e.g. referral or not or to whom), where information on the appropriateness of the final treatment plan is also reported

For included studies reporting any of the above outcome measures, the following outcomes will also be considered if reported:

Acceptability of tests to patients

Adverse events associated with testing

Study designs

The following types of studies will be included:

Randomised or non-randomised controlled trials.

Observational studies reporting change to treatment plan or clinical outcome subsequent to intervention or testing.

Prognostic studies that have included a multivariable analysis (evaluating risk factors or signs in an analysis that includes other relevant factors or signs, rather than an unadjusted correlation).

The following study/publication types will be excluded:

Pre-clinical, animal studies

Reviews, editorials, and opinion pieces

Case reports

Studies reporting only technical aspects of the test

Studies with <20 participants

Data abstraction strategy

Included studies were summarised using evidence tables for prognostic studies (see appendix K3 of the NICE guidelines manual)..

Critical appraisal strategy

Quality and strength of evidence of included studies was assessed using the methodology checklist for prognostic studies (see appendix J of the NICE guidelines manual)..

Methods of data synthesis

Not applicable

5.2 Results

5.2.1 Quantity and quality of research available

The searches of electronic searches yielded in 11,058 references. After screening of titles and abstracts, 10,951 references were excluded. The remaining 107 references were obtained and the full texts screened. Five studies were included with another 60 studies highlighted as possibly relevant for the background and/or the cost-effectiveness-analysis (CEA). A flow chart of the screening process is presented below..

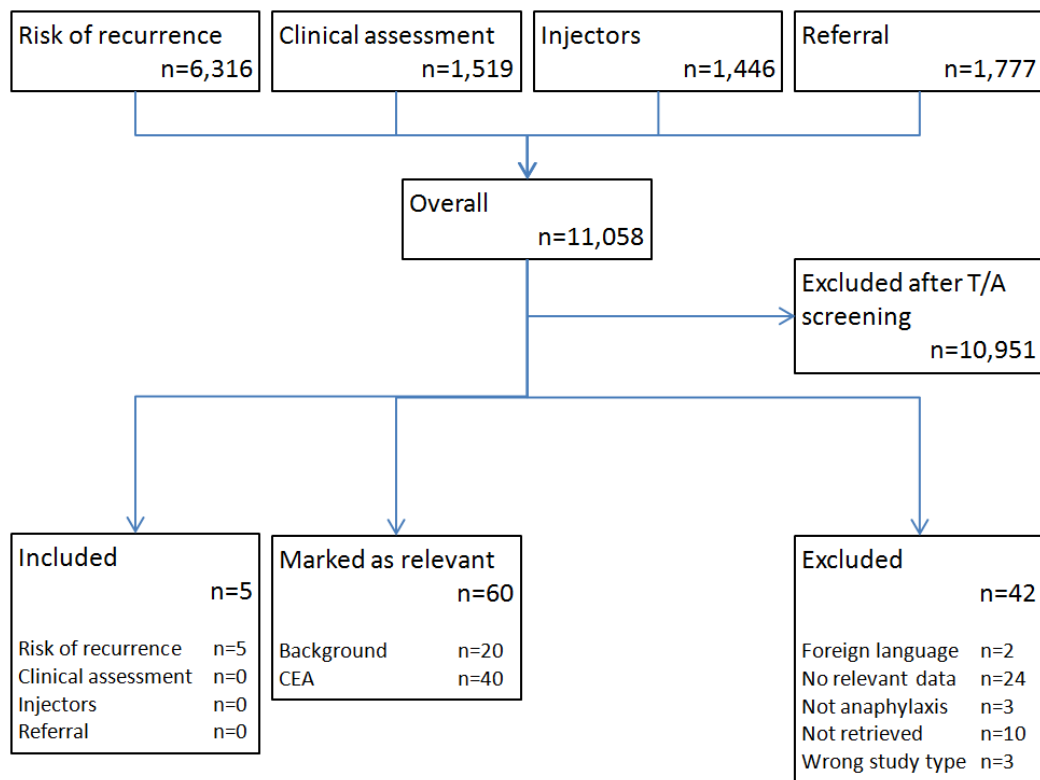


Figure 1: flow chart of study identification

Excluded studies

Alter SC, Kramps JA, Janoff A et al. (1990) Interactions of human mast cell tryptase with biological protease inhibitors. Archives of Biochemistry & Biophysics 276: 26-31.

EXC - no diagnostic test accuracy or timing

Assem ES (1993) Predictive value of in vitro tests for the IgE-dependent and the IgE-independent anaphylactoid reactions to muscle relaxants. Annales Francaises d Anesthesie et de Reanimation 12: 203-11.

EXC - no diagnostic accuracy and information on timing is for 1 patient

Bilo BM, Rueff F, Mosbech H et al. (2005) Diagnosis of Hymenoptera venom allergy. [Review] [144 refs]. Allergy 60: 1339-49.

EXC - narrative review

Brockow K, Jofer C, Behrendt H et al. (2008) Anaphylaxis in patients with mastocytosis: a study on history, clinical features and risk factors in 120 patients. Allergy 63: 226-32.

EXC - about risk factors for ana in mastocytosis

Bucher C, Uebelhart D, Wuthrich B et al. (2010) Bone mineral content in patients with anaphylactic reactions, signs of mastocytosis and elevated basal serum tryptase levels. Open Allergy Journal 3: 7-15.

EXC - about basal tryptase as risk factor

Caughey GH (2006) Tryptase genetics and anaphylaxis. [Review] [25 refs]. Journal of Allergy & Clinical Immunology 117: 1411-4.

EXC - narrative review

Enander I, Matsson P, Nystrand J et al. (1991) A new radioimmunoassay for human mast cell tryptase using monoclonal antibodies. *Journal of Immunological Methods* 138: 39-46.

EXC - case report

Ewan PW, Dugue P, Mirakian R et al. (2010) BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia. *Clinical & Experimental Allergy* 40: 15-31.

EXC - guidelines used to check references

Fernandez J, Blanca M, Moreno F et al. (1995) Role of tryptase, eosinophil cationic protein and histamine in immediate allergic reactions to drugs. *International Archives of Allergy & Immunology* 107: 160-2.

EXC - no reference standard

Fisher M (202) Anaphylaxis to anaesthetic drugs. [Review] [23 refs]. *Novartis Foundation Symposium* 257: 193-202.

EXC - narrative review

Gueant JL, Aimone-Gastin I, Namour F et al. (1998) Diagnosis and pathogenesis of the anaphylactic and anaphylactoid reactions to anaesthetics. [Review] [30 refs]. *Clinical & Experimental Allergy* 28: Suppl-70.

EXC - not enough information to extract a 2x2 table and no information on timing

Guenova E, Volz T, Eichner M et al. (2010) Basal serum tryptase as risk assessment for severe Hymenoptera sting reactions in elderly. *Allergy* 65: 919-23.

EXC - about basal tryptase as risk factor

Harper NJN, Dixon T, Dugue et al. (2009) Guidelines suspected anaphylactic reactions associated with anaesthesia. *Anaesthesia* 64: 199-211.

EXC - guidelines

Krishna MT, Fearby S, Annala I et al. (2001) Hymenoptera stings and serum tryptase. *Lancet* 357: 1527-8.

EXC - commentary

Lang R, Hawranek T (2006) Hymenoptera venom immunotherapy and field stings. *Journal of Investigational Allergology & Clinical Immunology* 16: 224-31.

EXC - about basal tryptase as risk factor

Laroche D, Namour F, Lefrancois C et al. (1999) Anaphylactoid and anaphylactic reactions to iodinated contrast material. [Review] [34 refs]. *Allergy* 54: Suppl-6.

EXC - narrative

Laroche D (2005) Immediate reactions to contrast media: mediator release and value of diagnostic testing. [Review] [10 refs]. *Toxicology* 209: 193-4.

EXC - narrative

Lin RY, Schwartz LB, Curry A et al. (2000) Histamine and tryptase levels in patients with acute allergic reactions: An emergency department-based study. *Journal of Allergy & Clinical Immunology* 106: t-71.

EXC - not clear if performed with allergic reaction or suspected anaphylaxis

McNeil HP, Adachi R, Stevens RL (2007) Mast cell-restricted tryptases: structure and function in inflammation and pathogen defense. [Review] [61 refs]. *Journal of Biological Chemistry* 282: 20785-9.

EXC - narrative review

Moreno F, Blanca M, Fernandez J et al. (1995) Determination of inflammatory markers in allergic reactions to drugs. *Allergy Proceedings* 16: 119-22.

EXC - looking at allergic reactions, not specifically suspected anaphylaxis

Muller UR (2009) Elevated baseline serum tryptase, mastocytosis and anaphylaxis. *Clinical & Experimental Allergy* 39: 620-2.

EXC - editorial/discussion

Ono E, Taniguchi M, Mita H et al. (2009) Increased production of cysteinyl leukotrienes and prostaglandin D2 during human anaphylaxis. *Clinical & Experimental Allergy* 39: 72-80.

EXC - no diagnostic accuracy or timing

Pakravan N, Waring WS, Sharma S et al. (2008) Risk factors and mechanisms of anaphylactoid reactions to acetylcysteine in acetaminophen overdose. *Clinical Toxicology: The Official Journal of the American Academy of Clinical Toxicology & European Association of Poisons Centres & Clinical Toxicologists* 46: 697-702.

EXC - no diagnostic test accuracy or timing

Potier A, Lavigne C, Chappard D et al. (2009) Cutaneous manifestations in Hymenoptera and Diptera anaphylaxis: relationship with basal serum tryptase. *Clinical & Experimental Allergy* 39: 717-25.

EXC - no diagnostic test accuracy or timing

Renz CL, Laroche D, Thurn JD et al. (1998) Tryptase levels are not increased during vancomycin-induced anaphylactoid reactions. *Anesthesiology* 89: 620-5.

EXC - no diagnostic test accuracy or timing

Rueff F, Przybilla B, Bilo MB et al. (2009) Predictors of severe systemic anaphylactic reactions in patients with Hymenoptera venom allergy: importance of baseline serum tryptase—a study of the European Academy of Allergology and Clinical Immunology Interest Group on Insect Venom Hypersensitivity. *Journal of Allergy & Clinical Immunology* 124: 1047-54.

EXC - about basal tryptase to predict future risk

Sastre J, Lluch-Bernal M, Quirce S et al. (2000) A double-blind, placebo-controlled oral challenge study with lyophilized larvae and antigen of the fish parasite, *Anisakis simplex*. *Allergy: European Journal of Allergy and Clinical Immunology* 55: 560-4.

EXC - no diagnostic test accuracy or timing

Schwartz HJ (2001) Anaphylaxis: issues in diagnosis. [Review] [13 refs]. *Current Opinion in Allergy & Clinical Immunology* 1: 357-9.

EXC - narrative review

Schwartz HJ (1995) Elevated serum tryptase in exercise-induced anaphylaxis. *Journal of Allergy & Clinical Immunology* 95: 917-9.

EXC - case report

Schwartz LB (2006) Diagnostic value of tryptase in anaphylaxis and mastocytosis. [Review] [77 refs]. *Immunology & Allergy Clinics of North America* 26: 451-63.

EXC - narrative review

Schwartz LB (1974) Effector cells of anaphylaxis: mast cells and basophils. [Review] [23 refs]. *Novartis Foundation Symposium* 257: 65-74.

EXC - narrative review

Schwartz LB, Irani AM (2000) Serum tryptase and the laboratory diagnosis of systemic mastocytosis. [Review] [100 refs]. *Hematology - Oncology Clinics of North America* 14: 641-57.

EXC - narrative review

Schwartz LB, Sakai K, Bradford TR et al. (1995) The alpha form of human tryptase is the predominant type present in blood at baseline in normal

subjects and is elevated in those with systemic mastocytosis. *Journal of Clinical Investigation* 96: 2702-10.

EXC - no diagnostic test accuracy or timing

Schwartz LB (1990) Tryptase, a mediator of human mast cells. [Review] [26 refs]. *Journal of Allergy & Clinical Immunology* 86: t-8.

EXC - narrative review

Seidel S, Voller B, Geusau A et al. (2010) Severe anaphylaxis to hymenoptera stings: does the basal serum tryptase concentration really matter? *Annals of Allergy, Asthma, & Immunology* 105: 185-7.

EXC - commentary

Shanmugam G, Schwartz LB, Khan DA (2006) Prolonged elevation of serum tryptase in idiopathic anaphylaxis. *Journal of Allergy & Clinical Immunology* 117: 950-1.

EXC - case report described in letter to editor

Sheffer AL, Tong AK, Murphy GF et al. (1985) Exercise-induced anaphylaxis: a serious form of physical allergy associated with mast cell degranulation. *Journal of Allergy & Clinical Immunology* 75: 479-84.

EXC - no tryptase test (just histamine)

Simons FE, Frew AJ, Ansotegui IJ et al. (2007) Risk assessment in anaphylaxis: current and future approaches. [Review] [150 refs]. *Journal of Allergy & Clinical Immunology* 120: Suppl-24.

EXC - narrative review

Stellato C, de CG, Patella V et al. (1996) Human basophil/mast cell releasability. XI. Heterogeneity of the effects of contrast media on mediator release. *Journal of Allergy & Clinical Immunology* 97: 838-50.

EXC - in vitro study

Sturm GJ, Heinemann A, Schuster C et al. (2007) Influence of total IgE levels on the severity of sting reactions in Hymenoptera venom allergy. *Allergy* 62: 884-9.

EXC - not relevant test

Tantikul C, Dhana N, Jongjarearnprasert K et al. (2008) The utility of the World Health Organization-The Uppsala Monitoring Centre (WHO-UMC) system for the assessment of adverse drug reactions in hospitalized children. *Asian Pacific Journal of Allergy & Immunology* 26: 77-82.

EXC - no diagnostic test accuracy or timing

Tanus T, Mines D, Atkins PC et al. (1994) Serum tryptase in idiopathic anaphylaxis: a case report and review of the literature. [Review] [22 refs]. *Annals of Emergency Medicine* 24: 104-7.

EXC - case report

Thirumala KM, Fearby S, Annila I et al. (2001) Hymenoptera stings and serum tryptase. *Lancet* 357: 1527-8.

EXC - commentary

Treudler R, Kozovska Y, Simon JC (2008) Severe immediate type hypersensitivity reactions in 105 German adults: when to diagnose anaphylaxis. *Journal of Investigational Allergology & Clinical Immunology* 18: 52-8.

EXC - timing of MCT not clear (ie. if the study reports basal serum levels or levels after anaphylaxis)

Van der Linden PW, Hack CE, Poortman J et al. (1992) Insect-sting challenge in 138 patients: relation between clinical severity of anaphylaxis and mast cell activation. *Journal of Allergy & Clinical Immunology* 90: 110-8.

EXC - no diagnostic test accuracy or timing

Watkins J (1994) Adverse reaction to neuromuscular blockers: frequency, investigation, and epidemiology. *Acta Anaesthesiologica Scandinavica Supplementum.*: 102-10.

EXC - results of tryptase tests not reported

Watkins J, Wild G (1993) Improved diagnosis of anaphylactoid reactions by measurement of serum tryptase and urinary methylhistamine. *Annales Francaises d'Anesthesie et de Reanimation* 12: 169-72.

EXC - no comparison with reference standard or timing

Watkins J (1992) Tryptase release and clinical severity of anaesthetic reactions. *Agents and Actions* 36: C203-C205.

EXC - no comparison with reference standard or timing

Whittington T, Fisher MM (1998) Anaphylactic and anaphylactoid reactions. *Bailliere's Clinical Anaesthesiology* 12: 301-23.

EXC - narrative review

Yunker J, Soar J (2010) Recognition and treatment of anaphylaxis. [Review] [11 refs]. *Nursing in Critical Care* 15: 94-8.

EXC - narrative review

Apter AJ, LaVallee HA (1994) How is anaphylaxis recognized? *Arch Fam.Med* 3: 717-22.

EXC - not evaluation of models of care

Bhutani S, Khan DA (2009) Allergist referrals for systemic reactions to imported fire ants: a community survey in an endemic area. *Annals of Allergy, Asthma, & Immunology* 102: 145-8.

EXC - survey of practice related to fire ants; not models of care

Dietrich JJ, Quinn JM, and England RW. (2009) Reasons for outpatient consultation in allergy/immunology. *Allergy & Asthma Proceedings* 30: 69-74.

EXC - description of reasons for referral; not models of care

England RW, Ho TC, Napoli DC et al. (2003) Inpatient consultation of allergy/immunology in a tertiary care setting. [Review] [12 refs]. *Annals of Allergy, Asthma, & Immunology* 90: 393-7.

EXC - description of reasons for referral; not models of care

Khan SN, Slavin RG (2000) Pediatricians' attitudes towards allergy: Past and present attitudes of pediatricians towards allergy. *Annals of Allergy, Asthma and Immunology* 85: 189-93.

EXC - reasons for referral (survey); not models of care

Lieberman P, Decker W, Camargo CA, Jr. et al. (2007) SAFE: a multidisciplinary approach to anaphylaxis education in the emergency department. [Review] [37 refs]. *Annals of Allergy, Asthma, & Immunology* 98: 519-23.

EXC - not evaluation of models of care

Nurmatov U, Worth A, Sheikh A (2008) Anaphylaxis management plans for the acute and long-term management of anaphylaxis: a systematic review. *Journal of Allergy and Clinical Immunology* 122(2): 353-61.

EXC - review of management plans; no exploration of the impact of the provider (specialist vs generalist care)

Sharma R, Sinha R, Menon PS et al. (2010) Management protocol for anaphylaxis. [Review] [43 refs]. *Journal of Oral & Maxillofacial Surgery* 68: 855-62.

EXC - narrative review; no details of model of care

Singh J, Aszkenasy OM (2003) Prescription of adrenaline auto-injectors for potential anaphylaxis--a population survey. *Public Health* 117: 256-9.

EXC - no comparison of the quality of care by setting

Walker S (2002) Managing anaphylaxis in general practice. *Practice Nursing* 13: 254-8.

EXC - narrative review; not models of care

These studies were excluded after reading the full text.

Proceedings: XVII International Congress of Allergology and Clinical Immunology, Sydney, Australia, 15-20 October 2000. *Allergy & Clinical Immunology International*. 2000:v-139.

No relevant data (no relevant studies identified).

Reduce anaphylactic reactions to anaesthetic drugs by identifying definite risk factors and preventing subsequent reactions. *Drugs and Therapy Perspectives*. 2005;21(2):24-6.

No relevant data.

Ahlbach S, Boehncke WH. Management of anaphylactic reactions in the allergological practice. *Allergologie*. 2003 Jul;26(7):294-302.

No relevant data.

Aleman A, Sastre J, Quirce S, de las Heras M, Carnes J, Fernandez-Caldas E, et al. Allergy to kiwi: A double-blind, placebo-controlled food challenge study in patients from a birch-free area. *Journal of Allergy and Clinical Immunology*. 2004 Mar;113(3):543-50.

No relevant data.

Al-Ghanem F, Al-Mutairi N. Spectrum of cutaneous adverse drug reactions seen in the Emergency Department (ED): A prospective study from Kuwait. *Middle East Journal of Emergency Medicine*. 2006;6(2):11-5.

Not anaphylaxis.

Bilo BM, Bonifazi F. Epidemiology of insect-venom anaphylaxis. *Current Opinion in Allergy and Clinical Immunology*. 2008 Aug;8(4):330-7.

No relevant data.

Boehncke WH, Ahlback S. Emergency management in the allergological practice: Prevention of iatrogenic anaphylactic reactions. *Allergologie*. 2003 Feb;26(2):78-83.

No relevant data.

Charpin D, Benzarti M, Birnbaum J, Hemon Y, Senft M, Alazia M, et al. RISK-FACTORS FOR ANAPHYLACTIC REACTIONS TO MUSCLE-RELAXANTS. *Journal of Allergy and Clinical Immunology*. 1987 Jan;79(1):239-.

No relevant data.

Chee R, Rattray L, Nagendran V, Bansal A, Hayman G, Warner A, et al. Assessing baseline serum plateletactivating factor acetylhydrolase levels in determining the risk of anaphylaxis in allergic patients. *Allergy*. 2008;63:1135.

No relevant data.

Collet E, Jeudy G. Clinical aspects of severe cutaneous allergies (excluding cutaneous drug eruptions). *Revue Francaise D Allergologie Et D Immunologie Clinique*. 2008 Apr;48(3):115-9.

Not anaphylaxis.

Dobbie A, Robertson CM. Provision of self-injectable adrenaline for children at risk of anaphylaxis: Its source, frequency and appropriateness of use, and effect. *Ambulatory Child Health*. 1998;4(3):283-8.

No relevant data.

Dykewicz MS, McGrath KG, Patterson R. IDENTIFICATION OF PATIENTS AT RISK FOR ANAPHYLAXIS FROM STREPTOKINASE. *Journal of Allergy and Clinical Immunology*. 1986 Jan;77(1):225-.

No relevant data.

13. El-Shanawany T, Seddon L, Jolles S, Carne E, Dowd H, Williams P. Patients with anaphylaxis in accident and emergency are not referred to specialised allergy services. *J Clin Pathol*. 2010 Apr;63(4):375.

No relevant data.

Ellsworth PI, Merguerian PA, Klein RB, Rozycki AA. EVALUATION AND RISK-FACTORS OF LATEX ALLERGY IN SPINA-BIFIDA PATIENTS - IS IT PREVENTABLE. *Journal of Urology*. 1993 Aug;150(2):691-3.

Not anaphylaxis.

Fisher Mc DM. The epidemiology of anaesthetic anaphylactoid reactions in Australasia. *Klinische Wochenschrift*. 1982;60(17):1017-20.

No relevant data.

Helbling A, Muller U, Hausmann O. Anaphylaxis - Reality of acute therapy and preventive measures. Analysis of 54 patients in a spezialized city hospital. [German]. *Allergologie*. 2009;32(9):358-64.

No relevant data.

Hompes S, Scherer K, Kohli A, Rueff F, Mahler V, Lange L, et al. Food anaphylaxis: Data from the anaphylaxis register. *Allergo Journal*. 2010;19(4):234-42.

Foreign language paper

Kanny G, Moneret-Vautrin DA, Flabbee J, Beaudouin E, Morisset M, Parisot L. Risk factors of food induced anaphylactic shock. *Journal of Allergy and Clinical Immunology*. 2002 Apr;109(4):743-.

Levy Y, Segal N, Danon YL. Trends in adrenaline (EpiPen) dispensing in Israel in 1997-2004. *PUBLIC HEALTH*. 2007 Feb;121(2):144-7.

No relevant data.

Lieberman P, Camargo CA, Jr., Bohlke K, Jick H, Miller RL, 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 Nov;97(5):596-602.

No relevant data.

Malinovsky JM, Vervloet D, Laxenaire MC. Are there risk factors of anaphylaxis related to patient factors, to treatments, and to anaesthetic procedures? - How identify the people at risk for anaphylactoid reactions in anaesthesia? *Annales Francaises D Anesthesie Et De Reanimation*. 2002 May;21:129S-50S.

Wrong study type.

Moneret-Vautrin DA, Kanny G. Food-induced anaphylactic shock. A French multicentric survey over 1991 and 1992. *Annales De Gastroenterologie Et D Hepatologie*. 1995 Sep;31(4):256-63.

Foreign language paper.

Muck AE, Bebartha VS, Borys DJ, Morgan DL. Six Years of Epinephrine Digital Injections: Absence of Significant Local or Systemic Effects. *Annals of Emergency Medicine*. 2010 Sep;56(3):270-4.

No relevant data.

Piromrat K, Chinratanapisit S, Trathong S. Anaphylaxis in an Emergency Department: A 2-Year Study in a Tertiary-Care Hospital. *Asian Pacific Journal of Allergy and Immunology*. 2008 Jun-Sep;26(2-3):121-8.

No relevant data.

Poachanukoon O, Paopairochanakorn C. Incidence of anaphylaxis in the emergency department: A 1-year study in a university hospital. *ASIAN PACIFIC JOURNAL OF ALLERGY AND IMMUNOLOGY*. 2006;24(2-3):111-6.

No relevant data.

Pritchard KI. Endocrine symptoms to predict risk of recurrence? *The Lancet Oncology*. 2008;9(12):1117-9.

Wrong study type.

Rusznak C, Peebles Jr RS. Anaphylaxis and anaphylactoid reactions. [Turkish]. *Sendrom*. 2003;15(6):57-64.

No relevant data.

Santaella ML, Cox PR, Ramos C, Disdier OM. Anaphylaxis: an analysis of cases evaluated at the Puerto Rico Medical Center over a ten-year period. *P R Health Sci J.* 2006 Jun;25(2):143-7.

No relevant data.

Schnadt S. Anaphylaxis - Data from patient's perspective. A national survey of the German Allergy and Asthma Association (DAAB). [German]. *Allergologie.* 2009;32(1):17-27.

No relevant data.

Schwartz HJ. Acute allergic disease in a hospital emergency room: a retrospective evaluation of one year's experience. *Allergy Proc.* 1995 Sep-Oct;16(5):247-50.

No relevant data.

Simons FER, Lieberman PL, Read EJ, Jr., Edwards ES. Hazards of unintentional injection of epinephrine from autoinjectors: a systematic review. *Ann Allergy Asthma Immunol.* 2009 Apr;102(4):282-7.

No relevant data.

Tejedor M, Moro M, Mugica M, Vila C, Rosado A, Gomez-Traseira C, et al. Referral to allergy unites of patients with anaphylaxis who attended to emergency departments. *Allergy.* 2008;63:292.

No relevant data.

Beaudoin E, Sergeant P, Flabbee J et al. (2007) Buckwheat allergy: Analysis of 22 cases recorded by the Allergy Vigilance Network (2002-2006). *European*

annals of allergy and clinical immunology 39: 303-6.

EXC - not biphasic anaphylaxis

Beck AM (2009) Leading through crisis. Hemodialysis International Conference: Annual Dialysis Conference - 29th Annual Conference on Peritoneal Dialysis, 15th International Symposium on Hemodialysis, and 20th Annual Symposium on Pediatric Dialysis Houston, TX United States. Conference Start: 20090308 Conference End: 20090310. Conference Publication: 136.

EXC - abstract

Beck AM (2009) Review of anaphylactoid cases in the dialysis unit at SLCH. Hemodialysis International Conference: Annual Dialysis Conference - 29th Annual Conference on Peritoneal Dialysis, 15th International Symposium on Hemodialysis, and 20th Annual Symposium on Pediatric Dialysis Houston, TX United States. Conference Start: 20090308 Conference End: 20090310. Conference Publication: 136.

EXC - abstract

Bellman B (2005) Immediate and delayed hypersensitivity reactions to restylane. Aesthetic Surgery Journal 25: 489-91.

EXC - no biphasic anaphylaxis

Bil B, Frontini F, Cinti B et al. (2009) Are mast-cell diseases risk factors for drug-induced biphasic anaphylaxis? a case report. Allergy: European Journal of Allergy and Clinical Immunology Conference: 28th Congress of the European Academy of Allergy and Clinical Immunology Abstract Book Warszawa Poland. Conference Start: 20090606 Conference End: 20090610. Conference Publication: 529-30.

EXC - abstract

Bilo BM, Bonifazi F (2008) Epidemiology of insect-venom anaphylaxis. Current Opinion in Allergy & Clinical Immunology 8: 330-8.

EXC - narrative review

Calvani M, Cardinale F, Martelli A et al. (2009) Efficiency of the new diagnostic criteria for food anaphylaxis in Italy. *Allergy: European Journal of Allergy and Clinical Immunology Conference: 28th Congress of the European Academy of Allergy and Clinical Immunology Abstract Book Warszawa Poland*. Conference Start: 20090606 Conference End: 20090610. Conference Publication: 566-7.

EXC - abstract

Chamberlin KW, Silverman AR (2009) Celecoxib-associated anaphylaxis. *Annals of Pharmacotherapy* 43: 777-81.

EXC - case report

Confino-Cohen R, Goldberg A (2009) Allergen immunotherapy-induced biphasic anaphylaxis: Incidence, characteristics and outcome- A prospective study. *Journal of Allergy and Clinical Immunology Conference: 2009 American Academy of Allergy, Asthma and Immunology*: S184.

EXC - abstract

Cortellini G, Corvetta A, Campi P et al. (2005) A case of fatal biphasic anaphylaxis secondary to multiple stings: Adrenalin and/or a longer observation time could have saved the patient? *European annals of allergy and clinical immunology* 37: 343-4.

EXC - case report

Cuniowski PA, Hunter CJ (2009) Would you recognize this patient's biphasic anaphylaxis? *Emergency Medicine (00136654)* 41: 30-5.

EXC - case report

Dijkman JH (1975) Observations on biphasic bronchial reactions due to inhalation of enzymes of *Bacillus subtilis*. *Clinical allergy* 5: 25-31.

EXC - not anaphylaxis

Ellis AK (2010) Biphasic anaphylaxis: A review of the incidence, characteristics and predictors. *Open Allergy Journal* 3: 24-8.

EXC - narrative review

Ellis AK, Day JH (2003) Diagnosis and management of anaphylaxis.
Canadian Medical Association Journal 169: 307-12.

EXC - case report

Ewan PW, Clark AT (2005) 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. Clinical and Experimental Allergy 35: 751-6.

EXC - not biphasic anaphylaxis

Goebel CW (1988) Anaphylaxis and anaphylactoid reaction: acute, biphasic and protracted. Indiana medicine : the journal of the Indiana State Medical Association 81: 526-7.

EXC - narrative review

Golden DB (157) Patterns of anaphylaxis: acute and late phase features of allergic reactions. Novartis Foundation symposium 257: 101-10.

EXC - narrative review

Gouvea G, Diaz R, Auler L et al. (2008) Evaluation of the right ventricular ejection fraction during orthotopic liver transplantation under propofol anaesthesia. British Journal of Anaesthesia 101: 161-5.

EXC - no biphasic anaphylaxis

Haden JR, Khan DA (2004) Anaphylaxis, part 2: management strategies. Journal of Respiratory Diseases 25: 113-7.

EXC - narrative review

Jairam A, Kumar RSV, Ghosh AK et al. (2010) Delayed Kounis syndrome and acute renal failure after wasp sting. International Journal of Cardiology 138: e12-e14.

EXC - not biphasic anaphylaxis

Jeong D, Leo H, Cunningham R et al. (2009) Knowledge of biphasic anaphylaxis and treatment for anaphylaxis among EMS providers in Southeast Michigan. Journal of Allergy and Clinical Immunology Conference:

2009 American Academy of Allergy, Asthma and Immunology: S187.

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EXC - no biphasic anaphylaxis

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EXC - not biphasic anaphylaxis

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EXC - narrative review

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EXC - case report

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EXC - abstract

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EXC - case report

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