Appendix C Guideline scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Hyperglycaemia in acute coronary syndromes: management of hyperglycaemia in people with acute coronary syndromes

1.1 Short title

Hyperglycaemia in acute coronary syndromes

2 The remit

The Department of Health has asked NICE: ‘to produce a short clinical guideline on the management of hyperglycaemia in acute coronary syndrome in patients both with and without diagnosed diabetes mellitus’.

3 Clinical need for the guideline

3.1 Epidemiology

Acute coronary syndromes (ACS) encompass a spectrum of unstable coronary artery disease from unstable angina to transmural myocardial infarction. All forms begin with an inflamed and complicated fatty deposit (known as an atheromatous plaque) in a blood vessel, and blood clots forming on the plaque. The principles behind the presentation, investigation and management of these syndromes are similar with important distinctions depending on the category of acute coronary syndrome.

Hyperglycaemia is common in patients when they are admitted to hospital with ACS. Recent studies found that approximately 65% of patients with acute
myocardial infarction (heart attack) who were not known to have diabetes had impaired glucose regulation when given a glucose tolerance test.

For patients both with and without diabetes mellitus, hyperglycaemia on admission is a powerful predictor of poorer survival and increased risk of complications while in hospital. Despite this, hyperglycaemia remains underappreciated as a risk factor in acute coronary syndromes and it is frequently untreated.

Persistently elevated blood glucose levels during acute myocardial infarction have been shown to be associated with increased in-hospital mortality, and to be a better predictor of outcome than admission blood glucose.

### 3.2 Current practice

Currently, the management of hyperglycaemia in people with acute coronary syndromes is inconsistent across the UK, whether or not the person has diagnosed diabetes.

The Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice recommend that:

- In people who present with an acute cardiovascular event, fasting glucose should be measured at least once, or an oral glucose tolerance test performed, during their hospital stay.
- Fasting glucose should be measured during the acute phase of the illness. If there is evidence of impaired fasting glucose (more than 6.0 mmol/litre but less than 7.0 mmol/litre) or an indication of diabetes (more than 7.0 mmol/litre) fasting glucose should be measured twice (or an oral glucose tolerance test performed once) between 8 and 12 weeks after discharge from hospital.

The SIGN guidelines on acute coronary syndromes recommend that patients with clinical myocardial infarction and diabetes or marked hyperglycaemia (more than 11 mmol/litre) should be given immediate intensive blood glucose control. This should be continued for at least 24 hours. The European Society
of Cardiology also recommends that patients with acute myocardial infarction and diabetes should be given tight glucometabolic control.

There is currently no relevant national guidance for England, Wales and Northern Ireland on the management of hyperglycaemia in people with acute coronary syndromes.

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 with acute coronary syndromes and hyperglycaemia with a diagnosis of diabetes.
- Adults with acute coronary syndromes and hyperglycaemia without a diagnosis of diabetes.
- Subgroups who are at higher risk of mortality and poorer outcomes associated with acute coronary syndrome will be considered as appropriate.

4.1.2 Groups that will not be covered

- Adults with hyperglycaemia who do not have acute coronary syndromes.
- Adults with acute coronary syndromes who do not have hyperglycaemia.
4.2 **Healthcare setting**
Secondary and tertiary care.

4.3 **Clinical management**

4.3.1 **Key clinical issues that will be covered**
- Threshold values of blood glucose levels for intervention.
- Inpatient glucometabolic management (glucose, potassium and insulin) of hyperglycaemia in patients with acute coronary syndrome, who have diagnosed diabetes mellitus.
- Inpatient glucometabolic management (glucose, potassium and insulin) of hyperglycaemia in patients with acute coronary syndrome, who do not have diagnosed diabetes mellitus.
- Timing and frequency of blood glucose level measures for monitoring purposes in hospital.
- Referral for subsequent investigation to confirm possible diabetes in patients without an existing diagnosis of diabetes.

4.3.2 **Clinical issues that will not be covered**
- Diagnosis of diabetes mellitus.
- Management of diabetes mellitus.
- Diagnosis of acute coronary syndromes.
- Management of acute coronary syndromes.
- Types of medical devices used to measure hyperglycaemia.
- Long-term management of hyperglycaemia and support beyond the acute phase.

4.4 **Main outcomes**
- All-cause mortality.
- Cardiovascular mortality.
- Cardiovascular events such as non-fatal reinfarction, heart failure and stroke.
- Measures and control of blood glucose levels.
• Health related quality of life.
• Adverse events associated with metabolic management of hyperglycaemia, including hypoglycaemia and hypokalaemia.
• Resource use and costs, such as length of hospital stay.

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 question is the cost effectiveness of intensive glucometabolic management of hyperglycaemia in inpatients with acute coronary syndromes and hyperglycaemia with or without diabetes. The full economic analysis will be developed in conjunction with the Clinical Review Group and the Guideline Development Group.

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 November 2010.
5 Related NICE guidance

5.1 Published guidance

5.1.1 Other related NICE guidance


### 5.2 Guidance under development

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


- Long-acting exenatide for the second-line (dual therapy) or third-line (triple therapy) treatment of type 2 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

- Buccal insulin for the management of type 1 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

### 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’.

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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.
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).

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 June 2010 and September 2010.

**Scoping searches**

Scoping searches were undertaken in May 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.

The below is a list of the related guidance used in the scoping searches

<table>
<thead>
<tr>
<th>Guidance/guidelines</th>
<th>Systematic reviews/economic evaluations</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Diabetes Association</td>
<td>Clinical Evidence</td>
</tr>
<tr>
<td>British Medical Association</td>
<td>Cochrane Database of Systematic Reviews (CDSR)</td>
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<tr>
<td>Canadian Medical Association Infobase</td>
<td>Database of Abstracts of Reviews of Effects (DARE)</td>
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<tr>
<td>Clinical Knowledge Summaries</td>
<td>Health Economic Evaluations Database (HEED)</td>
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<tr>
<td>Clinical Resource Efficiency Support Team</td>
<td>Health Technology Assessment database (HTA)</td>
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<tr>
<td>(CREST)</td>
<td>NHS Economic Evaluation Database (NHS EED)</td>
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<tr>
<td>Department of Health</td>
<td>NHS R&amp;D Service Delivery and Organisation Programme</td>
</tr>
<tr>
<td>Diabetes UK</td>
<td>National Institute for Health Research Health Technology Assessment Programme</td>
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<tr>
<td>Guidelines International Network (GIN)</td>
<td>(NIHR)</td>
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<tr>
<td>National Guideline Clearinghouse (US)</td>
<td>TRIP Database</td>
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<td>National Health and Medical Research Council (Australia)</td>
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<td>New Zealand Guidelines Group</td>
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<tr>
<td>NHS Evidence</td>
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<tr>
<td>Royal College of Physicians</td>
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<td>Royal Pharmaceutical Society</td>
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<tr>
<td>SIGN</td>
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<tr>
<td>University of Warwick</td>
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<td>World Health Organisation</td>
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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

What is the optimal inpatient metabolic management of patients presenting with hyperglycaemia and acute coronary syndrome (ACS) who have diagnosed diabetes mellitus and hyperglycaemia?

The following sources were searched to answer questions relating to:

Databases searched:

- Cochrane Central Register of Controlled Trials (Wiley)
- CINAHL (NHS Evidence)
- Cochrane Database of Systematic Reviews (Wiley)
- Database of Abstracts of Reviews of Effects (CRD)
- Embase (OVID)
- Health Technology Assessment database (CRD)
- Medline (OVID)
- Medline In-Process (OVID)

The searches were conducted on 10 August 2010.
Medline 1950 to July Week 4 2010

The Medline search strategy is presented below. It was translated for use in all of the other databases. Where appropriate, search filters for systematic reviews and randomised controlled trials were appended to the search strategies to retrieve high quality papers.

1. exp Hyperglycemia/
2. hyperglycemi$.tw.
3. hyperglycaemi$.tw.
4. (high$ adj3 plasma$ glucose$).tw.
5. (high$ adj3 blood$ glucose$).tw
7. (high$ adj3 blood$ sugar$).tw.
8. (impair$ adj3 blood$ sugar$ regulation$).tw.
9. or/1-8
10. Acute Coronary Syndrome/
11. (acute$ adj3 coronary$ syndrome$).tw.
12. acs.tw.
13. exp Myocardial Infarction/
15. mi.tw.
17. (heart$ adj3 infarction$).tw.
18. exp Angina, Unstable/
22. (unstable$ adj3 angina$ pectoris$).tw.
23. Myocardial Ischemia/
24. (myocardial$ adj3 ischemia$).tw.
25. (myocardial$ adj3 ischaemia$).tw.
27. (ischaemic$ adj3 heart$ disease$).tw.
28. (heart$ adj3 muscle$ ischemia$).tw.
29. (heart$ adj3 muscle$ ischaemi$a$).tw.
30. or/10-29
31. exp Insulin/
32. (intensive$ adj3 insulin$ therap$).tw.
33. (intensive$ adj3 insulin$ infusion$).tw.
34. Glucose/
35. glucose$.tw.
36. (glucose$ adj3 therap$).tw.
37. (glucose$ adj3 infusion$).tw.
38. potassium.tw.
39. or/31-38
40. Randomized Controlled Trial.pt.
41. Controlled Clinical Trial.pt.
42. Clinical Trial.pt.
43. exp Clinical Trials as Topic/
44. Placebos/
45. Random Allocation/
46. Double-Blind Method/
47. Single-Blind Method/
48. Cross-Over Studies/
49. ((random$ or control$ or clinical$) adj2 (trial$ or stud$)).tw.
51. placebo$.tw.
52. ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.
53. (crossover$ or (cross adj over$)).tw.
54. or/40-53
55. animals/ not humans/
56. 54 not 55
57. Meta-Analysis.pt.
58. Meta-Analysis as Topic/
59. Review.pt.
60. exp Review Literature as Topic/
61. (metaanaly$ or metanaly$ or (meta adj2 analy$)).tw.
62. (review$ or overview$).ti.
At what stage should patients with hyperglycaemia and ACS without
diagnosed diabetes be referred for subsequent investigations for possible
diabetes?

Databases searched:

- Cochrane Central Register of Controlled Trials (Wiley)
- CINAHL (NHS Evidence)
- Cochrane Database of Systematic Reviews (Wiley)
- Database of Abstracts of Reviews of Effects (CRD)
- Embase (OVID)
- Health Technology Assessment database (CRD)
- Medline (OVID)
- Medline In-Process (OVID)

The searches were conducted on 06 October 2010.

The Medline search strategy is presented below. It was translated for use in
all of the other databases.

Medline 1950 to September Week 3 2010

1. exp Hyperglycemia/
2. hyperglycemia.tw.
3. hyperglycaemia.tw.
4. (high adj3 plasma glucose).tw.
5. (high adj3 blood glucose).tw.
7. (high adj3 blood sugar).tw.
8. (impair adj3 blood sugar regulation).tw.
9. or/1-8
10. Acute Coronary Syndrome/
11. (acute adj3 coronary syndrome).tw.
12. acs.tw.
13. exp Myocardial Infarction/
15. mi.tw.
17. (heart adj3 infarction).tw.
18. exp Angina, Unstable/
22. (unstable adj3 angina pectoris).tw.
23. Myocardial Ischemia/
24. (myocardial adj3 ischemia).tw.
25. (myocardial adj3 ischaemia).tw.
27. (ischaemic adj3 heart disease).tw.
28. (heart adj3 muscle ischemia).tw.
29. (heart adj3 muscle ischaemia).tw.
30. or/10-29
31. exp Diabetes Mellitus/
32. diabetes.tw.
33. or/31-32
34. Risk Factors/
35. (risk adj3 factor).tw.
What information should patients with peri ACS and hyperglycaemia (who are at high risk of developing diabetes) be provided while waiting for a referral for diagnostic investigations for diabetes?

Databases searched:

- Cochrane Central Register of Controlled Trials (Wiley)
- CINAHL (NHS Evidence)
- Cochrane Database of Systematic Reviews (Wiley)
- Database of Abstracts of Reviews of Effects (CRD)
- Embase (OVID)
- Health Technology Assessment database (CRD)
- Medline (OVID)
The searches were conducted on 2 November 2010.

The Medline search strategy is presented below. It was translated for use in all of the other databases. Where appropriate, search filters for patient information were appended to the search strategies to retrieve high quality papers.

Medline 1950 to October Week 3 2010

1. exp Hyperglycemia/
2. hyperglycemi$.tw.
3. hyperglycaemi$.tw.
4. (high$ adj3 plasma$ glucose$).tw.
5. (high$ adj3 blood$ glucose$).tw.
7. (high$ adj3 blood$ sugar$).tw.
8. (impair$ adj3 blood$ sugar$ regulation$).tw.
9. or/1-8
10. Acute Coronary Syndrome/
11. (acute$ adj3 coronary$ syndrome$).tw.
12. acs.tw.
13. exp Myocardial Infarction/
15. mi.tw.
17. (heart$ adj3 infarction$).tw.
18. exp Angina, Unstable/
22. (unstable$ adj3 angina$ pectoris$).tw.
23. Myocardial Ischemia/
24. (myocardial$ adj3 ischemia$).tw.
25. (myocardial$ adj3 ischaemia$).tw.
27. (ischaemic$ adj3 heart$ disease$).tw.
28. (heart$ adj3 muscle$ ischemia$).tw.
29. (heart$ adj3 muscle$ ischaemia$).tw.
30. or/10-29
31. Qualitative Research/
32. Nursing Methodology Research/
33. exp Interviews as topic/
34. Questionnaires/
35. Narration/
36. Health Care Surveys/
37. (qualitative$ or interview$ or focus group$ or questionnaire$ or narrative$ or narration$ or survey$).tw.
38. (ethno$ or emic or etic or phenomenolog$ or grounded theory or constant compar$ or (thematic$ adj3 analys$) or theoretical sampl$ or purposive sampl$).tw.
39. (hermeneutic$ or heidegger$ or husserl$ or colaiuzzi$ or van kaam$ or van manen$ or giorgi$ or glaser$ or Strauss$ or ricouer$ or spiegelberg$ or merleau$).tw.
40. (metasynthes$ or meta-synthes$ or metasummar$ or meta-summar$ or metastud$ or meta-stud$).tw.
41. or/31-40
42. exp Patients/px
43. exp Parents/px
44. exp Family/px
45. Caregivers/px
46. Stress, Psychological/
47. (mental$ adj3 stress$).tw.
48. Adaptation, psychological/
49. (adaptive$ adj3 behaviour$).tw.
50. (adaptive$ adj3 behavior$).tw.
51. Emotions/
52. Anxiety/
53. Fear/
54. exp Consumer Satisfaction/
55. ((patient$ or parent$ or famil$ or carer$ or caregiver$ or care-giver$ or inpatient$ or in-patient$) adj2 (experience$ 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 attitude$ or satisfy$ or know$ or understand$ or aware$)).tw.
56. or/42-55
57. Pamphlets/
58. Needs Assessment/
59. Information Centers/
60. Information Services/
61. Health Education/
62. Information Dissemination/
63. Counseling/
64. Social Support/
65. Self-Help Groups/
66. Self Care/
67. Patient Education as Topic/
68. Patient Education Handout/
69. Consumer Health Information/
70. Life Style/
71. patient* diar*.tw.
72. (educat$ 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$).ti.
73. (counsel$ or selfhelp$ or self-help$ or self help$ or selfcar$ or self-car$ or self car$).ti.
74. or/57-73
75. 41 or 56 or 74
76. 9 and 30 and 75
77. limit 76 to english language
Economic search
The following sources were searched to identify economic evaluations and quality of life data.

Databases searched:

- Health Economic Evaluations Database (Wiley)
- NHS Economic Evaluation Database (CRD)
- Embase (OVID)
- Medline (OVID)
- Medline In-Process (OVID)

The searches were conducted on 25 August 2010.

Medline 1950 to August Week 2 2010

The Medline search strategy is presented below. It was translated for use in other databases except for Embase. Where appropriate, search filters for economic evaluations and quality of data were appended to the search strategies to retrieve high quality papers.

1. Acute Coronary Syndrome/
2. (acute$ adj3 coronary$ syndrome$).tw.
3. acs.tw.
4. exp Myocardial Infarction/
5. (myocardial$ adj3 infarction$).tw.
6. mi.tw.
7. (heart$ adj attack$).tw.
8. (heart$ adj3 infarction$).tw.
9. exp Angina, Unstable/
11. (preinfarction$ adj3 angina$).tw.
12. (myocardial$ adj3 preinfarction$).tw.
14. Myocardial Ischemia/
15. (myocardial$ adj3 ischemia$).tw.
16. (myocardial$ adj3 ischaemia$).tw.
17. (ischemic$ adj3 heart$ disease$).tw.
18. (ischaemic$ adj3 heart$ disease$).tw.
19. (heart$ adj3 muscle$ ischemia$).tw.
20. (heart$ adj3 muscle$ ischaemia$).tw.
21. or/1-20
22. exp Insulin/
23. (intensive$ adj3 insulin$ therap$).tw.
25. Glucose/
26. glucose$.tw.
27. (glucose$ adj3 therap$).tw.
29. potassium.tw.
30. or/22-29
31. 21 and 30
32. Economics/ use mesz
33. exp "Costs and Cost Analysis"/
34. Economics, Dental/
35. exp Economics, Hospital/
36. exp Economics, Medical/
37. Economics, Nursing/
38. Economics, Pharmaceutical/
39. Budgets/
40. exp Models, Economic/
41. Markov Chains/
42. Monte Carlo Method/
43. Decision Trees/
44. econom$.tw.
45. cba.tw.
46. cea.tw.
47. cua.tw.
48. markov$.tw.
49. (monte adj carlo).tw.
50. (decision adj2 (tree$ or analys$)).tw.
51. (cost or costs or costing$ or costly or costed).tw.
52. (price$ or pricing$).tw.
53. budget$.tw.
54. expenditure$.tw.
55. (value adj2 (money or monetary)).tw.
56. (pharmacoeconomic$ or (pharmaco adj economic$)).tw.
57. or/23-56
58. "Quality of Life"/ use mesz
59. quality of life.tw.
60. "Value of Life"/ use mesz
61 Quality-Adjusted Life Years/ use mesz
62. (qaly$ or qald$ or qale$ or qtime$).tw.
63. disability adjusted life.tw.
64. daly$.tw.
65. Health Status Indicators/ use mesz
66. (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.
67. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
68. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
69. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
70. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
71. (euroqol or euro qol or eq5d or eq 5d).tw.
72. (qol or hql or hqol or hrqol).tw.
73. (hye or hyes).tw.
74. health$ year$ equivalent$.tw.
75. utilit$.tw.
76. (hui or hui1 or hui2 or hui3).tw.
Review questions and review protocols

Review questions

- What is the optimal inpatient metabolic management of hyperglycaemia in a person presenting with acute coronary syndrome and hyperglycaemia and who also has a previous diagnosis of diabetes mellitus?
- What is the optimal inpatient metabolic management for a person presenting with acute coronary syndrome and hyperglycaemia and who does not have a previous diagnosis of diabetes?
- What risk factors are associated with the development of diabetes in people with hyperglycaemia in ACS?
- What information should patients with ACS and hyperglycaemia (who are at high risk for developing diabetes) be provided before diagnostic investigations for diabetes?

Review protocols

<table>
<thead>
<tr>
<th>REVIEW QUESTION 1</th>
<th>Details</th>
<th>Comments</th>
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<tbody>
<tr>
<td>REVIEW QUESTION 1</td>
<td>What is the optimal inpatient metabolic management of patients presenting</td>
<td></td>
</tr>
</tbody>
</table>
with hyperglycaemia and acute coronary syndrome (ACS) who have diagnosed diabetes mellitus and hyperglycaemia?

| OBJECTIVES | To compare the effectiveness and safety of standard practice with intensive insulin therapy in the management of hyperglycaemia in ACS in patients who have been diagnosed with diabetes  
To determine how and when glucose, potassium and/or insulin should be given to patients with hyperglycaemia and ACS  
To investigate clinically acceptable targets of whole blood glucose level or plasma glucose level required to achieve normoglycemia  
To determine when and how often whole blood or plasma glucose level should be measured in hospital | The wording of the objective was amended to include safety as adverse events such as hypoglycaemia were included as outcomes. |

| CRITERIA FOR CONSIDERING STUDIES | Inclusion:  
Hyperglycaemia & ACS  
Adults (> 18 years only)  
Previous diagnosis of diabetes (type 1 or type2)  
RCTs and MINAP  
Treatment in first 48 hours only (acute phase)  
Assessment of mortality and/or other primary/secondary outcome  
Exclusion:  
Other observational studies | |

| POPULATION | Adults with hyperglycaemia and ACS with diagnosed diabetes mellitus | |

| INTERVENTION | Intensive insulin therapy/infusion | |

| COMPARATORS | Standard practice/conventional treatment | |

| OUTCOMES | All cause mortality  
Cardiovascular mortality  
Cardiovascular events associated with hyperglycaemia such as non fatal reinfarction, heart failure and stroke  
Measures of whole blood or plasma glucose levels  
Health related quality of life  
Adverse events associated with metabolic management of hyperglycaemia including | |
<table>
<thead>
<tr>
<th>REVIEW QUESTION 2</th>
<th>Details</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>REVIEW QUESTION 2</td>
<td>What is the optimal inpatient metabolic management of patients presenting with hyperglycaemia and acute coronary syndrome (ACS) without a diagnosis of diabetes mellitus?</td>
<td>The wording of the objective was amended to include safety as adverse events such as hypoglycaemia were included as outcomes</td>
</tr>
</tbody>
</table>

| OBJECTIVES | To compare the effectiveness and safety of standard practice with intensive insulin therapy in the management of hyperglycaemia in ACS in patients without a diagnosis of diabetes mellitus To determine how and when glucose, potassium and/or insulin should be given to patients with hyperglycaemia and ACS To investigate clinically acceptable targets of whole blood glucose level or plasma glucose level required to achieve normoglycemia To determine when and how often whole blood or plasma glucose level should be measured in hospital |

| CRITERIA FOR CONSIDERING STUDIES | Inclusion: Hyperglycaemia & ACS Adults (> 18 years only) No previous diagnosis of diabetes RCTs and MINAP Treatment in first 48 hours only (acute phase) Assessment of mortality and/or other primary/secondary outcome Exclusion: Other observational studies |

<p>| POPULATION | Adults with hyperglycaemia and ACS without diagnosed diabetes mellitus |
| INTERVENTION | Intensive insulin therapy/infusion |
| COMPARATORS | Standard practice/ conventional |</p>
<table>
<thead>
<tr>
<th>OUTCOMES</th>
<th>treatment</th>
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<tbody>
<tr>
<td>Treatment outcomes</td>
<td>All cause mortality</td>
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<tr>
<td></td>
<td>Cardiovascular mortality</td>
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<tr>
<td></td>
<td>Cardiovascular events associated with hyperglycaemia such as non fatal</td>
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<td></td>
<td>reinfarction, heart failure and stroke</td>
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<td></td>
<td>Measures of whole blood or plasma glucose levels</td>
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<td>Health related quality of life</td>
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<td>Adverse events associated with metabolic management of hyperglycaemia</td>
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<td>including hypoglycaemia and hypokalemia</td>
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<td>Resource use and costs such as length of stay</td>
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### REVIEW QUESTION 3

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<tr>
<td>REVIEW QUESTION 3</td>
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<tr>
<td></td>
<td>hyperglycaemia and ACS who have not previously been diagnosed?</td>
</tr>
<tr>
<td></td>
<td>The GDG reworded this question to focus on the risk factors for</td>
</tr>
<tr>
<td></td>
<td>progression to diabetes rather than the time at which patients should</td>
</tr>
<tr>
<td></td>
<td>be referred.</td>
</tr>
<tr>
<td>OBJECTIVES</td>
<td>To investigate if the presence of additional risk factors which would</td>
</tr>
<tr>
<td></td>
<td>prompt referral for investigations for diabetes</td>
</tr>
<tr>
<td>CRITERIA FOR CONSIDERING STUDIES</td>
<td>Inclusion:</td>
</tr>
<tr>
<td></td>
<td>Adults (&gt; 18 years only)</td>
</tr>
<tr>
<td></td>
<td>No previous diagnosis of diabetes</td>
</tr>
<tr>
<td></td>
<td>No restrictions on study design</td>
</tr>
<tr>
<td></td>
<td>Risk factors for diabetes (in ACS)</td>
</tr>
<tr>
<td></td>
<td>Signs and symptoms</td>
</tr>
<tr>
<td></td>
<td>Exclusion:</td>
</tr>
<tr>
<td></td>
<td>Already diagnosed with diabetes</td>
</tr>
<tr>
<td>POPULATION</td>
<td>Adults with hyperglycaemia and ACS without diagnosed diabetes mellitus</td>
</tr>
<tr>
<td>INTERVENTION</td>
<td>Intensive insulin therapy/infusion</td>
</tr>
<tr>
<td>COMPARATORS</td>
<td>Standard practice/ conventional treatment</td>
</tr>
<tr>
<td>OUTCOMES</td>
<td>Clinical signs and symptoms that lead to a referral for further</td>
</tr>
<tr>
<td></td>
<td>investigation of possible diabetes</td>
</tr>
</tbody>
</table>
Measures of whole blood or plasma glucose levels
Health related quality of life
Resource use and costs such as length of stay
Appropriate referral for subsequent investigations to confirm possible diabetes in patients without an existing diagnosis of diabetes.

### REVIEW QUESTION 4

<table>
<thead>
<tr>
<th>Details</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>REVIEW QUESTION 4</td>
<td>What information should patients with peri ACS and hyperglycaemia (who are at high risk of developing diabetes) be provided while waiting for a referral for diagnostic investigations for diabetes?</td>
</tr>
</tbody>
</table>
| OBJECTIVES | To determine what information should be provided relating to the types of diagnostic investigations for diabetes
To determine what lifestyle advice should be provided |
| CRITERIA FOR CONSIDERING STUDIES | Inclusion:
- Adults (> 18 years only)
- No previous diagnosis of diabetes
- No restrictions on study design
- Patient information/support
Exclusion:
- Already diagnosed with diabetes |
| POPULATION | Adults with hyperglycaemia and ACS without diagnosed diabetes mellitus |
| INTERVENTION | Intensive insulin therapy/infusion |
| COMPARATORS | Standard practice/ conventional treatment |
| OUTCOMES | Patient and carer information and support needs
Health related quality of life
Appropriate referral for subsequent investigations to confirm possible diabetes in patients without an existing diagnosis of diabetes. |
Flow diagram of excluded studies for hyperglycaemia review

Question 1

The flow diagram below shows an overview of the studies that were identified, included and excluded for review question 2, which focuses on the metabolic management of patients with ACS and hyperglycaemia who have diagnosed diabetes.
Excluded studies

List of excluded studies for review question 1 (diabetes)

Ref ID: 12A
EXC-NARRATIVE REVIEW

Ref ID: 13A
EXC-REVIEW WITHOUT PERI ACS AND HYPERGLYCAEMIA AND FOCUS ON TYPE 2 DIABETES

Ref ID: 15A
EXC-FOCUS ON PROGNOSTIC SIGNIFICANCE OF HYPERGLYCAEMIA ON ADMISSION

Ref ID: 18A
EXC-PROTOCOL FOR INTENSIVE INSULIN AND NOT AN RCT


Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)   Page 29 of 106
intensive insulin therapy. [Review] [28 refs]. Revista Portuguesa de Cardiologia, 28, (1) 49-61
Ref ID: 22A
EXC-NARRATIVE REVIEW

Ref ID: 26A
EXC-REVIEW

Ref ID: 30A
EXC-FOCUS ON ECG CHANGES AS AN OUTCOME

Ref ID: 35A
EXC-REVIEW

Ref ID: 49A
EXC-NARRATIVE REVIEW

Ref ID: 50A
EXC-NARRATIVE REVIEW

with angiographic and clinical outcomes among patients with ST-segment elevation myocardial infarction (from the CLARITY-TIMI-28 study). American Journal of Cardiology, 101, (3) 303-307
Ref ID: 53A

EXC-FOCUS ON USE OF CLOPIDOGREL

Ref ID: 62A

EXC-COMBINED ANALYSIS OF CREATE ECLA AND OASIS-6. CREATE ECLA PAPER HAS BEEN EXCLUDED

Ref ID: 63A

EXC-NARRATIVE REVIEW

Ref ID: 73A

EXC-REVIEW

Cheung, N.W., Wong, V.W., & McLean, M. 2006. Insulin infusion therapy for myocardial infarction. [Review] [41 refs]. Expert Opinion on Pharmacotherapy,
Ref ID: 95A

Ref ID: 100A

Ref ID: 129A

Zarich, S.W. 2005. The role of intensive glycemic control in the management of patients who have acute myocardial infarction. [Review] [65 refs]. Cardiology Clinics, 23, (2) 109-117
Ref ID: 131A


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Dandona, P., Aljada, A., & Bandyopadhyay, A. 2003. The potential therapeutic role of insulin in acute myocardial infarction in patients admitted to intensive care and in those with unspecified hyperglycemia. [Review] [60 refs]. Diabetes Care, 26, (2) 516-519

McNulty, P.H. 2002. Glucose and insulin management in the post-MI setting. [Review] [51 refs]. Current Diabetes Reports, 2, (1) 37-44


**EXC-NARRATIVE REVIEW**


**EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO BASELINE BLOOD GLUCOSE LEVELS**


**EXC-NO FOCUS ON PRIMARY OUTCOMES**


**EXC-SYSTEMATIC REVIEW ON CRITICALLY ILL PATIENTS: NOT SPECIFIC TO ACS AND HYPERGLYCAEMIA**


**EXC-REVIEW**


---

Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)
Ref ID: 297A

Ref ID: 305A

Ref ID: 306A

Ref ID: 308A

Ref ID: 314A

Ref ID: 320A
EXC-NARRATIVE REVIEW

Ref ID: 333A
EXC-NARRATIVE REVIEW

Ref ID: 335A
EXC-NO INTERVENTION OF INTENSIVE INSULIN

Ref ID: 357A
EXC-NO FOCUS ON PRIMARY OUTCOMES & COMPARING NORMOGLYCAEMIA WITH HYPERGLYCAEMIA

Ref ID: 484A
EXC-EDITORIAL

Ref ID: 518A
EXC-PROTOCOL
Ref ID: 520A
EXC-LETTER

Ref ID: 521A
EXC-LETTER

Ref ID: 522A
EXC-LETTER

Ref ID: 592A
EXC-NOT PROVIDED BY THE BRITISH LIBRARY

Ref ID: 612A
EXC-REVIEW WITH FOCUS ON STROKE

Ref ID: 614A
EXC-EDITORIAL
Narain, V.S., Puri, A., & Ahuja, A. 2006. 10 Years of clinical trials in diabetic patient with coronary artery disease. Journal of Internal Medicine of India, 9, (1) 20-26
Ref ID: 620A
EXC-NARRATIVE REVIEW

Ref ID: 632A
EXC-NARRATIVE REVIEW

Hirsch, I.B. 2006. Inpatient diabetes: Review of data from the cardiac care unit. Endocrine Practice, 12, (SUPPL. 3) 27-34
Ref ID: 635A
EXC-NARRATIVE REVIEW

Hasin, T., Eldor, R., & Hammerman, H. 2006. Intensive insulin therapy in the intensive cardiac care unit. Acute Cardiac Care, 8, (4) 181-185
Ref ID: 637A
EXC-NARRATIVE REVIEW

Ref ID: 654A
EXC-REVIEW

Ref ID: 656A
EXC-COMMENTARY


Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011) Page 38 of 106
randomized controlled trials. Journal of Parenteral and Enteral Nutrition, 30, (2) 164-172
Ref ID: 665A
EXC-REVIEW

Furnary, A.P. & Braithwaite, S.S. 2006. Effects of Outcome on In-Hospital Transition from Intravenous Insulin Infusion to Subcutaneous Therapy. American Journal of Cardiology, 98, (4) 557-564
Ref ID: 671A
EXC-NARRATIVE REVIEW

Ref ID: 673A
EXC-REVIEW

Ref ID: 696A
EXC-FOCUS ON ASSOCIATION BETWEEN HIGH DOSE INSULIN INFUSION AND REFRACTORY HYPERGLYCAEMIA

Ref ID: 697A
EXC-REVIEW

Ref ID: 724A

Holt, R.I.G. 2005. DIGAMI-2 - The optimal management of hyperglycaemia remains controversial. Diabetes, Obesity and Metabolism, 7, (1) 110-116
Ref ID: 754A

Ref ID: 778A

Ref ID: 782A

Ref ID: 852A

Ref ID: 927A
Ref ID: 958A
EXC-PROTOCOL

Ref ID: 983A
EXC-NON-ENGLISH

Ref ID: 1
EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 81
EXC-NOT AN RCT

Ref ID: 135
EXC-NO FOCUS ON PRIMARY OUTCOMES AND NO RECORD OF BLOOD GLUCOSE STATES


EXC-NOT PERI ACS AND HYPERGLYCAEMIA


EXC-NO FOCUS ON PRIMARY OUTCOMES AND CONTROL GROUP ALSO RECEIVED INSULIN IF BLOOD GLUCOSE ABOVE SPECIFIC THRESHOLD


EXC-NOT PROVIDED BY THE BRITISH LIBRARY


EXC-FIBRINOLYTIC FUNCTION IS NOT A PRIMARY OUTCOME
Ref ID: 349
EXC-NO DEFINITION OF HYPERGLYCAEMIA

Yang, Z.H., Yang, K.H., Ma, B., & Yin, S.F. 2008. Effect of glucose-insulin-potassium on heart function of patients with acute myocardial infarction: a systematic review. Chinese Journal of Evidence-Based Medicine, 8, (2) 97-101
Ref ID: 556
EXC-NON-ENGLISH

Ref ID: 574
EXC-REVIEW WITH NO FOCUS ON HYPERGLYCAEMIA

Ref ID: 734
EXC-LETTER

Ref ID: 735
EXC-LETTER
Ref ID: 736
EXC-LETTER

Ref ID: 778
EXC-NOT AN RCT

Ref ID: 825
EXC-CONFERENCE POSTER

Ref ID: 878
EXC-LETTER TO EDITOR

Yusuf, S. 2005. Intensive insulin-glucose infusion regimens with long-term or standard glucose control did not differ for reducing mortality in type 2 diabetes mellitus and MI. ACP Journal Club, 143, (2) 43-44
Ref ID: 919
EXC-SUMMARY OF DIGAMI 2

Berger, P.B. 2005. A glucose-insulin-potassium infusion did not reduce, mortality, cardiac arrest, or cardiogenic shock after acute MI. ACP Journal Club, 143, (1) 4-6


Ref ID: 1082
EXC-FOCUS ON FIBRINOLYSIS

1999. AMI treatment rejected in ’60s draws new attention: GIK cuts death rate in half. Cost Management in Cardiac Care, 4, (2) 21-23
Ref ID: 1104
EXC-COMMENT

Ref ID: 1189
EXC-REVIEW

Ref ID: 1223
EXC-BRITISH LIBRARY NOT ABLE TO SUPPLY

Ref ID: 1262
EXC-REVIEW-NO FOCUS ON THE ACUTE PHASE OF ACS


Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)
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Ref ID: 1464
EXC-NARRATIVE REVIEW

Ref ID: 1531
EXC-REVIEW OF CARDIAC SURGERY

Ref ID: 1642
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO BASELINE RECORD OF BLOOD GLUCOSE

Ref ID: 1682
EXC-REVIEW

Ref ID: 1796
EXC-EDITORIAL COMMENT


Apstein, C.S. & Opie, L.H. 1999. Glucose-insulin-potassium (GIK) for acute myocardial infarction: a negative study with a positive value. [Review] [38 refs]. Cardiovascular Drugs & Therapy, 13, (3) 185-189


Fisher, M. 1999. Diabetes and myocardial infarction. [Review] [56 refs]. Best Practice & Research Clinical Endocrinology & Metabolism, 13, (2) 331-343


diabetes in Japan. BMJ, 315, (7107) 544
Ref ID: 2168
EXC-EDITORIAL

Surawicz, B. 1968. Evaluation of treatment of acute myocardial infarction with potassium, glucose and insulin. [Review] [110 refs]. Progress in Cardiovascular Diseases, 10, (6) 545-560
Ref ID: 2692
EXC-NARRATIVE REVIEW

Ref ID: 2877
EXC-ABSTRACT ONLY

Ref ID: 2921
EXC-ABSTRACT ONLY

Ref ID: 3462
EXC-BRITISH LIBRARY CANNOT PROVIDE A COPY

Ref ID: 3525
EXC-EDITORIAL

Ref ID: 3585
EXC-REVIEW

Ref ID: 3696
EXC-LETTER

Ref ID: 3697
EXC-LETTER

Ref ID: 4253
EXC-PARTICIPANTS UNDERGOING CABG

Ref ID: 4456
EXC-NO FOCUS ON PRIMARY OUTCOMES
Ref ID: 4535
EXC-COMMENT

Ref ID: 4555
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO EVALUATION OF BASELINE BLOOD GLUCOSE

Ref ID: 4601
EXC-NOT MENTION OF BASELINE BLOOD GLUCOSE

Ref ID: 4630
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO EVALUATION OF BASELINE BLOOD GLUCOSE

potassium) and low-molecular-weight heparin in acute myocardial infarction. American heart journal, 148, (6) 1068-1078
Ref ID: 4705

EXC-RELATES TO STUDY DESIGN

Kastrati, A. & Bellandi, F. 2004. Trial finds routine intravenous glucose-insulin-potassium does not improve myocardial salvage in people with acute myocardial infarction. Evidence-based Cardiovascular Medicine, 8, (4) 339-342
Ref ID: 4707

EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 4850

EXC-PARTICIPANTS UNDERGOING CABG

Ref ID: 5004

EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 5150

EXC-HYPERGLYCAEMIC POPULATION NOT WELL DEFINED AND DOES NOT DEFINE BLOOD GLUCOSE ON RECRUITMENT
Ref ID: 5220
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND OXIDATIVE STRESS NOT A PRIMARY OUTCOME

Ref ID: 5511
EXC-REVIEW ARTICLE NOT FOCUSING ON PERI ACS AND HYPERGLYCAEMIA

Ref ID: 5571
EXC-REVIEW

Ref ID: 5618
EXC-FOCUS ON TREATMENT FOLLOWING DISCHARGE (NOT ACUTE PHASE)

EXC-NO CUT OFF POINT FOR HYPERGLYCAEMIA OR BLOOD GLUCOSE


EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO EVALUATION OF BASELINE BLOOD GLUCOSE


EXC-PATIENTS UNDERGOING CABG


EXC-NO PERI ACS AND HYPERGLYCAEMIA

EXC-RESULTS FOR GIK INFUSION NOT REPORTED HERE. NOT PERI ACS AND HYPERGLYCAEMIA

Ref Type: Generic
Ref ID: 6050

EXC-NOT SPECIFIC TO ACS

Ref Type: Generic
Ref ID: 6051

EXC-NOT SPECIFIC TO ACS

Ref Type: Generic
Ref ID: 6052

EXC-NOT SPECIFIC TO ACS

Ref ID: 6013

EXC-NO DEFINITION OF HYPERGLYCAEMIA
Flow diagram of excluded studies for hyperglycaemia review

Question 2

The flow diagram below shows an overview of the studies that were identified, included and excluded for review question 2 which focuses on the metabolic management of patients with ACS and hyperglycaemia without diagnosed diabetes.

Records identified through database searching (initial & preferred search) (n = 7035)

Additional records identified through other sources (systematic review references) (n = 5)

Records after duplicates removed (n = 5554)

Records excluded based on abstract (n = 5407)

Records screened (n = 5554)

Full-text articles assessed for eligibility (n = 147)

Full-text articles excluded, with reasons (n = 144)

88 = abstract/protocol/review/editorial/study design/commentary/poster/letter/summary
13 = not ACS and hyperglycaemia or no baseline blood glucose
5 = alternative focus
7 = no focus on primary outcomes
5 = unable to access
5 = not intensive insulin intervention or not RCT
4 = no/ inadequate definition of hyperglycaemia
6 = participants undergoing CABG or not acute phase of ACS
11 = other

Studies included in quantitative summary (n = 3)
Excluded studies

List of excluded studies for review question 2 (non-diabetes)

Ref ID: 12A
EXC-NARRATIVE REVIEW

Ref ID: 13A
EXC-REVIEW WITHOUT PERI ACS AND HYPERGLYCAEMIA AND FOCUS ON TYPE 2 DIABETES

Ref ID: 15A
EXC-FOCUS ON PROGNOSTIC SIGNIFICANCE OF HYPERGLYCAEMIA ON ADMISSION

Ref ID: 18A
EXC-PROTOCOL FOR INTENSIVE INSULIN AND NOT AN RCT

intensive insulin therapy. [Review] [28 refs]. Revista Portuguesa de Cardiologia, 28, (1) 49-61
Ref ID: 22A

EXC-NARRATIVE REVIEW

Ref ID: 26A

EXC-REVIEW

Ref ID: 30A

EXC-FOCUS ON ECG CHANGES AS AN OUTCOME

Ref ID: 35A

EXC-REVIEW

Ref ID: 49A

EXC-NARRATIVE REVIEW

Ref ID: 50A

EXC-NARRATIVE REVIEW

with angiographic and clinical outcomes among patients with ST-segment elevation myocardial infarction (from the CLARITY-TIMI-28 study). American Journal of Cardiology, 101, (3) 303-307

Ref ID: 53A

EXC-FOCUS ON USE OF CLOPIDOGREL


Ref ID: 62A

EXC-COMBINED ANALYSIS OF CREATE ECLA AND OASIS-6. CREATE ECLA PAPER HAS BEEN EXCLUDED


Ref ID: 63A

EXC-NOT PERI ACS AND HYPERGLYCAEMIA


Ref ID: 70A

EXC-NARRATIVE REVIEW


Ref ID: 73A

EXC-REVIEW

Cheung, N.W., Wong, V.W., & McLean, M. 2006. Insulin infusion therapy for myocardial infarction. [Review] [41 refs]. Expert Opinion on Pharmacotherapy,
Ref ID: 95A

Ref ID: 100A

Ref ID: 129A

Zarich, S.W. 2005. The role of intensive glycemic control in the management of patients who have acute myocardial infarction. [Review] [65 refs]. Cardiology Clinics, 23, (2) 109-117
Ref ID: 131A


Dandona, P., Aljada, A., & Bandyopadhyay, A. 2003. The potential therapeutic role of insulin in acute myocardial infarction in patients admitted to intensive care and in those with unspecified hyperglycemia. [Review] [60 refs]. Diabetes Care, 26, (2) 516-519

McNulty, P.H. 2002. Glucose and insulin management in the post-MI setting. [Review] [51 refs]. Current Diabetes Reports, 2, (1) 37-44


Ref ID: 209A
EXC-NARRATIVE REVIEW

Ref ID: 250A
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO BASELINE BLOOD GLUCOSE LEVELS

Ref ID: 253A
EXC-NO FOCUS ON PRIMARY OUTCOMES

Ref ID: 275A
EXC-SYSTEMATIC REVIEW ON CRITICALLY ILL PATIENTS- NOT SPECIFIC TO ACS AND HYPERGLYCAEMIA

Ref ID: 287A
EXC-REVIEW


Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)


Ref ID: 520A
EXC-LETTER

Ref ID: 521A
EXC-LETTER

Ref ID: 522A
EXC-LETTER

Ref ID: 592A
EXC-NOT PROVIDED BY THE BRITISH LIBRARY

Ref ID: 612A
EXC-REVIEWS WITH FOCUS ON STROKE

Ref ID: 614A
EXC-EDITORIAL

Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)
Narain, V.S., Puri, A., & Ahuja, A. 2006. 10 Years of clinical trials in diabetic patient with coronary artery disease. Journal of Internal Medicine of India, 9, (1) 20-26
Ref ID: 620A
EXC-NARRATIVE REVIEW

Ref ID: 632A
EXC-NARRATIVE REVIEW

Hirsch, I.B. 2006. Inpatient diabetes: Review of data from the cardiac care unit. Endocrine Practice, 12, (SUPPL. 3) 27-34
Ref ID: 635A
EXC-NARRATIVE REVIEW

Hasin, T., Eldor, R., & Hammerman, H. 2006. Intensive insulin therapy in the intensive cardiac care unit. Acute Cardiac Care, 8, (4) 181-185
Ref ID: 637A
EXC-NARRATIVE REVIEW

Ref ID: 654A
EXC-REVIEWS

Ref ID: 656A
EXC-COMMENTARY

randomized controlled trials. Journal of Parenteral and Enteral Nutrition, 30, (2) 164-172
Ref ID: 665A
EXC-REVIEW

Furnary, A.P. & Braithwaite, S.S. 2006. Effects of Outcome on In-Hospital Transition from Intravenous Insulin Infusion to Subcutaneous Therapy. American Journal of Cardiology, 98, (4) 557-564
Ref ID: 671A
EXC-NARRATIVE REVIEW

Ref ID: 673A
EXC-REVIEW

Ref ID: 696A
EXC-FOCUS ON ASSOCIATION BETWEEN HIGH DOSE INSULIN INFUSION AND REFRACTORY HYPERGLYCAEMIA

Ref ID: 697A
EXC-REVIEW

Ref ID: 724A

Holt, R.I.G. 2005. DIGAMI-2 - The optimal management of hyperglycaemia remains controversial. Diabetes, Obesity and Metabolism, 7, (1) 110-116
Ref ID: 754A

Ref ID: 778A

Ref ID: 782A

Ref ID: 852A

Ref ID: 927A
Ref ID: 958A
EXC-PROTOCOL

Ref ID: 983A
EXC-NON-ENGLISH

Ref ID: 1
EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 81
EXC-NOT AN RCT

Ref ID: 135
EXC-NO FOCUS ON PRIMARY OUTCOMES AND NO RECORD OF BLOOD GLUCOSE STATES

Ref ID: 174

EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 238

EXC-NO FOCUS ON PRIMARY OUTCOMES AND CONTROL GROUP ALSO RECEIVED INSULIN IF BLOOD GLUCOSE ABOVE SPECIFIC THRESHOLD

Ref ID: 253

EXC-NOT PROVIDED BY THE BRITISH LIBRARY

Ref ID: 320

EXC-FIBRINOLYTIC FUNCTION IS NOT A PRIMARY OUTCOME
Ref ID: 349
EXC-NO DEFINITION OF HYPERGLYCAEMIA

Yang, Z.H., Yang, K.H., Ma, B., & Yin, S.F. 2008. Effect of glucose-insulin-potassium on heart function of patients with acute myocardial infarction: a systematic review. Chinese Journal of Evidence-Based Medicine, 8, (2) 97-101
Ref ID: 556
EXC-NON-ENGLISH

Ref ID: 574
EXC-REVIEW WITH NO FOCUS ON HYPERGLYCAEMIA

Ref ID: 734
EXC-LETTER

Ref ID: 735
EXC-LETTER


Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)
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Yusuf, S. 2005. Intensive insulin-glucose infusion regimens with long-term or standard glucose control did not differ for reducing mortality in type 2 diabetes mellitus and MI. ACP Journal Club, 143, (2) 43-44

Berger, P.B. 2005. A glucose-insulin-potassium infusion did not reduce, mortality, cardiac arrest, or cardiogenic shock after acute MI. ACP Journal Club, 143, (1) 4-6
Ref ID: 929
EXC-COMMENTARY AND NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 937
EXC-LETTER

Ref ID: 941
EXC-COMMENTARY

Ref ID: 951
EXC-NO PRECISE DEFINITION OF HYPERGLYCAEMIA AND BLOOD GLUCOSE LEVELS

Ref ID: 1082
EXC-FOCUS ON FIBRINOLYSIS

1999. AMI treatment rejected in ’60s draws new attention: GIK cuts death rate in half. Cost Management in Cardiac Care, 4, (2) 21-23
Ref ID: 1104
EXC-COMMENT

Ref ID: 1189
EXC-REVIEW

Ref ID: 1223
EXC-BRITISH LIBRARY NOT ABLE TO SUPPLY

Ref ID: 1262
EXC-REVIEW-NO FOCUS ON THE ACUTE PHASE OF ACS

Ref ID: 1464
EXC-NARRATIVE REVIEW
Ref ID: 1531
EXC-REVIEW OF CARDIAC SURGERY

Ref ID: 1642
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO BASELINE RECORD OF BLOOD GLUCOSE

Ref ID: 1682
EXC-REVIEW

Ref ID: 1796
EXC-EDITORIAL COMMENT

Ref ID: 1887
EXC-NARRATIVE REVIEW
Ref ID: 2044

EXC-NO PERI ACS AND HYPERGLYCAEMIA

Apstein, C.S. & Opie, L.H. 1999. Glucose-insulin-potassium (GIK) for acute myocardial infarction: a negative study with a positive value. [Review] [38 refs]. Cardiovascular Drugs & Therapy, 13, (3) 185-189
Ref ID: 2045
EXC-EDITORIAL

Ref ID: 2050
EXC-CORRESPONDENCE

Fisher, M. 1999. Diabetes and myocardial infarction. [Review] [56 refs]. Best Practice & Research Clinical Endocrinology & Metabolism, 13, (2) 331-343
Ref ID: 2078
EXC-NARRATIVE REVIEW

Ref ID: 2102
EXC-EDITORIAL

Ref ID: 2168
EXC-EDITORIAL

Hyperglycaemia in acute coronary syndromes: DRAFT appendix D (August 2011)
Surawicz, B. 1968. Evaluation of treatment of acute myocardial infarction with potassium, glucose and insulin. [Review] [110 refs]. Progress in Cardiovascular Diseases, 10, (6) 545-560
Ref ID: 2692
EXC-NARRATIVE REVIEW

Ref ID: 2877
EXC-ABSTRACT ONLY

Ref ID: 2921
EXC-ABSTRACT ONLY

Ref ID: 3462
EXC-BRITISH LIBRARY CANNOT PROVIDE A COPY

Ref ID: 3525
EXC-EDITORIAL

and ongoing randomised trials with important clinical end points. Diabetes and Vascular Disease Research, 5, (4) 276-284
Ref ID: 3585
EXC-REVIEW

Ref ID: 3696
EXC-LETTER

Ref ID: 3697
EXC-LETTER

Ref ID: 4253
EXC-PARTCIPANTS UNDERGOING CABG

Ref ID: 4456
EXC-NO FOCUS ON PRIMARY OUTCOMES


Ref ID: 4705
EXC-RELATES TO STUDY DESIGN

Kastrati, A. & Bellandi, F. 2004. Trial finds routine intravenous glucose-insulin-potassium does not improve myocardial salvage in people with acute myocardial infarction. Evidence-based Cardiovascular Medicine, 8, (4) 339-342
Ref ID: 4707
EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 4850
EXC-PARTICIPANTS UNDERGOING CABG

Ref ID: 5004
EXC-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 5150
EXC-HYPERGLYCAEMIC POPULATION NOT WELL DEFINED AND DOES NOT DEFINE BLOOD GLUCOSE ON RECRUITMENT

insulin-potassium infusion. Critical care medicine, 30, (2) 417-421
Ref ID: 5220
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND OXIDATIVE STRESS
NOT A PRIMARY OUTCOME

Fath-Ordoubadi, F., Markides, V., & Beatt, K.J. 1998. Meta-analysis of
glucose-insulin-potassium therapy for myocardial infarction. Cardiology
Review, 15, (4) 41-44
Ref ID: 5511
EXC-REVIEW ARTICLE NOT FOCUSING ON PERI ACS AND
HYPERGLYCAEMIA

treatment of acute myocardial infarction: An overview of randomized placebo-
controlled trials. Circulation, 96, (4) 1152-1156
Ref ID: 5571
EXC-REVIEW

The impact of glucose lowering treatment on long-term prognosis in patients
with type 2 diabetes and myocardial infarction: A report from the DIGAMI 2
trial. European heart journal, 29, (2) 166-176
Ref ID: 5618
EXC-FOCUS ON TREATMENT FOLLOWING DISCHARGE (NOT ACUTE
PHASE)

Rasoul, S., Ottervanger, J.P., Timmer, J.R., Svilaas, T., Henrigues, J.P.S.,
after glucose-insulin-potassium in ST elevation myocardial infarction. The
Glucose-insulin-potassium study II. International journal of cardiology, 122, (1)
52-55
Ref ID: 5703
EXC-NO CUT OFF POINT FOR HYPERGLYCAEMIA OR BLOOD GLUCOSE

Marano, L., Bestetti, A., Lomuscio, A., Tagliabue, L., Castini, D., Tarricone, D.,
Dario, P., Tarolo, G.L., & Fiorentini, C. 2000. Effects of infusion of glucose-

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insulin-potassium on myocardial function after a recent myocardial infarction.
Acta Cardiologica, 55, (1) 9-15
Ref ID: 5804
EXC-NOT PERI ACS AND HYPERGLYCAEMIA AND NO EVALUATION OF BASELINE BLOOD GLUCOSE

Ref ID: 5996
EXC-PATIENTS UNDERGOING CABG

Ref Type: Generic
Ref ID: 6048
EXC-NO PERI ACS AND HYPERGLYCAEMIA

Ref Type: Generic
Ref ID: 6049
EXC-RESULTS FOR GIK INFUSION NOT REPORTED HERE. NOT PERI ACS AND HYPERGLYCAEMIA

Ref Type: Generic
Ref ID: 6050
EXC-NOT SPECIFIC TO ACS

Ref Type: Generic
Ref ID: 6051
EXC-NOT SPECIFIC TO ACS

Ref Type: Generic
Ref ID: 6052
EXC-NOT SPECIFIC TO ACS

Ref ID: 6013
EXC-NO DEFINITION OF HYPERGLYCAEMIA

Ref ID: 396
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)
Ref ID: 378
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)

Ref ID: 2181
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)

Ref ID: 367
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)

Ref ID: 3363
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)

Ref ID: 144
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)
Ref ID: 207
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)

Ref ID: 6053
EXC-ASSESSED FOR RQ1 (PATIENTS WITH DIABETES)
Flow diagram of excluded studies for hyperglycaemia review question 3

The flow diagram below shows an overview of the studies that were identified, included and excluded for review question 3, which focuses on risk factors for diabetes in patients with ACS and hyperglycaemia.

Records identified through database searching (n = 2036)  
Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 1462)

Records screened (n = 1462)  
Records excluded (n = 1398)

Full-text articles assessed for eligibility (n = 64)  
Full-text articles excluded, with reasons (n = 59)  
news article/editorial/review/comment = 22  
already diagnosed with diabetes = 2  
Not focused on risk factors for diabetes = 17  
not peri ACS and hyperglycaemia = 8  
not accessible = 5  
other = 5

Studies included in evidence synthesis (n = 4)
Excluded studies

Full list of excluded studies for RQ3-Risk factors for diabetes

Ref ID: 1964
EXCLUDE-NEWS ARTICLE

Ref ID: 1100
EXCLUDE-PARTICIPANTS ALREADY DIAGNOSED WITH DIABETES

Ref ID: 905
EXCLUDE-FOCUS ON PREVALANCE OF DIABETES NOT RISK FACTORS FOR ITS DEVELOPMENT

Aquilante, C.L. & Griend, J.R.V. 2008. Understanding metabolic syndrome: Knowing the risks. Pharmacy Times, 74, (7) 61-68
Ref ID: 386
EXCLUDE-REVIEW

Ref ID: 1902
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA
Barry, H. 2002. How often does diabetes occur within 3 months of an acute myocardial infarction? Evidence-Based Practice, 5, (10) -NaN
Ref ID: 2023
EXCLUDE-NOT ACCESSIBLE

Ref ID: 211
EXCLUDE-REVIEW ARTICLE

Belknap, S. 2008. Review: beta-blockers for hypertension increase risk of new onset diabetes: Commentary. Evidence-Based Medicine, 13, (2) 50
Ref ID: 418
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 769
EXCLUDE-REVIEW FOCUSING ON CARDIOVASCULAR RISK

Ref ID: 828
EXCLUDE-REVIEW FOCUSING ON RISK OF CARDIOVASCULAR DISEASE

Ref ID: 415
EXCLUDE-REVIEW FOCUSING ON EFFECT ON MORTALITY

Brancati, F. 2000. Resolving the glucose response curve: The underestimated importance of postprandial glucose. American Journal of Managed Care, 6, (21 SUPPL.) S1082-S1088
Ref ID: 1071
EXCLUDE-FOCUS ON RISK OF MORTALITY

Ref ID: 369
EXCLUDE-DETAILS OF TRIAL DESIGN

Ref ID: 1093
EXCLUDE-FOCUS ON RISK OF MORTALITY NOT PROGRESSION TO DIABETES

Ref ID: 51
EXCLUDE-NO FOCUS ON DEVELOPMENT OF DIABETES

Ref ID: 647
EXCLUDE-NARRATIVE REVIEW

Ref ID: 895
EXCLUDE-EDITORIAL WITH NO FOCUS ON SUBSEQUENT DEVELOPMENT OF DIABETES

Ref ID: 501
EXCLUDE-REVIEW NOT FOCUSING ON PERI ACS AND HYPERGLYCAEMIA

Ref ID: 66
EXCLUDE-COMMENT

Ref ID: 1295
EXCLUDE-NOT FOCUSED ON RISK FACTORS FOR DIABETES

Engberg, S., Vlmetis, D., Lau, C., Glumer, C., Joergensen, T., Pedersen, O., & Borch-Johnsen, K. 2009. Progression to impaired glucose regulation and
diabetes in the population-based inter99 study. Diabetes Care, 32, (4) 606-611
Ref ID: 167
EXCLUDE-PATIENTS FROM GENERAL POPULATION WITH HYPERGLYCAEMIA WITHOUT ACS. HIGH RISK GROUP HAVE ABSOLUTE RISK OF ISCHEMIC HEART DISEASE

Ref ID: 1664
EXCLUDE-FOCUS ON PREDICTORS OF MORTALITY

Ref ID: 599
ASSESS FOR RQ4 (PATIENT INFO)

Ref ID: 667
EXCLUDE-FOCUS ON RISK OF MORTALITY NOT PROGRESSION TO DIABETES

Ref ID: 871
EXCLUDE-LETTER

Cardiovascular Medicine, 10, (4) 202-208
Ref ID: 12
EXCLUDE-REVIEW FOCUSING ON RISK FACTORS FOR CARDIOVASCULAR DISEASE NOT PROGRESSION TO DIABETES

Ref ID: 587
EXCLUDE-LETTER

Ref ID: 276
EXCLUDE-CONFERENCE PAPER

Ref ID: 1231
EXCLUDE-NOT FOCUSED ON RISK FACTORS FOR DEVELOPMENT OF DIABETES

Ref ID: 358
EXCLUDE-EDITORIAL

Ref ID: 990
EXCLUDE-DATA FOR PROGRESSION TO DIABETES IN PATIENTS WITH ELEVATED GLYCAEMIA BUT NO ACS

Ref ID: 1108
EXCLUDE-LETTER

Ref ID: 374
EXCLUDE-NOT ACCESSIBLE

Ref ID: 1214
EXCLUDE-FOCUS ON PREVALANCE OF DIABETES NOT RISK FACTORS FOR PROGRESSION TO DIABETES

Ref ID: 8
EXCLUDE-FOCUS ON RISK OF MORTALITY NOT PROGRESSION TO DIABETES

Ref ID: 1388
EXCLUDE-FOCUSED ON RISK FACTORS FOR PROGRESSION TO DIABETES IN PATIENTS WITH ACS (NO SPECIFIC REFERENCE TO BASELINE BLOOD GLUCOSE)

Ref ID: 582
EXCLUDE-REVIEW FOCUSING ON PREVALENCE OF DIABETES NOT RISK FACTORS FOR DEVELOPMENT OF DIABETES

Ref ID: 486
EXCLUDE-REVIEW FOCUSING ON RISK OF CHRONIC HEART DISEASE
Ref ID: 657
EXCLUDE-PATIENTS WITH HYPERGLYCAEMIA NOT INCLUDED

Ref ID: 11
EXCLUDE-EDITORIAL AND PATIENTS ALREADY DIAGNOSED WITH DIABETES

Ref ID: 1223
EXCLUDE-NOT FOCUSED ON RISK FACTORS FOR PROGRESSION TO DIABETES

Ref ID: 1200
EXCLUDE-TEMPORARILY UNAVAILABLE

Ref ID: 644
EXCLUDE-NOT SPECIFIC TO PROGRESSION TO DIABETES. FOCUSES ON GLYCOMETABOLIC DISTURBANCE IN GENERAL WHICH INCLUDES BOTH IFG OR DIABETES

Ref ID: 1239
EXCLUDE-FOCUSED ON PREVALANCE OF DIABETES NOT RISK FACTORS FOR PROGRESSION TO DIABETES

Ref ID: 455
EXCLUDE-GUIDELINE

Ref ID: 755
EXCLUDE-UNCLEAR IF PARTICIPANTS WERE HYPERGLYCAEMIC ON ADMISSION
Ref ID: 1914
EXCLUDE-NOT SPECIFIC TO ACS

Ref ID: 850
EXCLUDE-CASE STUDY/EDITORIAL

Ref ID: 323
EXCLUDE-NOT ACCESSIBLE

Ref ID: 251
EXCLUDE-NOT ACCESSIBLE

Ref ID: 876
EXCLUDE-FOCUS ON RISK OF MORTALITY


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EXCLUDE-FOCUS ON PREVALANCE OF DIABETES NOT RISK FACTORS FOR PROGRESSION TO DIABETES

Ref ID: 1050
EXCLUDE-CONFERENCE PAPER

Ref ID: 1368
EXCLUDE-FOCUS ON RELIABILITY OF OGTT

Ref ID: 403
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA. FOCUS ON RISK OF CHRONIC HEART DISEASE AND DIABETES IN PARTICIPANTS WITHOUT HISTORY OF THESE CONDITIONS

Ref ID: 365
EXCLUDE-NARRATIVE REVIEW
Flow diagram of excluded studies for hyperglycaemia review question 4

The flow diagram below shows an overview of the studies that were identified, included and excluded for review question 4, which focuses on the information or support that should be provided for patients with ACS and hyperglycaemia (who are at high risk for developing diabetes) while they are waiting for a referral for diabetic investigations.

<table>
<thead>
<tr>
<th>Records identified through database searching (n = 762)</th>
<th>Additional records identified through other sources (n = 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Records after duplicates removed (n = 668)</td>
<td></td>
</tr>
<tr>
<td>Records screened (n = 668)</td>
<td>Records excluded (n = 637)</td>
</tr>
<tr>
<td>Full-text articles assessed for eligibility (n = 31)</td>
<td></td>
</tr>
<tr>
<td>Studies included in qualitative synthesis (n = 0)</td>
<td></td>
</tr>
<tr>
<td>Studies included in quantitative synthesis (meta-analysis) (n = 0)</td>
<td>Full-text articles excluded, with reasons (n = 31)</td>
</tr>
<tr>
<td></td>
<td>8=conference abstract/news article/editorial</td>
</tr>
<tr>
<td></td>
<td>11=not peri ACS and hyperglycaemia</td>
</tr>
<tr>
<td></td>
<td>6=not focused on patient information</td>
</tr>
<tr>
<td></td>
<td>2=protocol/overview of intervention</td>
</tr>
<tr>
<td></td>
<td>3=patients already diagnosed with diabetes</td>
</tr>
<tr>
<td></td>
<td>1=other</td>
</tr>
</tbody>
</table>
**Excluded studies**

**List of excluded studies for review question 4 (patient information)**

Ref ID: 64
EXCLUDE-FOCUS ON RISK FACTORS FOR CHRONIC HEART DISEASE
NOT PATIENT INFORMATION

Ref ID: 546
EXCLUDE-NEWS ARTICLE

Ref ID: 445
EXCLUDE-NOT FOCUSED ON PATIENT INFORMATION FOR HYPERGLYCAEMIA

Ref ID: 492
EXCLUDE-FOCUS ON MANAGEMENT OF DIAGNOSED DIABETES

Ref ID: 508
EXCLUDED-OVERVIEW OF DIABETES EDUCATION PROGRAM
Ref ID: 266
EXCLUDE-CONFERENCE ABSTRACT

Ref ID: 328
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Engberg, S., Vistisen, D., Lau, C., Glumer, C., Jorgensen, T., Pedersen, O., & Borch-Johnsen, K. 2009. Progression to impaired glucose regulation and diabetes in the population-based Inter99 study.[Erratum appears in Diabetes Care. 2009 Sep;32(9):1751]. Diabetes Care, 32, (4) 606-611
Ref ID: 10
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 656
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 470
EXCLUDE-NOT FOCUSED ON PATIENT INFO FOR POTENTIAL DIABETES

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Ref ID: 12
EXCLUDE-NOR FOCUSED ON PATIENT INFORMATION/ADVICE

Ref ID: 371
EXCLUDE-FOCUS ON PATIENTS ALREADY DIAGNOSED WITH DIABETES

Ref ID: 244
EXCLUDE-CONFERENCE ABSTRACT

Ref ID: 654
EXCLUDE-NOT FOCUSED ON PATIENT INFORMATION

Ref ID: 164
EXCLUDE-CONFERENCE ABSTRACT


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Ref ID: 322
EXCLUDE-FOCUS ON LINK BETWEEN SMOKING AND DIABETES NOT PATIENT INFORMATION

Ref ID: 28
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Ref ID: 623
EXCLUDE-NOT SPECIFIC TO PATIENTS WITH ACS AND HYPERGLYCAEMIA

Ref ID: 613
EXCLUDE-PROTOCOL
Ref ID: 617
EXCLUDE-PAPERS DONT INCLUDE PATIENTS WITH ACS (HYPERGLYCAEMIA ONLY)

Ref ID: 180
EXCLUDE-CONFERENCE ABSTRACT

Ref ID: 63
EXCLUDE-NOT SPECIFIC TO PATIENTS WITH ACS AND HYPERGLYCAEMIA

Rosenstock, J. 2007. Reflecting on type 2 diabetes prevention: More questions than answers! Diabetes, Obesity and Metabolism, 9, (SUPPL.1) 3-11
Ref ID: 502
EXCLUDE-NOT PERI ACS AND HYPERGLYCAEMIA

Ref Type: Generic
Ref ID: 655

Ref ID: 362

Ref ID: 653

Ref ID: 637

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