Guideline Summary NGC-10568

Guideline Title
Acute heart failure: diagnosing and managing acute heart failure in adults.

Bibliographic Source(s)

Guideline Status
This is the current release of the guideline.
This guideline meets NGC's 2013 (revised) inclusion criteria.

Scope

Disease/Condition(s)
Acute heart failure

Note: The guideline does not cover long-term management of underlying diseases (such as congenital heart disease) and comorbidities of acute heart failure, management of perioperative acute heart failure, and long-term management of acute heart failure in pregnant women.

Guideline Category
Diagnosis
Evaluation
Management
Treatment

Clinical Specialty
Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Pulmonary Medicine
Radiology
Thoracic Surgery

Intended Users
Advanced Practice Nurses
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians

Guideline Objective(s)
- To offer best practice advice on the care of adults (aged 18 years and over) with acute heart failure or possible...
Acute heart failure is a clinical crisis (age > 18 years) characterized by severe volume overload in patients with chronic heart failure.

To consider the following key clinical issues:
- The role of early natriuretic peptide testing and echocardiography
- The role of specialist management units
- The use of ventilatory support, pharmacological therapy and ultra-filtration
- Treatment after stabilisation, including selected surgical interventions and initiation of the pharmacological therapies that are used in the management of chronic heart failure

**Target Population**

Adults (aged 18 years or older) who have a diagnosis of acute heart failure, or have possible acute heart failure, or are being investigated for acute heart failure.

**Note:** Specific consideration is given to subgroups with pulmonary oedema, cardiogenic shock, acute right-sided heart failure or acute decompensated heart failure.

**Interventions and Practices Considered**

**Diagnosis/Evaluation**
1. Clinical examination
2. Electrocardiography
3. Chest X-ray
4. Blood test
5. Serum natriuretic peptide (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NT proBNP])
6. Transthoracic Doppler two-dimensional (2D) echocardiography
7. Pulmonary artery catheterisation (not recommended routinely)

**Management/Treatment**
1. Use of a specialist heart failure team on hospital admission and follow-up
2. Initial pharmacological treatment
   - Opiates (not recommended routinely)
   - Intravenous diuretic therapy, with monitoring of renal function, weight, and urine output
   - Nitrates (not recommended routinely)
   - Sodium nitroprusside (not recommended)
   - Inotropes and vasopressors (not recommended routinely)
3. Initial non-pharmacological treatment
   - Non-invasive ventilation (continuous positive airways pressure [CPAP] or non-invasive positive pressure ventilation [NIPPV])
   - Invasive ventilation
   - Ultrafiltration for confirmed diuretic resistance
4. Treatment after stabilisation
   - Beta-blocker
   - Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker
   - Aldosterone antagonist
   - Close monitoring of renal function, electrolytes, heart rate, blood pressure and overall clinical status during treatment
5. Valvular surgery and percutaneous intervention
   - Surgical aortic valve replacement
   - Transcatheter aortic valve implantation (TAVI) in selected people
   - Surgical mitral valve repair or replacement
6. Mechanical assist devices

**Major Outcomes Considered**
- Length of hospitalization and readmission rates
- Major cardiovascular events
- Mortality
- Need for invasive ventilation
- Quality of life
- Readmission and complications related to heart failure
Sensitivity and specificity of diagnostic tests
- Serious adverse events
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NGCC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews; in a framework of population, index tests, reference standard and target condition for reviews of diagnostic test accuracy; and using population, presence or absence of factors under investigation (for example prognostic factors) and outcomes for prognostic reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the NGCC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (Appendix A in the full version of the guideline [see the “Availability of Companion Documents” field]).

A total of 25 review questions were originally identified. Some of these were later combined into one review when the protocols were agreed, resulting in an overall list of 18 review topics (see Table 1 in the full version of the guideline). Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken in accordance with the Guidelines Manual 2012 (see the "Availability of Companion Documents" field) to identify evidence within published literature to answer the review questions. Clinical databases were searched using relevant medical subject headings, free-text terms and study-type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. All searches were conducted on three core databases: Medline, EMBASE, and The Cochrane Library. An additional subject specific database (HMIC, Health Management Information Consortium) was used for the question on specialist management units. All searches were updated on 28th January 2014. No papers published added to above databases after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews and asking the GDG for known studies. The questions, the study type filters applied, the databases searched and the years covered can be found in Appendix F in the full version of the guideline.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria as defined by the protocol for each question.

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (www.guideline.gov)
- National Institute for Health and Care Excellence (NICE) (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (www.consensus.nih.gov)
- National Library for Health (www.library.nhs.uk)
- Trip Database (www.tripdatabase.com)

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to acute heart failure in the National Health Service Economic Evaluation Database (NHS EED), the Health Technology Assessment database (HTA) and the Health Economic Evaluations Database (HEED) with no date restrictions. Additionally, the search was run on Medline and EMBASE using a specific economic filter, from 2010, to ensure recent publications that had not yet been indexed by the economic databases were identified. This was supplemented by additional searches that looked for economic papers specifically relating to valvular surgery on Medline, EMBASE, NHS EED, HTA and HEED as it became apparent that some papers in this area were not being identified through the first search. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English.

The health economic search strategies are included in Appendix F in the full version of the guideline. All searches were updated on 28th January 2014. No papers published after this data were considered.
Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the guideline:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.

- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C in the full version of the guideline).

Inclusion and Exclusion Criteria

The inclusion and exclusion of studies was based on the review protocols, which can be found in Appendix C in the full version of the guideline. Excluded studies by review question (with the reasons for their exclusion) are listed by review question in Appendix K in the full version of the guideline. The GDG was consulted about any uncertainty regarding inclusion or exclusion.

Randomised trials, non-randomised trials, and observational studies (including diagnostic or prognostic studies) were included in the evidence reviews as appropriate.

The GDG agreed that randomised controlled trials were the most appropriate study design for intervention reviews. However, there were exceptions to this where observational studies were accepted as evidence since randomisation would be unethical or when GDG members were aware that little or no evidence was available for a particular topic. In most of these cases observational studies were only included if they were of sufficient size (n>2000) and made multivariable adjustments for confounding baseline characteristics between treatment and control groups. This was the case for the following reviews:

- Beta-blocker reduction or discontinuation (Chapter 8.1 in the full version of the guideline)
- Commencing beta-blocker, angiotensin converting enzyme inhibitor or mineralocorticoid receptor antagonist therapy (Chapter 8.1 in the full version of the guideline)

Smaller observational studies (n<2000) were accepted as evidence in the following reviews:

- Specialist management units (restricted to those with multivariable adjustments) (Chapter 11.1 in the full version of the guideline)
- Opiates (Chapter 6.2 in the full version of the guideline)

In the review on specialist acute heart failure management in Chapter 11.1 in the full version of the guideline, the GDG decided to restrict evidence from the year 1999 onwards, because specialist services were considered to have gone through substantial changes and earlier evidence would no longer be applicable. Interventions focusing exclusively on specialist nursing services were also excluded from this review because the GDG considered this evidence not generalisable to an overall specialist management approach.

People with cardiogenic shock were included as a subgroup of people with acute heart failure. The GDG agreed to include evidence which described people with myocardial infarction complicated by cardiogenic shock, but considered this to be an indirect population.

In Chapter 11.1 in the full version of the guideline, because there was a lack of evidence for a comparison between left ventricular assist devices and medical care, evidence from an indirect randomised trial was included. This study included people with 'chronic end stage heart failure' and used the procedure as destination therapy which is not current practice in the United Kingdom (UK).

Conference abstracts were not automatically excluded from the review but were initially assessed against the inclusion criteria and then further processed only if no other full publication was available for that review question, in which case the authors of the selected abstracts were contacted for further information. The reviews that included abstracts were:

- In Chapter 6 in the full version of the guideline: Inotropes (dobutamine) - for this review a trial which was not fully published (Zairis et al., 2004 CASINO trial as described in Ciełand 2004) was included. The authors did not reply to a request for further information on methods and additional outcomes.
- Abstracts were also included in pharmacological treatment after stabilisation in Chapter 8 in the full version of the guideline. For the timing of beta-blocker and mineralocorticoid receptor antagonists (MRA) commencement reviews one abstract each was included as they described results of data from the OPTIMIZE registry. The design, rationale and methods of analysis of this registry were described in depth in other publications.

Composite outcomes were usually excluded. However, an exception was made for the composite endpoint of 'mortality or heart failure hospitalisation' for reviews where limited or no other evidence was available.

Literature reviews, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

The review protocols are presented in Appendix C in the full version of the guideline.

Type of Studies

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. If the GDG believed RCT data were not appropriate or there was limited evidence from RCTs, well-conducted non-randomised studies were included. Please refer to Appendix C in the full version of the guideline for full details on the study design of studies selected for each review question.

Where data from observational studies were included, the GDG decided that the results for each outcome should be presented separately for each study and meta-analysis not conducted.

For diagnostic reviews, cross-sectional and retrospective studies were included. For prognostic reviews, prospective and retrospective cohort studies were included. Case-control studies were not included.

Evidence of Cost-effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost-effectiveness.
Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their cost-effectiveness\(^\text{\textdagger}\)) rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature
- Undertook a new cost-effectiveness analysis to cover priority areas

**Literature Review**

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against pre-specified inclusion and exclusion criteria to identify relevant studies (see below for details)

**Inclusion and Exclusion Criteria**

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost–benefit and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially includable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were always excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Remaining studies were prioritized for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available, then other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (see Appendix F in the Guidelines Manual and the health economics review protocol in Appendix C in the full version of the guideline).

When no relevant economic studies were found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implications of the recommendations.

**Number of Source Documents**

The number of studies identified for each aspect of clinical and health economics literature is provided in Appendices D and E in the full version of the guideline, respectively (see the "Availability of Companion Documents\(^\text{\textdagger}\) field).

**Methods Used to Assess the Quality and Strength of the Evidence**

**Weighting According to a Rating Scheme (Scheme Given)**

**Rating Scheme for the Strength of the Evidence**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change confidence in the estimate of effect</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate</td>
</tr>
<tr>
<td>Very Low</td>
<td>Any estimate of effect is very uncertain</td>
</tr>
</tbody>
</table>

**Methods Used to Analyze the Evidence**

- Meta-Analysis
- Review of Published Meta-Analyses
- Systematic Review with Evidence Tables

**Description of the Methods Used to Analyze the Evidence**

**Note from the National Guideline Clearinghouse (NGC):** This guideline was developed by the National Clinical Guideline Centre (NGCC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents\(^\text{\textdagger}\) field for the full version of this guidance.

**Evidence of Effectiveness**

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the guideline:

- Relevant studies were critically appraised using the appropriate checklist as specified in the Guidelines Manual. For diagnostic questions, the QUADAS-2 checklist was followed (http://www.bris.ac.uk/quadas/quadas-2/\(^\text{\textdagger}\)).
- Key information was extracted on the study's methods, PICO (patients, intervention, comparison and outcome) factors and results. These were presented in summary tables (in each review chapter of the full guideline) and evidence tables (in Appendix G in the full version of the guideline [see the "Availability of Companion Documents\(^\text{\textdagger}\) field]).
• Summaries of evidence were generated by outcome (included in the relevant review protocols) and were presented in Guideline Development Group (GDG) meetings:
  • Randomised studies: data were meta-analysed where appropriate and reported in Grading of Recommendations, Assessment, Development and Evaluation (GRADE) profiles (for intervention reviews).
  • Observational studies: data were presented as a range of values in GRADE profiles.
  • Prognostic studies: data were presented as a range of values, usually in terms of the relative effect as reported by the authors.
  • Diagnostic studies were presented as measures of diagnostic test accuracy (sensitivity, specificity, positive and negative predictive value). Coupled values of sensitivity and specificity were summarised in receiver operating characteristic (ROC) curve to allow visual comparison between different index tests (plotting data at different thresholds) and to investigate heterogeneity more effectively (given data were reported at the same thresholds). Diagnostic meta-analyses were carried out whenever data from at least 5 studies were available. See Chapter 1 and Appendix J in the full version of the guideline for details.

A 20% sample of each of the above stages of the reviewing process was quality assured by a second reviewer to eliminate any potential of reviewer bias or error.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes.

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. Data for continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences and, where the studies had different scales, standardised mean differences were used. The generic inverse variance option in RevMan5 is used if any studies reported solely summary statistics and 95% confidence interval (95% CI) or standard error; this included any hazard ratios reported. When the only evidence available was based on studies that summarised results by presenting medians (and interquartile ranges), or only p values were given, this information was used in terms of the study and its sample size and was included in the GRADE tables without calculating the relative or absolute effects. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for evidence of this type. Where reported, time-to-event data was presented as a hazard ratio.

Stratified analyses were predefined for some review questions at the protocol stage when the GDG identified that these strata are different in terms of biological and clinical characteristics and the interventions were expected to have a different effect on subpopulations. It was decided at the outset that acute heart failure refers to distinct subpopulations, i.e., acute heart failure with pulmonary oedema, cardiogenic shock, acute right-sided heart failure, and acute decompensated chronic heart failure.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at p<0.1 or an I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, the authors carried out predefined subgroup analyses – see protocols in Appendix C in the full version of the guideline.

Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random-effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. Absolute risk differences were presented in the GRADE profiles and in clinical summary of findings tables, for discussion with the GDG.

For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

Data Synthesis for Prognostic Factor Reviews

Odds ratios (ORs), risk ratios (RRs) or hazard ratios (HRs), with their 95% confidence intervals (95% CIs) for the effect of the pre-specified prognostic factors were extracted from the papers. Studies at lower risk of bias were preferred, taking into account the analysis and the study design. In particular, prospective cohort studies were preferred that reported multivariable analyses, including key confounders as identified by the GDG at the protocol stage for that outcome. A narrative summary of results from univariate analyses was also given, highlighting the very high risk of bias as there was a high chance of unknown real effect due to lack of controlling for potential confounders. Data were not combined in meta-analyses for prognostic studies.

Data Synthesis for Diagnostic Test Accuracy Review

Data and Outcomes

For the reviews of diagnostic test accuracy, a positive result on the index test was found if the patient had values of the measured quantity above a threshold value, and different thresholds could be used. Diagnostic test accuracy measures used in the analysis were: sensitivity, specificity, positive and negative predictive value, area under the ROC curve. The threshold of a diagnostic test is defined as the value at which the test can best differentiate between those with and without the target condition and, in practice, the thresholds used varies amongst studies. In the one diagnostic review for this guideline, sensitivity was given more importance than specificity since natriuretic peptide testing is used as a ‘rule out’ test. This means that the test is carried out to minimise the false negative test results. The GDG defined the clinically relevant natriuretic thresholds to be used in the analysis based on the thresholds described in the current European heart failure guideline (see Chapter 5.1 in the full version of the guideline for details).

Data Synthesis

Coupled forest plots of sensitivity and specificity with their 95% CIs across studies (at various thresholds) were produced for each test, using RevMan5. In order to do this, 2x2 tables (the number of true positives, false positives, true negatives and false negatives) were directly taken from the study if given, or else were derived from raw data or calculated from the...
set of test accuracy statistics (calculated 2x2 tables can be found in Appendix I in the full version of the guideline).

To allow comparison between tests, summary ROC curves (by type of natriuretic peptide and by threshold level) were generated for each diagnostic test from the pairs of sensitivity and specificity calculated from the 2x2 tables, selecting threshold per study. A ROC plot shows true positive rate (sensitivity) as a function of false positive rate (1 minus specificity). Data were entered into RevMan5 and ROC curves were fitted using the Moses Littenberg approach. In order to compare diagnostic tests, 2 or more tests were plotted on the same graph. The performance of the different diagnostic tests was then assessed by examining the summary ROC curves visually: the test that had a curve lying closest to the upper left corner (100% sensitivity and 100% specificity) was interpreted as the best test.

A second analysis was conducted on studies that used two types of natriuretic peptides in the same study population. Results were plotted on one graph indicating paired results for each study. Paired results could show whether one peptide performed consistently better within study populations.

For those studies that reported area under the ROC curve (AUC) data, these were also plotted on a graph, for each diagnostic test. The AUC describes the overall diagnostic accuracy across the full range of thresholds. The GDG agreed on the following criteria for AUC:

- ≤0.50: worse than chance
- 0.50-0.60: very poor
- 0.61-0.70: poor
- 0.71-0.80: moderate
- 0.81-0.90: good
- 0.91-1.00: excellent or perfect test

Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots where appropriate (only when there were similar thresholds).

When data from 5 or more studies were available, a diagnostic meta-analysis was carried out. Study results were pooled using the bivariate method for the direct estimation of summary sensitivity and specificity using a random effects approach (in WinBUGS® software - for the program code see Appendix I in the full version of the guideline). This model also assesses the variability between studies by incorporating the precision by which sensitivity and specificity have been measured in each study. A confidence ellipse is shown in the graph that indicates the confidence region around the summary sensitivity/specificity point.

**Appraising the Quality of Evidence by Outcomes**

The evidence for outcomes from the included RCTs and, where appropriate, observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles (GRADE tables), which consist of 2 sections: the 'Clinical evidence profile' table includes details of the quality assessment while the 'Clinical evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation, or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was only taken into consideration in the quality assessment and included in the 'Clinical evidence profile' table if it was apparent.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2 in the full version of the guideline. Each element was graded using the quality levels listed in Table 3 in the full version of the guideline. For each of these quality elements evidence for each outcome is downgraded where applicable using the following levels:

- The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems.
- The ratings for each component are summed to obtain an overall assessment for each outcome. The grades described above lead to an overall quality rating as described in the "Rating Scheme for the Strength of the Evidence" field. For example if the quality element 'risk of bias' is downgraded twice and 'imprecision' downgraded once an overall rating of 'very low' is given for this outcome and any further low or high risks in other quality elements will not change this rating.
- The GRADE toolbox is currently designed only for intervention reviews using randomised trials and observational studies but the authors adapted the quality assessment elements and outcome presentation for diagnostic accuracy studies.

**Grading the Quality of Clinical Evidence**

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start as High, observational studies as Low, and uncontrolled case series as Low or Very low.
2. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed in the full version of the guideline. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
3. The downgraded or updated marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in the Sections 3.3.6 to 3.3.10.
The details of the clinical used for each of the main quality elements are discussed further in the online tool to choose in the full version of the guideline.

**Assessing Clinical Importance (Benefit, Harm or No Difference)**

The GDG assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

The GDG considered a minimal important difference (MID) based on the point estimate of the absolute effect for intervention studies. For all outcomes the GDG used the robustness of the evidence, i.e., GRADE rating, as well as the absolute effect (if positive) of the outcome of interest to decide whether the intervention could be considered beneficial for this outcome. The same point estimate, but in the opposite direction would apply if the outcome was negative.

This assessment was carried out by the GDG for each critical outcome, and an evidence summary table was produced to compile the GDG's assessments of clinical importance per outcome, alongside the evidence quality.

**Evidence Statements**

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:

- The number of studies and the number of participants for a particular outcome
- A brief description of the participants
- An indication of the direction of effect (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the 2 tested treatments)
- A description of the overall quality of evidence (GRADE overall quality)

**Evidence of Cost-effectiveness**

The GDG is required to make decisions based on the best available evidence of both clinical and cost-effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their 'cost-effectiveness') rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature
- Undertook a new cost-effectiveness analysis to cover priority areas

**Literature Review**

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in the Guidelines Manual
- Extracted key information about the studies' methods and results into evidence tables (included in Appendix H in the full version of the guideline)
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter for each review question)

**NICE Economic Evidence Profiles**

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows an assessment of applicability and methodological quality for each economic evaluation, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from the Guidelines Manual. It also shows the incremental costs, incremental effects (for example, quality-adjusted life years [QALYs]) and incremental cost-effectiveness ratio for the base case analysis in the evaluation, as well as information about the assessment of uncertainty in the analysis. See Appendix H in the full version of the guideline for more details.

If a non-United Kingdom (UK) study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

**Methods Used to Formulate the Recommendations**

- Expert Consensus
- Informal Consensus

**Description of Methods Used to Formulate the Recommendations**

**Note from the National Guideline Clearinghouse (NGC):** This guideline was developed by the National Clinical Guideline Centre (NGCC) on behalf of the National Institute for Health and Care Excellence (NICE). See the “Availability of Companion Documents” field for the full version of this guidance.

A multidisciplinary Guideline Development Group (GDG) comprising health professionals and researches as well as lay members developed this guideline. The group met every 5 to 6 weeks during the development of the guideline. Staff from the NGCC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and Information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

**Developing Recommendations**
Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices II and I in the full version of the guideline (see the “Availability of Companion Documents” field).
- Summary of clinical and economic evidence and quality (as presented in Chapters 5-11 in the full version of the guideline)
- Forest plots and summary receiver operating characteristics (ROC) curves (Appendices I-I in the full version of the guideline)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix M in the full version of the guideline)

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the GDG took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GDG’s values and preferences), and the confidence the GDG had in the evidence (evidence quality).

Secondly, it was assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs compared to the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were agreed through discussions in the GDG meeting. The GDG also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

Members of the GDG reviewed all recommendations at the end of guideline development in a confidential online survey to gauge the level of support and provide space for free text comments. Recommendations where one or more members disagreed with the wording of a recommendation or where particular issues were raised in the free text comments were discussed again to resolve any particular concerns.

The wording of recommendations was agreed by the GDG and focused on the following factors:

- The actions health professionals need to take
- The information readers need to know
- The strength of the recommendation (for example the word ‘offer’ was used for strong recommendations and ‘consider’ for weak recommendations)
- The involvement of patients (and their carers if needed) in decisions on treatment and care
- Consistency with NICE’s standard advice on recommendations about drugs, waiting times and ineffective interventions

The main considerations specific to each recommendation are outlined in the ‘Recommendations and link to evidence’ sections within each chapter.

Rating Scheme for the Strength of the Recommendations

**Strength of Recommendations**

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some Interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

**Interventions That Must (or Must Not) Be Used**

The GDG usually uses ‘must’ or ‘must not’ only if there is a legal duty to apply the recommendation. Occasionally the GDG uses ‘must’ (or ‘must not’) if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

**Interventions That Should (or Should Not) Be Used – a ‘Strong’ Recommendation**

The GDG uses ‘offer’ (and similar words such as ‘refer’ or ‘advise’) when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, ‘Do not offer...’) are used when the GDG is confident that an intervention will not be of benefit for most patients.

**Interventions That Could Be Used**

The GDG uses ‘consider’ when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient’s values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

**Cost Analysis**

**Undertaking New Health Economic Analysis**

As well as reviewing the published economic literature for each review question, as described above, a new economic analysis was undertaken by the health economist to cover selected areas. Priority areas for new health economic analysis were agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.
The GDG identified acute heart failure and specialist management units as the highest priority areas for original economic modelling. Early echocardiography was also prioritised but this was not subsequently modelled because there was not the data to quantify the incremental costs and benefits. These areas were prioritised because they potentially have a higher patient and cost impact than other areas of the guideline, and because of significant variation in clinical practice.

The following general principles were adhered to in developing the cost-effectiveness analysis:
- Methods were consistent with the National Institute for Health and Care Excellence (NICE) reference case.
- The GDG was involved in the design of the model, selection of inputs and interpretation of the results.
- Model inputs were based on the systematic review of the clinical literature supplemented with other published data sources where possible.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at the National Clinical Guideline Centre (NCGC).

Full methods for the combined cost-effectiveness analysis of natriuretic peptide testing and specialist management units, are described in Appendix M in the full version of the guideline (see the "Availability of Companion Documents" field).

Cost-effectiveness Criteria

NICE’s report ‘Social value judgements: principles for the development of NICE guidance’ sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):
- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the ‘Recommendations and link to evidence’ section of the relevant chapter, with reference to issues regarding the plausibility of the estimate or to the factors set out in ‘Social value judgements: principles for the development of NICE guidance’.

In the Absence of Economic Evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant United Kingdom National Health Service (UK NHS) unit costs, alongside the results of the clinical review of effectiveness evidence.

Method of Guideline Validation
- External Peer Review
- Internal Peer Review

Description of Method of Guideline Validation

This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) website when the pre-publication check of the full guideline occurs.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NGCG) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guideline.

The wording used in the recommendations in this guideline (for example, words such as ‘offer’ and ‘consider’) denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Organisation of Care

All hospitals admitting people with suspected acute heart failure should provide a specialist heart failure team that is based on a cardiology ward and provides outreach services.

Ensure that all people being admitted to hospital with suspected acute heart failure have early and continuing input from a dedicated specialist heart failure team.

Plan the following with people with acute heart failure in line with the NGC summary of the NICE guideline Chronic heart failure. Management of chronic heart failure in adults in primary and secondary care (NICE clinical guideline 108):
- Discharge from hospital after the acute phase and
- Subsequent management in primary care, including ongoing monitoring and care provided by the multidisciplinary team and
Information and communication about their condition, its treatment and prognosis.

A follow-up clinical assessment should be undertaken by a member of the specialist heart failure team within 2 weeks of the person being discharged from hospital.

**Diagnosis, Assessment and Monitoring**

Take a history, perform a clinical examination and undertake standard investigations – for example, electrocardiography, chest X-ray and blood tests – in line with the NICE summary of the NICE guideline Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care (NICE clinical guideline 108).

In people presenting with new suspected acute heart failure, use a single measurement of serum natriuretic peptides (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NT-proBNP]) and the following thresholds to rule out the diagnosis of heart failure:

- BNP less than 100 ng/litre
- NT-proBNP less than 300 ng/litre

In people presenting with new suspected acute heart failure with raised natriuretic peptide levels (see recommendation above), perform transthoracic Doppler two-dimensional (2D) echocardiography to establish the presence or absence of cardiac abnormalities.

In people presenting with new suspected acute heart failure, consider performing transthoracic Doppler 2D echocardiography within 48 hours of admission to guide early specialist management.

Do not routinely offer pulmonary artery catheterisation to people with acute heart failure.

**Initial Pharmacological Treatment**

For guidance on patient consent and capacity follow recommendations 1.2.12 and 1.2.13 in Patient experience in adult NHS services (NICE clinical guideline 138).

Do not routinely offer opiates to people with acute heart failure.

Offer intravenous diuretic therapy to people with acute heart failure. Start treatment using either a bolus or infusion strategy.

For people already taking a diuretic, consider a higher dose of diuretic than that on which the person was admitted unless there are serious concerns with patient adherence to diuretic therapy before admission.

Closely monitor the person's renal function, weight and urine output during diuretic therapy.

Discuss with the person the best strategies of coping with an increased urine output.

Do not routinely offer nitrates to people with acute heart failure.

If intravenous nitrates are used in specific circumstances, such as for people with concomitant myocardial ischaemia, severe hypertension or regurgitant aortic or mitral valve disease, monitor blood pressure closely in a setting where at least level 2 care can be provided. Level 2 care is for people needing more detailed observation or intervention, including support for a single failing organ system or postoperative care and for those stepping down from higher levels of care (from the Intensive Care Society guideline Levels of critical care for adult patients).

Do not offer sodium nitroprusside to people with acute heart failure.

Do not routinely offer inotropes or vasopressors to people with acute heart failure.

Consider inotropes or vasopressors in people with acute heart failure with potentially reversible cardiogenic shock. Administer these treatments in a cardiac care unit or high dependency unit or an alternative setting where at least level 2 care can be provided.

**Initial Non-pharmacological Treatment**

Do not routinely use non-invasive ventilation (continuous positive airways pressure [CPAP] or non-invasive positive pressure ventilation [NIPPV]) in people with acute heart failure and cardiogenic pulmonary oedema.

If a person has cardiogenic pulmonary oedema with severe dyspnoea and acidaemia consider starting non-invasive ventilation without delay:

- At acute presentation or
- As an adjunct to medical therapy if the person's condition has failed to respond.

Consider invasive ventilation in people with acute heart failure that, despite treatment, is leading to or is complicated by:

- Respiratory failure or
- Reduced consciousness or physical exhaustion

Do not routinely offer ultrafiltration to people with acute heart failure.

Consider ultrafiltration for people with confirmed diuretic resistance. Diuretic resistance is defined as dose escalation beyond a person's previously recognised dose ceiling or a dose approaching the maximum recommended daily dose without incremental improvement in diuresis (from the American College of Cardiology paper Diuretics and ultrafiltration in acute decompensated heart failure).

**Treatment after Stabilisation**

In a person presenting with acute heart failure who is already taking beta-blockers, continue the beta-blocker treatment unless they have a heart rate less than 50 beats per minute, second or third degree atrioventricular block, or shock.

Start or restart beta-blocker treatment during hospital admission in people with acute heart failure due to left ventricular systolic dysfunction, once their condition has been stabilised – for example, when intravenous diuretics are no longer needed.

Ensure that the person's condition is stable for typically 48 hours after starting or restarting beta-blockers and before discharging from hospital.
Offer an angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker if there are intolerable side effects) and an aldosterone antagonist during hospital admission to people with acute heart failure and reduced left ventricular ejection fraction. If the angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker) is not tolerated an aldosterone antagonist should still be offered.

Closely monitor the person’s renal function, electrolytes, heart rate, blood pressure and overall clinical status during treatment with beta-blockers, aldosterone antagonists or angiotensin-converting enzyme inhibitors.

Valvular Surgery and Percutaneous Intervention
Offer surgical aortic valve replacement to people with heart failure due to severe aortic stenosis assessed as suitable for surgery.

Consider transcatheter aortic valve implantation (TAVI) in selected people, with heart failure caused by severe aortic stenosis, who are assessed as unsuitable for surgical aortic valve replacement. Details of all people undergoing TAVI should be entered into the United Kingdom (UK) Central Cardiac Audit database. For information about patient selection, see Transcatheter aortic valve implantation for aortic stenosis (NICE interventional procedure guidance 421).

For guidance on coronary revascularisation see the NGC summary of the NICE guideline Chronic heart failure in adults in primary and secondary care.

Consider surgical mitral valve repair or replacement for people with heart failure due to severe mitral regurgitation assessed as suitable for surgery.

Mechanical Assist Devices
At an early stage, the specialist should have a discussion with a centre providing mechanical circulatory support about:

- People with potentially reversible severe acute heart failure or
- People who are potential candidates for transplantation

Definitions:

Strength of Recommendations
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Clinical Algorithm(s)

An algorithm titled “Diagnostic and Treatment Algorithm for Clinical Suspicion of Acute Heart Failure” is included in the full version of the guideline (see the “Availability of Companion Documents” field).

A NICE pathway titled “Acute Heart Failure Overview” is available from the National Institute for Health and Care Excellence (NICE) Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations
The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of individuals with acute heart failure
See the “Trade-off between clinical benefits and harms” sections in the full version of the guideline (see the “Availability of Companion Documents” field) for additional details about benefits of specific interventions.

Potential Harms

As with any diagnostic test, there will be false-negative and false-positive results in the use of natriuretic peptide...
As with any diagnostic test, there will be false-negative and false-positive results in the use of natriuretic peptide testing. The use of high-dose loop diuretics raised concerns relating to ototoxicity, but the group were reassured that no ototoxicity was demonstrated in the DOSE trial. The Guideline Development Group (GDG) noted that there is likely to be a rise in serum creatinine during diuretic therapy so close monitoring is required. There is a trend to harm in terms of increased mortality, myocardial infarction and arrhythmia associated with inotrope or vasopressor use. However, the data are relatively weak in the acute heart failure setting. The GDG noted that use of vasopressors and/or inotropes may be most appropriate in rescuing patients from life-threatening systemic hypoperfusion, in order to allow other therapies to act and address potentially reversible causes. Both nitrates and nitroprusside may increase the risk of harm in patients with hypotension, in particular in those with aortic stenosis. Ultrafiltration was associated with more serious adverse events than diuretic therapy. Risks of major stroke were higher in the transcatheter aortic valve implantation (TAVI) group compared to the traditional treatment group (at 30 days and 1 year follow-up times). Short- and long-term physical health-related quality of life as well as short-term mental health-related quality of life were rated more highly by people who received TAVI. Readmission rates were higher in the medical care group.

See the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for additional details about harms of specific interventions.

Qualifying Statements

This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of the Guideline

Implementation Strategy

Implementation tools and resources to help you put the guideline into practice are also available from the National Institute for Health and Care Excellence (NICE) Web site.

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Organisation of Care

All hospitals admitting people with suspected acute heart failure should provide a specialist heart failure team that is based on a cardiology ward and provides outreach services.

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Ensure that the person's condition is stable for typically 48 hours after starting or restarting beta-blockers and before discharging from hospital.

Offer an angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker if there are intolerable side effects) and an aldosterone antagonist during hospital admission to people with acute heart failure and reduced left ventricular ejection fraction. If the angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker) is not tolerated an aldosterone antagonist should still be offered.

Implementation Tools

- Clinical Algorithm
- Foreign Language Translations
- Mobile Device Resources
- Patient Resources
- Resources

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

- Getting Better

IOM Domain

- Effectiveness
- Patient-centeredness
- Timeliness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

- 2014 Oct

Guideline Developer(s)

National Clinical Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group Members: Jonathan Mant (GDG Chair), Professor of Primary Care Research and Honorary Consultant, University of Cambridge; Abdallah Al-Mohammad, Consultant Cardiologist and Honorary Senior Clinical Lecturer, Sheffield Teaching Hospitals NHS Trust; Peter Bolton, Patient member; Jane Butler, Heart Failure Specialist Consultant Nurse, Barts Health NHS Trust; Martin Cowie, Professor of Cardiology and Honorary Consultant Cardiologist, Imperial College London; Suzanne Hardman, Consultant Cardiologist, Whittington Health and Honorary Senior Lecturer, University College, London; Nicholas Ioannou, Consultant Intensivist and Anaesthetist, Guy's and St Thomas' NHS Foundation Trust, London; Christopher Jones (October 2012 to February 2014), Patient member; Jason Kendall,
Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B in the full version of the guideline (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site.

Availability of Companion Documents

The following are available:


Patient Resources

The following is available:


Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline’s content.

NGC Status

This NGC summary was completed by ECRI Institute on February 12, 2015.

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