NICE National Institute for Health and Care Excellence

NICE

Surveillance report 2016 – Unstable angina and NSTEMI (2010) NICE guideline CG94 and Myocardial infarction with ST-segment elevation (2013) NICE guideline CG167

Surveillance report

Published: 29 September 2016
nice.org.uk

Contents

Surveillance decision

This report describes the joint surveillance review of clinical guidelines on the early management of unstable angina and non-ST-elevation myocardial infarction (NSTEMI) NICE guideline CG94 and early management of myocardial infarction with ST-segment elevation (STEMI) NICE guideline CG167.

Following the joint surveillance review of CG94 and CG167 and a recent review of the clinical guideline on management of hyperglycaemia in acute coronary syndromes (CG130), it is proposed that the 3 guidelines should be combined to ensure that recommendations on the management of acute coronary syndromes fall under 1 clinical guideline.

Unstable angina and NSTEMI: early management (CG94)

We will plan an update of the following clinical areas:

1. Antiplatelet therapy

- Which antiplatelet is most effective for managing patients with unstable angina (UA) or NSTEMI? (Note: this clinical question has been amended after reviewing new evidence on antiplatelet therapy.)

2. Management strategies

- In adults with UA or non-ST elevation myocardial infarction (MI) does early invasive investigation (that is, angiography) with intent to assess for (and in those patients deemed suitable, to perform) revascularisation improve outcomes in comparison with initial conservative treatment, with or without later angiography?

We propose adding the following new question to the guideline:

- What is the clinical and cost effectiveness of drug-eluting stents in patients with unstable angina or NSTEMI undergoing percutaneous coronary intervention (PCI)?

Myocardial infarction with ST-segment elevation: acute management (CG167)

We will plan an update of the clinical question relating to culprit versus complete revascularisation:

- What is the clinical and cost effectiveness of multivessel PCI compared to culprit-only primary PCI (PPCI) in people with STEMI and multivessel coronary disease undergoing PPCI?

We propose adding the following new questions to the guideline:

- What is the clinical and cost effectiveness of PPCI using drug-eluting stents in people with STEMI?
- What is the clinical and cost effectiveness of antithrombins (such as bivalirudin) in patients with STEMI undergoing PPCI?

We propose that the combined guideline incorporates recommendations from NICE technology appraisal guidance that was developed after the clinical guideline was published: prasugrel with percutaneous coronary intervention for treating acute coronary syndromes. Recommendations will be incorporated subject to the outcome of a technology appraisal review proposal (expected in 2017).

Reason for the decision

We found 132 new studies through surveillance: 8 new studies for CG94 and 124 new studies for CG167.

Unstable angina and NSTEMI: early management (CG94)

Although none of the identified new evidence was thought to impact recommendations, topic experts, including those who helped to develop the guideline, advised us that the following sections of the guideline should be updated.

Antiplatelet therapy

- Which antiplatelet is most effective for managing patients with UA or NSTEMI? (Note: this clinical question has been amended after reviewing new evidence on antiplatelet therapy.)

There was a strong indication from topic experts that the guideline needed to be updated. Experts stated that although no new evidence has been identified from literature searches, clinical practice indicates that ticagrelor and prasugrel are more potent and predictable antiplatelets than clopidogrel, but they also carry an increased risk of bleeding. As a result, cardiologists need to consider the predicted ischaemic risk and the estimated risk of bleeding. A further consideration is the duration of dual antiplatelet therapy. Experts stated that European Society of Cardiology and

American Heart Association guidelines incorporated these issues into their revised guideline, which makes the prescription of antiplatelet therapy more individualised.

Decision: This review question should be updated.

Management strategies

- In adults with UA or non-ST elevation MI does early invasive investigation (that is, angiography) with intent to assess for (and in those patients deemed suitable, to perform) revascularisation improve outcomes in comparison with initial conservative treatment, with or without later angiography?

Topic experts stated that there is an ongoing debate about whether angiography centres should have 24/7 capabilities for interventional procedures (angioplasty). They felt that this presents a substantive question about the structure of service provision. Some experts suggested that early angiography results in less radiation to the patient, less renal nephropathy, reduced tariff and shorter length of stay. They suggested that this is likely to have an impact on health economic modelling. Another topic expert suggested that patients with suspected non-ST elevation acute coronary syndromes are increasingly being offered coronary angiography (invasive strategy) and systematic use of risk stratification is not widely used. Furthermore, experts felt that evidence highlights that patients who are at highest risk of ischaemia benefit most from early angiography; however, data from registries suggests that cardiologists do not always select these patients

Decision: This review question should be updated.

New question: Drug-eluting stents

- What is the clinical and cost effectiveness of drug-eluting stents in patients with UA or NSTEMI undergoing PCI? (Note: this question was derived from technology appraisal guidance on drug-eluting stents for the treatment of coronary artery disease.)

During the 6-year surveillance review of CG94, 1 new study on drug-eluting stents was identified; however, it was considered not to have an impact on guideline recommendations. A considerable amount of new evidence was identified from randomised controlled trials (RCTs) during the 2-year surveillance review of CG167 (see below). The new evidence indicated that CG167 needed updating. Because both guidelines are due to be combined, it is proposed that this clinical question should be added to ensure that the combined guideline covers the use of drug-eluting stents for different types of acute coronary syndromes.

Decision: This review question should be added.

Myocardial infarction with ST-segment elevation: acute management (CG167)

New evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated and any new sections added.

Culprit versus complete revascularisation

- What is the clinical and cost effectiveness of multivessel PCI compared to culprit-only PPCI in people with STEMI and multivessel coronary disease undergoing PPCI?

Currently, CG167 makes no recommendations on the use of multivessel PCI in people with STEMI and multivessel coronary disease.

One large RCT indicated some benefit of multivessel PCI whereas the remaining identified studies reported no significant differences between multivessel PCI and culprit-only PPCI in people with STEMI and multivessel coronary disease undergoing PPCI. In combination with the opinions of topic experts, the identified new evidence suggests that recommendations on the role of multivessel PCI could inform future clinical practice.

Decision: This review question should be updated.

New question: Drug-eluting stents

- What is the clinical and cost effectiveness of PPCI using drug-eluting stents in people with STEMI? (Note: this question was derived from NICE's technology appraisal guidance on drug-eluting stents for the treatment of coronary artery disease.)

CG167 makes recommendations on PPCI using bare-metal stents but does not make any recommendations on PPCI using drug-eluting stents in patients with STEMI.

A considerable amount of evidence was identified that assessed the safety and efficacy of drug-eluting stents. The identified new evidence comparing drug-eluting stents and bare-metal stents was inconsistent: some studies indicated that drug-eluting stents were safer and more effective than bare-metal, whereas other studies reported no significant differences between the 2 types of stent. When different types of drug-eluting stents were compared against each other results tended to favour everolimus-eluting stents. Studies also reported that new stent designs conferred better outcomes than older designs. Topic experts highlighted that drug-eluting stent prices have

decreased significantly since their initial introduction and bare-metal stents are generally no longer used for patients with STEMI. They felt that this may have cost implications on procurement.

It was considered that an extensive review of the evidence base on drug-eluting stents would ensure that their role in treatment of patients with STEMI is clearly defined.

Decision: This review question should be added.

New question: Antithrombin therapy

- What is the clinical and cost effectiveness of antithrombins (such as bivalirudin) in patients with STEMI undergoing PPCI?

CG167 incorporates a recommendation from NICE's technology appraisal guidance on bivalirudin for the treatment of ST-segment-elevation myocardial infarction:

1.2.2 Bivalirudin in combination with aspirin and clopidogrel is recommended for the treatment of adults with STEMI undergoing primary PCI.

The new evidence was inconsistent in reporting the direction of the treatment effect of bivalirudin when used during PPCI. Some studies reported that bivalirudin was more effective than other antithrombins; some reported that it was less effective and others reported no difference in outcomes. Topic experts highlighted uncertainties about older studies and felt that new evidence suggests that heparin is superior to bivalirudin. The inconsistent evidence in addition to uncertainties outlined by topic experts indicates that this question should be updated to clarify the role bivalirudin and other antithrombins in patients with STEMI.

Decision: This review question should be added subject to agreement to update the technology appraisal on bivalirudin.

Recommendations from NICE technology appraisals

We identified that NICE technology appraisal guidance on prasugrel with percutaneous coronary intervention for treating acute coronary syndromes was developed after the clinical guideline was published. It was considered that the technology appraisal was a relevant NICE guidance.

Decision: We propose that the clinical guideline incorporates recommendations from the technology appraisal subject to the outcome of a technology appraisal review proposal (expected in 2017).

Other clinical areas

Unstable angina and NSTEMI: early management (CG94)

We found new evidence for CG94 that was not thought to have an effect on current recommendations. This evidence related to the efficacy and safety of adding a glycoprotein inhibitor (GPI; tirofiban, eptifibatide and abciximab) to aspirin and heparin therapy as adjunct therapy to patients with UA/ NSTEMI undergoing primary coronary intervention (PPCI).

We did not find any new evidence related to:

- Tables, equations, engines or scoring systems for patient-risk stratification.
- The efficacy and safety of aspirin therapy compared to placebo.
- The efficacy and safety of adding a low-molecular-weight heparin (LMWH) compound to aspirin (with or without clopidogrel).
- The efficacy and safety of adding a factor Xa inhibitor (fondaparinux) to aspirin.
- The efficacy and safety of adding a synthetic pentasaccharide (fondaparinux and enoxaparin) to aspirin as adjunct therapy to patients undergoing PCI.
- The efficacy and safety of adding a thrombin inhibitor (bivalirudin) to the combination of aspirin, with or without a glycoprotein inhibitor (GPI).
- The efficacy and safety of adding a thrombin inhibitor (hirudin and bivalirudin) to the combination of aspirin and a GPI as adjunct therapy in patients undergoing PCI.
- Comparisons between coronary artery bypass grafting and PCI.
- Intra-aortic balloon pump counterpulsation.
- Investigation for myocardial ischaemia prior to hospital discharge in patients who do not undergo angiography.
- Pre-discharge assessment of left ventricular function.
- Psychosocial and educational interventions, mobilisation and discharge planning (cardiac rehabilitation – phase 1).

Myocardial infarction with ST-segment elevation: acute management (CG167)

We found new evidence related to CG167 that was not thought to have an effect on current recommendations. This evidence related to time to perfusion, pre-hospital versus in-hospital fibrinolysis, facilitated PPCI, radial versus femoral access, thrombus extraction during PPCI, hospital volumes of PPCI, rescue PCI and routine early angiography following fibrinolysis.

We did not find any new evidence related to cardiogenic shock and treatment of people who remain unconscious after a cardiac arrest.

Equalities

No equalities issues were identified during the surveillance reviews of both guidelines.

Overall decision

After considering all the new evidence and views of topic experts, we decided that partial updates were necessary for both guidelines.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 3 studies related to STEMI (CG167) for further commentary and no studies relating to unstable angina and NSTEMI (CG94).

Culprit versus complete revascularisation

We selected a randomised controlled trial (RCT) by Wald et al. (2013) for a full commentary because it highlights potential benefits of multivessel percutaneous coronary intervention (PCI) which may impact on the guideline.

What the guideline recommends

CG167 currently makes no recommendations on the use of multivessel PCI in people with STEMI and multivessel coronary disease.

Methods

Wald et al. (2013) performed a multicentre RCT including 465 patients with STEMI treated by immediate multivessel PCI (n=234) or culprit-only primary PCI (PPCI; n=231).

Patients of any age with acute STEMI and multivessel coronary disease, identified at the time of emergency PCI, were included. They were considered eligible if the infarct artery was treated successfully but 1 or more coronary artery other than the infarct artery had greater than 50% stenosis and the stenosis was considered treatable by PCI. Patients with cardiogenic shock, a history of previous coronary artery bypass grafting (CABG), non-infarct-artery stenosis greater than 50% in the left main stem or the ostia of both the left anterior descending and circumflex arteries or non-infarct stenosis caused by chronic total occlusion were excluded. Patients were randomly allocated to receive no further treatment or to undergo preventative PCI in non-infarct arteries following PCI of the infarcted artery.

The primary outcome was the composite of cardiac-related mortality, non-fatal myocardial infarction, or refractory angina. Each outcome was also assessed separately. Secondary outcomes were all-cause mortality and the need for repeat revascularisation (PCI or CABG).

Results

Authors report that recruitment was stopped early due to recommendations from an overseeing committee which noted highly significant differences ($p<0.001$) between groups in favour of

multivessel PCI. Patients were followed-up for a mean of 23 months: 67% of patients were followed-up for at least 1 year and 46% of patients were followed-up for at least 2 years. Ten patients in the multivessel PCI and 8 patients in the culprit-only PPCI group were lost to follow-up.

The primary outcome (composite of cardiac-related mortality, non-fatal myocardial infarction, or refractory angina) was reported in 21 out of 234 patients in the multivessel PCI group and 53 out of 231 patients in the culprit-only PPCI group at follow-up (hazard ratio [HR] 0.35; 95% confidence interval [CI] 0.21 to 0.58; p<0.001). Significant differences in favour of multivessel PCI were still observed when analyses were limited to the composite of cardiac-related mortality and non-fatal myocardial infarction (HR 0.36; 95% CI 0.18 to 0.73; p=0.004). Authors reported that Kaplan–Meier analysis revealed that the risk reduction in the multivessel PCI group was evident within 6 months and maintained thereafter.

In relation to individual outcome measures, no significant differences in the risks of cardiac-related mortality (HR 0.34; 95% CI 0.11 to 1.08; p=0.07) and non-cardiac mortality (HR 1.10; 95% CI 0.38 to 3.18; p=0.86) were observed between groups at mean follow-up of 23 months. The rate of non-fatal myocardial infarction was 7 out of 234 patients in the multivessel PCI group and 20 out of 231 patients in the culprit-only PPCI group (HR 0.32; 95% CI 0.13 to 0.75; p=0.009). Refractory angina rates were reported in 12 out of 234 and 30 out of 231 patients in the multivessel and culprit-only PPCI groups, respectively (HR 0.35; 95% CI 0.18 to 0.69; p=0.002). Repeat revascularisation was needed in 6.8% (16/234) and 19.9% (46/231) of patients in the multivessel and culprit-only PPCI groups, respectively (HR 0.30; 95% CI 0.17 to 0.56; p<0.001). With respect to procedure-related adverse events, no significant differences in rates of procedure-related stroke, bleeding requiring transfusion or surgery and contrast-induced neuropathy requiring dialysis were observed between groups.

None of the reported outcome measures were significantly associated with age, sex, presence/absence of diabetes, infarct location or the number of coronary arteries with stenosis.

Strengths and limitations

Strengths

The following strengths were identified:

- Clear inclusion and exclusion criteria were specified.
- An independent cardiologist and cardiac surgeon, who were not aware of treatment allocations, assessed the occurrence of outcomes.

- No significant differences in baseline characteristics, use of bare-metal stents, drug-eluting stents and medical therapies were observed between groups.
- Analysis was performed using the intention-to-treat approach.

Limitations

The following limitations were identified:

- Authors acknowledge that although the study highlights the benefits of multivessel PCI, it does not explore differences between immediate and delayed multivessel PCI.

Impact on guideline

Currently CG167 makes no recommendations on when to perform multivessel PCI. This study indicates that immediate multivessel PCI confers significant benefits over culprit-only PPCI in patients with STEMI. Topic experts stated that the question of when to use multivessel PCI or culprit-only PPCI is an important question in interventional cardiology. They suggested that the extensive use of multivessel PCI could have an impact on clinical practice. One expert highlighted that if practice changes high-risk groups may also change and the impact of these changes will need to be fully understood.

Drug-eluting stents

We selected the COMFORTABLE-AMI trial by Raber et al. (2014) for a full commentary because it assesses the safety and efficacy of a contemporary drug-eluting stent in patients with STEMI. This is currently not covered by the clinical guideline.

What the guideline recommends

CG167 currently makes no recommendations on the use of drug-eluting stents in people with STEMI.

Methods

Raber et al. (2014) performed a multicentre RCT including 1,116 patients with STEMI treated by biolimus-eluting stents with biodegradable polymer (n=575) or bare-metal stents (n=582).

Patients over 18 years with acute STEMI of more than 1 mm in greater than 2 contiguous leads, true posterior myocardial infarction, or new left bundle branch block were included. All patients

had more than 1 culprit lesion within the infarct vessel. Exclusion criteria were presence of mechanical complications of acute STEMI, known allergy to any study medication, use of vitamin K-antagonists, history of bleeding diathesis or known coagulopathy, and non-cardiac comorbid conditions with life expectancy below 1 year.

Whenever feasible, manual thrombus aspiration was performed before stent implantation. Pre-dilation of the culprit lesion was left to the discretion of the operator. When available, prasugrel was used during and after PCI. If prasugrel was not available or contraindicated, clopidogrel was administered. Furthermore, patients received either unfractionated heparin or bivalirudin during treatment. Complete revascularisation of all lesions within the infarct vessel had to be performed with the randomly allocated stent. Following PCI, all patients received dual antiplatelet therapy for at least 1 year. The primary endpoint was the composite of death, target-vessel reinfarction, and ischaemia-driven target-vessel revascularisation.

Results

Patients were followed-up for up to 2 years: data were available for over 95% of patients from each group at final follow-up. The primary outcome (composite of cardiac-related mortality, target-vessel reinfarction and target-lesion revascularisation) was reported in 5.8% (33/575) of patients in the drug-eluting stent group and 11.9% (68/582) of patients in the bare-metal stent group (HR 0.48; 95% CI 0.31 to 0.72; p<0.001). The composite rate of all-cause mortality, any reinfarction and any revascularisation was 14.5% (82/575) of patients in the drug-eluting stent group and 19.3% (110/582) of patients in the bare-metal stent group (HR 0.73; 95% CI 0.55 to 0.97; p=0.03).

In relation to individual outcome measures, no significant differences in the risks of cardiac-related mortality (HR 0.69; 95% CI 0.37 to 1.27; p=0.23) and all-cause mortality (HR 0.79; 95% CI 0.53 to 1.46; p=0.62) were observed between groups at 2-year follow-up. Significantly fewer patients experienced target-vessel reinfarction in the drug-eluting stent group (1.3%; 7/575) compared to the bare-metal stent group (3.4%; 19/582), HR 0.37 (95%CI 0.15 to 0.87; p=0.023). No difference in the proportions of patients who had any reinfarction was observed between groups (HR 0.64; 95% CI 0.35 to 1.16; p=0.14). Ischaemia-driven target-lesion revascularisation was needed in 3.1% (17/575) of patients in the drug-eluting stent group and 8.2% (46/582) of patients in the bare-metal stent group (HR 0.36; 95% CI 0.21 to 0.63; p<0.001). Similarly, significant differences in the occurrence of any target-lesion revascularisation were also observed between groups (HR 0.35; 95% CI 0.21 to 0.59; p<0.001). With respect to procedure-related adverse events, no significant differences in rates of procedure-related stroke and stent thrombosis were observed between groups.

Strengths and limitations

Strengths

The following strengths were identified:

- Baseline clinical and procedural characteristics were well balanced between both treatment groups.
- Independent outcome assessors were blinded to treatment allocations to minimise bias.
- Analysis was performed using the intention-to-treat approach.
- After the procedure rates of compliance to recommended medications were similar between groups at each follow-up period.

Limitations

The following limitations were identified:

- Authors stated that the use of glycoprotein inhibitor (GPI) was left to the discretion of the operator. It was not clear how many patients in each group received GPIs.
- Patients and treating physicians were not blinded to treatment allocations.
- The trial indicated that biolimus-eluting stents were superior to bare-metal stents in relation to composite outcome measures; however, authors acknowledge that the trial was not sufficiently powered to address individual components of safety and efficacy.

Impact on guideline

CG167 makes recommendations on PPCI using bare-metal stents in patients with STEMI but does not make any recommendations on PPCI using drug-eluting stents. Raber et al (2014) highlights the potential benefits of using contemporary drug-eluting stents over bare-metal stents in patients with STEMI. Topic experts highlighted that drug-eluting stent prices have decreased significantly since their initial introduction and felt that this may have cost implications on procurement. Experts also highlighted that there are various types of drug-eluting stents available and they may not have comparable safety and efficacy profiles.

Antithrombin therapy

We selected Shahzad et al. (2014) for a full commentary because it assesses the safety and efficacy of 2 antithrombins (bivalirudin versus unfractionated heparin) commonly used during PPCI in patients with STEMI.

What the guideline recommends

CG167 incorporates recommendations from NICE's technology appraisal guidance on bivalirudin for the treatment of ST-segment-elevation myocardial infarction:

1.2.2 Bivalirudin in combination with aspirin and clopidogrel is recommended for the treatment of adults with STEMI undergoing primary PCI.

Methods

Shahzad et al. (2014) performed an open-label RCT including 1,812 patients with STEMI who received bivalirudin or unfractionated heparin during PPCI.

Patients over 18 years with STEMI were enrolled unless they had intolerance, hypersensitivity, or contraindications to trial medications; active bleeding at presentation; artificial ventilation; reduced consciousness level or other factors precluding administration of oral antiplatelet therapy or their physician refused to administer antiplatelet loading. Patients were randomly allocated to groups at presentation, before entry to the catheterisation laboratory. Randomisation was stratified by age and presence of cardiogenic shock.

All patients received dual antiplatelet therapy before PPCI. Subsequently, patients received the assigned medication (bolus dose of 70U/Kg of heparin or 0.75mg/Kg of bivalirudin) after entry to the catheter laboratory but before angiographic findings were known. PPCI was performed by 1 of 14 interventional cardiologists who were blinded to treatment allocations. Primary outcome measures were the incidence of major bleeding as well as the composite rate of mortality, cerebrovascular accident, reinfarction and target- lesion revascularisation. Secondary outcome measures included minor bleeding, stent thrombosis and cardiac enzyme release. Analysis was performed using the intention-to-treat approach.

Results

Patients were followed-up for 28 days. The primary outcome (composite of mortality, cerebrovascular accident, reinfarction and target-lesion revascularisation) was reported in 8.7%

(79/905) of patients in the bivalirudin group and 5.7% (52/905) of patients in the heparin group (risk ratio [RR] 1.52; 95% CI 1.09 to 2.13; p=0.01). In relation to individual major adverse cardiac events, no significant differences in mortality rates and cardiovascular accident rates were observed between groups. The incidence of new myocardial infarction or reinfarction was significantly higher in the bivalirudin group (RR 3.01; 95% CI 1.36 to 6.66; p=0.004). Additionally, the incidence of additional unplanned revascularisation was reported in 2.7% (24/905) of patients in the bivalirudin group and 0.7% (6/907) of patients in the heparin group (RR 4.01; 95% CI 1.65 to 9.76; p=0.001).

The risk of stent thrombosis was significantly higher in the bivalirudin group compared to the heparin group (RR 3.91; 95% CI 1.61 to 9.52; p=0.001). Similar rates of bleeding events were observed between groups. No significant differences in major and minor bleeding rates were observed between groups. Furthermore, no significant differences in thrombocytopenia rates and door to device times were reported between groups.

Strengths and limitations

Strengths

The following strengths were identified:

- Randomisation was stratified to ensure that confounding factors were evenly distributed between groups.
- All outcome measures were assessed by an independent committee which was blinded to treatment allocations.
- Similar proportions of patients in each group underwent thrombus aspiration or received glycoprotein inhibitor (abciximab) as bailout treatment during PPCI.
- Similar numbers of patients in each group were lost to follow-up or excluded from analysis at the end of the study period. Reasons for losses to follow-up and exclusion were clearly outlined by authors.

Limitations

The following limitations were identified:

- Authors acknowledged that a number of patients died after randomisation but before consent was obtained.

Impact on guideline

The guideline states that bivalirudin in combination with aspirin and clopidogrel is recommended for the treatment of adults with STEMI undergoing PPCI. This study suggests that unfractionated heparin confers better outcomes than bivalirudin. Topic experts stated that this study was the first study to compare bivalirudin and heparin with equal use of GPI inhibitors in both study arms.

How we made the decision

We check our guidelines regularly to ensure they remain up to date.

- In relation to unstable angina and NSTEMI: early management (2010) NICE guideline CG94, we based the decision on surveillance 6 years after the publication of the guideline.
- In relation to myocardial infarction with ST-segment elevation: acute management (2013) NICE guideline CG167, we based the decision on surveillance 2 years after the publication of the guideline.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Previous surveillance update decisions for CG94 are on our website. No previous surveillance was performed for CG167.

New evidence for CG94

We found 6 new studies in a search for systematic reviews published between 10 May 2012 and 26 January 2016. We also considered 2 additional studies identified by members of the guideline committee who originally worked on this guideline.

Evidence identified in previous surveillance 2 years after publication of the guideline was also considered. This included 76 studies identified by search. No studies were identified in comments received during consultation on the 2-year surveillance decision.

From all sources, 84 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A1: summary of new evidence from surveillance and references for all new evidence considered.

New evidence for CG167

We found 123 new studies in a search for RCTs published between 1 November 2012 and 22 January 2016. We also considered 1 additional study identified by members of the guideline committee who originally worked on this guideline.

From all sources, 124 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A2: summary of new evidence from surveillance and references for all new evidence considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders are consulted only if we decide to update the guideline following checks at 4 and 8 years after publication. Because 2- and 6-year surveillance reviews were performed, and the decision was to update both guidelines, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

NICE Surveillance programme project team

Sarah Willett
Associate Director

Philip Alderson
Consultant Clinical Adviser

Katrina Sparrow
Technical Adviser

Jeffrey T Essuman
Technical Analyst

The NICE project team would like to thank the topic experts who participated in the surveillance process.

ISBN: 978-1-4731-2061-7