6-year surveillance 2016 – Unstable angina and NSTEMI: early management

Appendix A: Decision matrix

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
Assessment of a patient's risk of future adverse cardiovascular events			
94 – 01 Which tables, equations, engines or scoring systems for patient-risk stratification are most predictive of death, re-infarction or other vascular events in patients with UA/NSTEMI? (1.2.1-1.2.5) **1.2.1 As soon as the diagnosis of unstable angina or NSTEMI is made, and aspirin and antithrombin therapy have been offered, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, Global Registry of Acute Cardiac Events [GRACE]).** **1.2.2 Include in the formal risk assessment:** • **a full clinical history (including age, previous myocardial infarction [MI] and previous percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG])** • **a physical examination (including measurement of blood pressure and heart rate)** • **resting 12-lead electrocardiography (ECG) (looking particularly for dynamic or unstable patterns that indicate myocardial ischaemia)** • **blood tests (such as troponin I or T, creatinine, glucose and haemoglobin).** **1.2.3 Record the results of the risk assessment in the patient's care record.** **1.2.4 Use risk assessment to guide clinical management, and balance the benefit of a treatment against any risk of related adverse events in the light of this assessment.** **1.2.5 Use predicted 6-month mortality to categorise the risk of future adverse cardiovascular events as follows**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, feedback from topic experts did not			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
indicate that the guideline should be updated. This review question should not be updated.			
<u>3-year surveillance (2012)</u> A systematic review)[1] was identified which evaluated the use of risk scores in clinical decision making in acute coronary syndromes (ACS). Analysis of GRACE scores revealed pooled c-statistic values of 0.83 and 0.80 at short- and long-term follow-up, respectively: follow-up duration was not specified. Analysis of TIMI scores revealed pooled c-statistic values of 0.54 and 0.67 at short- and long-term follow-up, respectively. The review indicated that other scores may also be potentially useful and should be investigated further. One non-randomised comparative study[2] was identified which investigated the accuracy of the SYNTAX score, CSS score, NERS score, ACEF score, GRACE score and the TIMI score for risk assessment of 1-year mortality, cardiac mortality, myocardial infarction, target vessel revascularization and stent thrombosis in patients with non-ST elevation acute coronary syndromes (NSTE-ACS) undergoing percutaneous coronary intervention. The study	No relevant evidence identified.	One topic expert highlighted that more cardiovascular centres are starting to use GRACE and CRUSADE scores in patients with NSTEMI who receive antithrombotic medications. Conversely, 2 topic experts stated that risk stratification is not used widely and many clinicians prefer to offer an invasive strategy to the majority of patients with a diagnosis of NSTEMI.	No new evidence was identified that would affect recommendations. Topic experts were unable to provide consistent feedback indicating that the guideline should be updated.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
concluded that risk scores incorporating clinical and angiographic variables had the highest predictive accuracy for a broad spectrum of ischaemic end points. One case series[3] aimed to develop a practical risk score to predict the risk and implications of major bleeding in ACS. The study concluded that a simple risk score based on 6 baseline measures plus anticoagulation regimen identifies patients at increased risk for non-coronary artery bypass grafting-related bleeding and subsequent 1-year mortality. The development of a clinical risk algorithm to predict patient risk in patients undergoing percutaneous coronary intervention (PCI) was discussed in 1 study[4]. The authors concluded that further study is warranted to confirm the application of the algorithm in clinical practice. The predictive value of the SYNTAX score for risk assessment of 1-year clinical outcomes in patients with NSTE-ACS undergoing PCI was assessed in 1 study[5]. The results of the study indicated that, in this population, the SYNTAX score was an independent predictor of the			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
1-year rates of death, cardiac death, myocardial infarction and target vessel revascularization. Topic experts stated that the guidance highlighted the importance of assessing the risk of bleeding. There was additional research in this area but experts were unaware whether comparisons had been made between different risk assessment scores. The identified new evidence evaluated a range of risk scoring systems. It was considered that there was insufficient consistent new evidence in this area of the guideline. Additionally, the new evidence was considered unlikely to invalidate the guideline recommendation which states: As soon as the diagnosis of unstable angina or NSTEMI is made, and aspirin and antithrombin therapy have been offered, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, GRACE).			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
Antiplatelet therapy			
94 – 02 What is the efficacy and safety of aspirin therapy in the medical management of patients with UA or NSTEMI compared to placebo? (1.3.1-1.3.3) **1.3.1 Offer aspirin as soon as possible to all patients and continue indefinitely unless contraindicated by bleeding risk or aspirin hypersensitivity.** **1.3.2 Offer patients a single loading dose of 300 mg aspirin as soon as possible unless there is clear evidence that they are allergic to it.** **1.3.3 For patients with aspirin hypersensitivity, clopidogrel monotherapy should be considered as an alternative treatment. (This recommendation is from 'MI – secondary prevention', NICE clinical guideline 172.)**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
94 – 03 Which antiplatelet is most effective for managing patients with UA or NSTEMI? (1.3.4-1.3.8) Note: this clinical question has been amended after reviewing new evidence on antiplatelet therapy. **1.3.4 As soon as the risk of adverse cardiovascular events has been assessed, offer a loading dose of 300 mg clopidogrel in addition to aspirin to patients with a predicted 6-month mortality of more than 1.5% and no contraindications (for example, an excessive bleeding risk).** **1.3.5 Offer a 300-mg loading dose of clopidogrel to all patients with no contraindications who may undergo PCI within 24 hours of admission to hospital.** **1.3.6 Offer clopidogrel as a treatment option for up to 12 months to people who have had an NSTEMI, regardless of treatment. (This recommendation is from MI – secondary prevention, NICE clinical guideline 172.)** **1.3.7 Consider discontinuing clopidogrel treatment 5 days before CABG in patients who have a low risk of adverse cardiovascular events.** **1.3.8 For patients at intermediate or higher risk of adverse cardiovascular events, discuss the continuation of clopidogrel before CABG with the cardiac surgeon and base the decision on the balance of ischaemic and bleeding risk.**			
Surveillance decision No new evidence was identified from literature searches. One systematic review was highlighted by topic experts; however, it was not specific to clopidogrel. Feedback from topic experts strongly indicated that the guideline needs to be updated because newer antiplatelets are being recommended by specialist societies. This review question should be updated.			
3-year surveillance (2012) An RCT[6] evaluated the impact of upstream clopidogrel in patients with NSTE-ACS requiring coronary artery bypass grafting (CABG). In patients treated with clopidogrel, a 5-day wash-out period (off clopidogrel) was recommended before CABG. The study concluded that administration of clopidogrel before catheterisation in	No relevant evidence identified.	Topic experts highlighted a systematic review[18] which compared upstream administration of thienopyridines (prasugrel or clopidogrel) with placebo in patients with NSTEMI undergoing PCI. Pooled data from randomised controlled trials revealed no significant difference in mortality rates between patients treated by thiendopyridines and those who received no treatment. Compared to no	New evidence identified that may change current recommendations. No relevant evidence was identified from literature searches. Furthermore, the study proffered by 1 topic expert assessed the efficacy of 1 class of medications (thienopyridines) and was not specific to clopidogrel. There was a strong indication from topic experts that the guideline may need updating. They

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
patients with NSTE-ACS requiring CABG is associated with fewer 30-day adverse ischaemic events without significantly increasing major bleeding. One RCT[7] was identified which compared a loading dose of 600mg clopidogrel with 300mg clopidogrel in 256 patients with NSTE-ACS undergoing early PCI. The results of the study indicated that there was a modest incremental antiplatelet effect of a 600mg loading dose of clopidogrel, however, 600mg compared with 300mg clopidogrel did not reduce adverse clinical outcomes to 6 months. One RCT[8] compared double-dose clopidogrel with standard dose clopidogrel and either higher or lower dose aspirin in 25, 086 patients with ACS. The study concluded that there was no significant difference in primary outcomes for the treatment regimens tested. A subgroup analysis of the RCT[9] investigated the effect of various clopidogrel and aspirin regimens in prevention of major cardiovascular events in patients with ACS undergoing PCI. The results of the study indicated that a double-dose clopidogrel regimen was		treatment, upstream administration of thienopyridines was associated with higher major bleeding rates and lower rates of major adverse cardiac events. There was a strong indication from topic experts that the guideline needed to be updated. Although no new evidence has been identified, experts stated that in practice it is considered 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. 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. Experts also highlighted that although ticarelor and prasugrel are more expensive than clopidogrel many cardiology centres have started using them instead of clopidogrel. Topic experts also suggested that there is some evidence that dual antiplatelet therapy (DAPT) should be considered for	highlighted that newer antiplatelets are considered more efficacious than clopidogrel and aspirin; however, clinicians need to balance potential risk and benefits. They highlighted that European and American guidelines have now incorporated these considerations in their recommendations. The identified new evidence, in combination with topic expert feedback, indicates that a full review of the evidence base on antiplatelets is needed to ensure that their role in treating NSTEMI is clearly defined.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
associated with a reduction in cardiovascular events compared with the standard dose. A meta-analysis[10] evaluated the risk of CABG in patients with ACS continuing clopidogrel therapy. The study concluded that further multinational trials are required to fully determine the balance of ischaemia and bleeding. A systematic review[11] was identified which assessed the use of clopidogrel in combination with aspirin for patients with NSTE-ACS. Clopidogrel was found to be effective in reducing adverse cardiovascular events in patients with NSTE-ACS at intermediate and high risk of ischaemic events. A meta-analysis[12] was identified which concluded that new oral antiplatelet regimens are associated with a reduction in mortality, reinfarction and in-stent thrombosis in patients with ACS without an overall increase in major bleeding. <u>Clopidogrel versus ticagrelor</u> In the PLATO trial[13] 18, 624 patients with acute ST elevation (STEMI) and NSTE-ACS were randomised to either ticagrelor or clopidogrel in addition to aspirin. Total		prolonged periods of time (over 12 months) in patients treated by drug eluting stents.	

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
major bleeding was similar between both groups although ticagrelor was associated with increased non-procedure-related major bleeding after 30 days of treatment. Furthermore, sub-studies of the PLATO trial reported the following: Ticagrelor is a preferred option compared with clopidogrel for patients with ACS in whom an early invasive strategy is planned.[14] A pre-specified analysis in 5216 patients admitted to hospital for ACS who were specified as planned for non-invasive management benefited from ticagrelor treatment with results consistent with those from the overall PLATO results.[15] Treatment with ticagrelor compared with clopidogrel significantly reduced the rate of death from vascular causes or myocardial infarction without an increase in the rate of overall major bleeding but with an increase in the rate of non-procedure-related bleeding.[16] <u>Clopidogrel versus prasugrel</u> A sub-group analysis of the TRITON-TIMI 38 trial[17] evaluated treatment with aspirin plus clopidogrel or prasugrel in patients with ACS undergoing PCI without stent			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
implantation. The study concluded that prasugrel reduced ischaemic events and increased bleeding events to a similar magnitude as among patients who received stents. Topic experts highlighted that clopidogrel had reached the end of its patent and was commercially available in generic form. They suggested that this have an impact on cost-effectiveness. Experts also revealed that enoxaparin was due to reach the end of its patent. One topic expert suggested that the guideline could consider the use of potent antiplatelet agents (such as prasugrel and ticagrelor), and small molecule glycoproteins. Another topic expert noted that newer antiplatelets and antithrombins may be more effective than clopidogrel in certain sub-sets of patients. In summary, several studies were identified comparing different doses of clopidogrel; however, they reported conflicting results. Ticagrelor and Prasugrel were the subject of separate Technology Appraisals and were not considered in CG94. • TA236: Ticagrelor for the treatment			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
of acute coronary syndromes (2011) • TA182: Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention, (2009) It was considered that the identified new evidence was unlikely to change the direction of the guideline recommendations which state: As soon as the risk of adverse cardiovascular events has been assessed, offer a loading dose of 300mg clopidogrel in addition to aspirin to patients with a predicted 6-month mortality of more than 1.5% and no contraindications (for example, an excessive bleeding risk) Offer a 300mg loading dose of clopidogrel to all patients with no contraindications who may undergo PCI within 24 hours of admission to hospital.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
94 – 04 What is the efficacy and safety of adding a GPI (tirofiban, eptifibatide and abcixmab) to aspirin and heparin therapy in the medical management of patients with UA or NSTEMI compared to the combination of aspirin and LMWH? (1.3.9-1.3.11) **1.3.9 Consider intravenous eptifibatide or tirofiban as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.** **1.3.10 Consider abciximab as an adjunct to PCI for patients at intermediate or higher risk of adverse cardiovascular events who are not already receiving a GPI.** **1.3.11 Balance the potential reduction in a patient's ischaemic risk with any increased risk of bleeding, when determining whether a GPI should be offered**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Feedback from topic experts did not indicate that the guideline should be updated. This review question should not be updated.			
3-year surveillance (2012) Glycoprotein IIb/IIIa inhibitors A Cochrane systematic review[19] was identified which assessed the effects and safety of glycoprotein IIb/IIIa inhibitors (GPIs) when administered during PCI and as an initial medical treatment for patients with NSTE-ACS. The review concluded that glycoprotein IIb/IIIa inhibitors failed to reduce mortality rates when administered as initial medical treatment. However, when administered during PCI, intravenous GPIs reduced the risk of death at 30 days and at six months although the risk of severe bleeding is	No relevant evidence identified.	Topic experts highlighted that the use of GPIs has reduced and cheaper alternatives are now available. No additional information was provided.	No new evidence was identified that would affect recommendations. None of the comments from topic experts contradicted guideline recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
increased. A second systematic review[20] found that triple antiplatelet therapy based on intravenous GPIs was more effective than aspirin-based dual therapy in reducing vascular events in patients with NSTEMI. One systematic review[21] evaluated whether intracoronary administration of GPIs was superior to intravenous administration for patients with ACS undergoing PCI. The review indicated that intracoronary administration of GPIs significantly increased target coronary flow and myocardial reperfusion without increasing the risk of bleeding complication; however, no significant differences in clinical outcomes were observed when compared with intravenous administration. Similar results were reported in a meta-analysis.[22] One systematic review[23] evaluated the use of GPIs as part of early medical management in patients with NSTE-ACS. Three additional systematic reviews were identified that reported conflicting results, with one study concluding that upstream administration of GPIs did not improve clinical outcomes compared to			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
downstream selective administration[24] whilst two other systematic reviews indicated that in NSTE-ACS treatment with upstream GPIs provided ischaemic benefit[25],[26]. An RCT[27] assessed immediate and early outcomes in patients with NSTE-ACS who received tirofiban with conventional therapy compared with those who received conventional therapy (combination of aspirin, clopidogrel, heparin with or without beta-blockers and angiotensin-converting enzyme inhibitors) only. The study concluded that tirofiban improved the outcome of patients with high-risk NSTE-ACS. A systematic review[28] was identified which assessed the efficacy of tirofiban compared with usual care or other GPIs. Tirofiban was found to be more effective than usual care for NSTE-ACS patients receiving planned PCI and medical management. One RCT[29] which evaluated the efficacy and safety of tirofiban in high-risk patients with NSTE-ACS after PCI reported that tirofiban administration was safe and effective in this population.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
A post-hoc analysis of an RCT[30] examined efficacy and safety of early eptifibatide in the setting of concurrent upstream clopidogrel use in patients with NSTE-ACS. The results of the study revealed that early eptifibatide use reduced 30-day death/myocardial infarction among patients with intended upstream clopidogrel but not among those without intended upstream clopidogrel use. An RCT[31] evaluated the long-term efficacy of abciximab bolus-only with aspirin and clopidogrel pretreatment and systematic coronary stenting. The results of the study indicated that similar efficacy, up to 3 years after PCI, was observed in subgroup analysis including patients with unstable angina and NSTEMI. In summary, several systematic reviews and meta-analyses were identified focusing on the use of GPIs. The timings of treatments, patient populations, use of adjunctive therapies and invasive strategies varied across the literature making it difficult to make comparisons between the studies. As a result, it was considered that the identified new literature was unlikely to change the			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
direction of the guideline recommendation which states: Consider intravenous eptifibatide or tirofiban as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.			
94 – 05 What is the efficacy and safety of adding a GPI (tirofiban, eptifibatide and abcixmab) to aspirin and heparin therapy as adjunct therapy to patients with UA/ NSTEMI undergoing PCI compared to the combination of aspirin and LMWH? (1.3.9-1.3.11) **1.3.9 Consider intravenous eptifibatide or tirofiban as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.** **1.3.10 Consider abciximab as an adjunct to PCI for patients at intermediate or higher risk of adverse cardiovascular events who are not already receiving a GPI.** **1.3.11 Balance the potential reduction in a patient's ischaemic risk with any increased risk of bleeding, when determining whether a GPI should be offered.**			
Surveillance decision Since the previous surveillance review, 1 systematic review has been identified from literature searches which supports guideline recommendations. Feedback from topic experts did not indicate that the guideline should be updated. This review question should not be updated.			
3-year surveillance (2012) A Cochrane systematic review[19] was identified which assessed the effects and safety of glycoprotein IIb/IIIa inhibitors	One systematic review[35] of 60 RCTs, including 66,689 patients, compared the efficacy of add-on intravenous GPI during PCI with that of placebo or usual care.	Topic experts stated that evidence does not indicate a need for major changes to the guideline. One topic expert felt that the use of GPIs has reduced because	New evidence is consistent with guideline recommendations. The identified new study highlighted the

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
(GPIs) when administered during PCI and as an initial medical treatment for patients with NSTE-ACS. The review concluded that glycoprotein IIb/IIIa inhibitors failed to reduce mortality rates when administered as initial medical treatment. However, when administered during PCI, intravenous GPIs reduced the risk of death at 30 days and at six months although the risk of severe bleeding is increased. One systematic review[21] evaluated whether intracoronary administration of GPIs was superior to intravenous administration for patients with ACS undergoing PCI. The review indicated that intracoronary administration of GPIs significantly increased target coronary flow and myocardial reperfusion without increasing the risk of bleeding complication; however, no significant differences in clinical outcomes were observed when compared with intravenous administration. Similar results were reported in a meta-analysis.[22] One RCT[32] was identified which revealed that although abciximab reduced the 30-day and 1-year incidence of major adverse cardiac events in patients with	Myocardial infarction rates were significantly lower in the in the GPI group at 30-day but not at 6-month follow-up. At 6 months, GPIs significantly reduced the composite rate of all-cause mortality or myocardial infarction. Conversely, GPIs significantly increased the odds of severe bleeding. Authors stated that results were were less marked for patients pre-treated with clopidogrel.	cheaper alternatives are now available.	benefits of adding GPI to standard blood thinning agents in patients with NSTEMI. This is broadly in line with guideline recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
NSTE-ACS undergoing PCI, treatment did not improve the impact of left ventricular ejection fraction over 6-8 months of follow-up. One RCT[33] evaluated the efficacy and safety of abciximab in Japanese patients undergoing PCI for unstable angina. No significant difference in the incidence of coronary events was reported between between the abciximab group and the placebo group. One RCT[34] compared a strategy of early, routine administration of eptifibatide with delayed, provisional administration in patients with NSTE-ACS assigned to an invasive strategy. The results of the study indicated that the use of eptifibatide 12 or more hours before angiography was not superior to the provisional use of eptifibatide after angiography and was associated with an increased risk of non-life threatening bleeding. In summary, several systematic reviews and meta-analyses were identified focusing on the use of GPIs. However, as timings of treatments, patient populations, use of adjunctive therapies and invasive strategies varied across the literature,			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
making it difficult to make comparisons between the studies. As a result, it was considered that the identified studies were unlikely to impact on guideline recommendations.			
Antithrombin therapy			
94 – 06 What is the efficacy and safety of adding a LMWH compound to aspirin (with or without clopidogrel) in the medical management of patients with UA or NSTEMI compared to the combination of unfractionated heparin and aspirin (with or without clopidogrel)? (1.4.2, 1.4.4, 1.4.5) **1.4.2 Offer unfractionated heparin as an alternative to fondaparinux to patients who are likely to undergo coronary angiography within 24 hours of admission.** **1.4.4 Consider unfractionated heparin, with dose adjustment guided by monitoring of clotting function, as an alternative to fondaparinux for patients with significant renal impairment (creatinine above 265 micromoles per litre).** **1.4.5 Offer systemic unfractionated heparin (50–100 units/kg) in the cardiac catheter laboratory to patients receiving fondaparinux who are undergoing PCI.**			
Surveillance decision Since the previous surveillance review, no new evidence that would affect guideline recommendations has been identified from literature searches. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
94 – 07 What is the efficacy and safety of adding a factor Xa inhibitor (fondaparinux) to aspirin in the medical management of patients with UA or NSTEMI compared to the combination of LMWH/ UFH and aspirin therapy? (1.4.1, 1.4.2) **1.4.1 Offer fondaparinux to patients who do not have a high bleeding risk, unless coronary angiography is planned within 24 hours of admission.** **1.4.2 Offer unfractionated heparin as an alternative to fondaparinux to patients who are likely to undergo coronary angiography within 24 hours of admission.**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Feedback from topic experts did not indicate that the guideline should be updated. However, it was suggested that the guideline could refer to a Technology appraisal on Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome (March 2015) TA335. This review question should not be updated. Instead, the guideline should list TA335 as related NICE guidance			
3-year surveillance (2012) One study[36] was identified which evaluated the cost-effectiveness of anticoagulants in patients with ACS. The results of the analysis indicated that fondaparinux is cost effective compared with enoxaparin whilst bivalirudin in patients with ACS treated invasively is cost effective compared with heparin plus a GPI. A cost-effectiveness analysis[37] was identified which aimed to compare the short-term costs and long-term cost-effectiveness of fondaparinux and enoxaparin for NSTE-ACS. The study concluded that fondaparinux is a more	No relevant evidence identified.	One expert stated that the use of anti-thrombotic medication in acute coronary syndromes is a complex area and an updated guideline based on review of the contemporary evidence would be helpful. They pointed out that European Society of Cardiology and American College of Cardiology guidelines on acute coronary syndromes have recently been updated to take account of new evidence. One topic expert highlighted that the guideline should refer to the Technology Appraisal on Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome (March 2015) TA335.	No new evidence was identified that would affect recommendations. None of the comments from topic experts contradicted guideline recommendations. However, it was suggested that the guideline could refer to a Technology appraisal on Rivaroxaban (TA335). It must be noted that the Technology Appraisal focusses on management of NSTEMI after hospital discharge. This is currently outside the scope of CG94. Thus, it is recommended that this question should not be updated and CG167 could refer to TA335 as related nice guidance.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
cost-effective antithrombotic agent in NSTE-ACS. One RCT[38] was identified which compared the incidence of adverse cardiac outcomes of enoxaparin versus unfractionated heparin in the management of NSTE-ACS. The results of the study indicated that enoxaparin use led to a decrease in the incidence of ischaemic events. Several other studies were identified which indicated a benefit of fondaparinux treatment in patients with ACS.[39,40,41,42,43] Three studies[44,45,46] were identified which compared apixaban with placebo, in addition to standard antiplatelet therapy in patients with NSTE-ACS. In all the studies a dose-related increase in bleeding was observed. Authors concluded that further testing of apixaban was required. One RCT[47] compared rivaroxaban with placebo in patients with a recent ACS. The results of the study indicated that rivaroxaban reduced the risk of death from myocardial infarction or stroke however an increased risk of major bleeding was observed.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
In a RCT[48] which evaluated the efficacy and safety of otamixaban in patients with NSTE-ACS authors reported that otamixaban reduced ischaemic events however they suggested that further research was required. One RCT[49] assessed the safety and tolerability of different doses of darexaban for the prevention of ischaemic events in patients with ST-elevation acute coronary syndrome or NSTE-ACS. Results revealed higher bleeding rates in the darexaban arms of the study compared with the placebo arm. An RCT[50] was identified which compared the efficacy and safety of dalteparin, a low molecular weight heparin, with a standard unfractionated heparin in patients with unstable angina. The study concluded that dalteparin is as effective and safe as unfractionated heparin in the treatment of unstable angina. In summary, no consistent new evidence was identified which would invalidate the current guideline recommendations on anti-thrombin therapy. The identified new evidence indicated a beneficial effect of treatment with fondaparinux and other			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
factor Xa inhibitors. No studies comparing factor Xa inhibitors with aspirin were identified. Thus it was considered that the new evidence was unlikely to impact on guideline recommendations which state: Offer fondaparinux to patients who do not have a high bleeding risk, unless coronary angiography is planned within 24 hours of admission.			
94 – 08 What is the efficacy and safety of adding a synthetic pentasaccharide (fondaparinux and enoxaparin) to aspirin as adjunct therapy to patients with UA/ NSTEMI undergoing PCI compared to the combination of LMWH/UFH and aspirin therapy? (1.4.1, 1.4.2) **1.4.1 Offer fondaparinux to patients who do not have a high bleeding risk, unless coronary angiography is planned within 24 hours of admission.** **1.4.2 Offer unfractionated heparin as an alternative to fondaparinux to patients who are likely to undergo coronary angiography within 24 hours of admission.**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Feedback from topic experts did not indicate that the guideline should be updated. This review question should not be updated.			
3-year surveillance (2012) A subgroup analysis of the synergy trial[51] reported that patients who received enoxaparin before PCI had improved outcomes compared with those who did not. A subgroup analysis from the ACUITY	No relevant evidence identified.	One expert stated that the use of anti-thrombotic medication in acute coronary syndromes is a complex area and an updated guideline based on review of the contemporary evidence would be helpful. They pointed out that European Society of Cardiology and American College of	No new evidence was identified that would affect recommendations. None of the comments from topic experts contradicted guideline recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
trial[52] was unable to demonstrate an association between adverse ischaemic outcomes with the timing of antithrombin administration in patients with NSTE-ACS undergoing an early invasive management strategy. An RCT[53] compared the safety of two unfractionated heparin regimens during PCI in high-risk patients with NSTE-ACS initially treated with fondaparinux. The results of the study indicated that low-dose compared with standard-dose unfractionated heparin did not reduce major peri-PCI bleeding. A systematic review[54] was identified which assessed the efficacy and safety of unfractionated heparin plus GPIs compared with controls during revascularization for an ACS. Minor bleeding was increased in the groups taking unfractionated heparin plus GPIs although no difference in mortality between the two groups was observed. It was considered that the identified evidence was unlikely to impact on guideline recommendations.		Cardiology guidelines on acute coronary syndromes have recently been updated to take account of new evidence. The American College of Cardiology made no reference to synthetic pentasaccharides whereas the European Society of cardiology states: “Overall, fondaparinux is considered to be the parenteral anticoagulant with the most favourable efficacy–safety profile and is recommended regardless of the management strategy, unless the patient is scheduled for immediate coronary angiography.”	

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
94 – 09 What is the efficacy and safety of adding a Thrombin inhibitor (Bivalirudin) to the combination of aspirin, with or without a GPI, in the medical management of patients with UA or NSTEMI compared to the combination of LMWH/UFH, aspirin, with or without a GPI? (1.4.3, 1.4.6, 1.4.7) **1.4.3 Carefully consider the choice and dose of antithrombin in patients who have a high risk of bleeding associated with any of the following:** • **advancing age** • **known bleeding complications** • **renal impairment** • **low body weight.** **1.4.6 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients who:** • **are at intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3%), and** • **are not already receiving a GPI or fondaparinux, and** • **are scheduled to undergo angiography (with follow-on PCI if indicated) within 24 hours of admission.** **1.4.7 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients undergoing PCI who:** • **are at intermediate or higher risk of adverse cardiovascular events, and** • **are not already receiving a GPI or fondaparinux.**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) Several studies were identified which	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
compared bivalirudin with heparins in patients with NSTE-ACS. The results of 1 RCT [55] (which compared heparin plus GPIs versus bivalirudin in ACS patients pre-treated with 600mg clopidogrel) indicated that there were no differences between the groups for the outcomes measured although, in one study[56], treatment with bivalirudin led to a significant decrease in the risk of bleeding complications. One RCT[57] was identified which examined the impact of gender and antithrombotic therapy for NSTE-ACS. The results of the study indicated that, in women, bivalirudin therapy compared with a GPI-based strategy resulted in significantly decreased bleeding but similar rates of ischaemia and mortality. From an assessment of the abstracts it was not possible to determine the risk score of study populations and the background therapy used. Furthermore,, interpretation of bivalirudin trial data was complicated by differences in dosages, duration of therapy, adjunctive therapies and study populations. The guideline indicates that trials comparing bivalirudin with heparin and GPIs suggest that			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
bivalirudin may offer equivalent ischaemic protection with reduced bleeding. No new literature was identified which would change this conclusion.			

94 – 10 What is the efficacy and safety of adding a Thrombin inhibitor (Hirudin and Bivalirudin) to the combination of aspirin and a GPI as adjunct therapy to patients with UA/ NSTEMI undergoing PCI compared to the combination of LMWH/UFH, aspirin, and a GPI? (1.4.3, 1.4.6, 1.4.7)

1.4.3 Carefully consider the choice and dose of antithrombin in patients who have a high risk of bleeding associated with any of the following:

- **advancing age**
- **known bleeding complications**
- **renal impairment**
- **low body weight.**

1.4.6 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients who:

- **are at intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3%), and**
- **are not already receiving a GPI or fondaparinux, and**
- **are scheduled to undergo angiography (with follow-on PCI if indicated) within 24 hours of admission.**

1.4.7 As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients undergoing PCI who:

- **are at intermediate or higher risk of adverse cardiovascular events, and**
- **are not already receiving a GPI or fondaparinux.**

Surveillance decision

Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
question were provided by topic experts. This review question should not be updated.			
<u>3-year surveillance (2012)</u> Sub-group analyses of the ACUITY trial concluded that bivalirudin is an effective anticoagulant in PCI for ACS[58] and that bivalirudin significantly reduced bleeding complications compared with heparin without any negative impact on ischaemic outcomes at 1 year.[59] It was considered that the identified study was had no impact on guideline recommendations.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
Management strategies			
94 – 11 In adults with UA or non-ST elevation MI does early invasive investigation (i.e. angiography) with intent to assess for (and in those patients deemed suitable, to perform) revascularization improve outcomes in comparison with initial conservative treatment, with or without later angiography? (1.5.1-1.5.3, 1.1.1) **1.5.1 Offer coronary angiography (with follow-on PCI if indicated) within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%) if they have no contraindications to angiography (such as active bleeding or comorbidity). Perform angiography as soon as possible for patients who are clinically unstable or at high ischaemic risk.** **1.5.2 Offer conservative management without early coronary angiography to patients with a low risk of adverse cardiovascular events (predicted 6-month mortality 3.0% or less).** **1.5.3 Offer coronary angiography (with follow-on PCI if indicated) to patients initially assessed to be at low risk of adverse cardiovascular events (predicted 6-month mortality 3.0% or less) if ischaemia is subsequently experienced or is demonstrated by ischaemia testing.**			
Surveillance decision Studies identified in this 6-year review reported no differences in some outcomes of patients treated by early invasive investigation and those treated by conservative approaches. Topic expert feedback highlighted that early invasive management improves other outcome measures which, in turn, could impact on cost effectiveness. This review question should be updated.			
3-year surveillance (2012) Eleven studies were identified which concluded that an early invasive strategy is not superior to a selective or delayed invasive strategy in patients with NSTE-ACS.[60,61,62,63,64,65,66,67,68,69,70] However, one RCT[71] indicated that an immediate strategy was associated with an increased rate of myocardial infarction compared with a 24-48 hr delayed	One systematic review[78] of 8 RCTs assessed outcomes of 5,761 patients with a moderate to high risk of NSTEMI who received angiography within 96 hours of presentation. Results revealed that patients who received angiography within 2 hours had a higher risk of recurrent myocardial infarction than those who received angiography after 2 hours. Furthermore, no significant difference in	One topic expert highlighted an RCT[80] (RITA-3 trial) of 1,810 patients with NSTEMI treated by a routine early invasive strategy (coronary angiography and myocardial revascularisation within 72 hours of presentation) or selective invasive strategy (coronary angiography for recurrent ischemia only). Authors report that there was no significant difference in all-cause mortality rates	New evidence identified that may change current recommendations. The studies identified during this 6-year review highlighted no significant differences in stroke rates and mortality rates in patients treated by early invasive investigation compared to those treated by conservative treatment. Topic experts highlighted that there is an ongoing

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
strategy. In addition, a sub-group analysis of the ACUITY trial[72] indicated that delaying revascularization with PCI by 24 hours in patients with NSTE-ACS was an independent predictor of early and late mortality and adverse ischaemic outcomes. One study[61] which included an economic analysis demonstrated slightly increased costs associated with an early invasive strategy. A meta-analysis[73] evaluated whether a routine invasive strategy reduces the long-term frequency of cardiovascular death or nonfatal myocardial infarction in patients with NSTE-ACS. The results indicated that a routine invasive strategy reduces the long-term rates of cardiovascular deaths or myocardial infarction with the largest absolute effect seen in higher-risk patients. A Cochrane systematic review[74] investigated the benefits of an invasive compared with a conservative strategy for treating UA/NSTEMI. The review revealed that an invasive strategy is associated with reduced rates of refractory angina and rehospitalisation in the short term and decreased myocardial infarction in the long term plus an increased risk of	the rate of major bleeding events was observed in patients who received angiography within 2 hours and those who underwent the procedure after 2 hours. Major bleeding events decreased only with angiography performed within 12 compared to more than 12 hours. There were no significant differences in the odds of death or stroke between time-points (time-points not specified). One systematic review[79] compared clinical outcomes of patients with NSTEMI who underwent PCI within 24 hours of presentation (early PCI) against those who received PCI more than 24 hours after presentation (delayed PCI). Meta-analysis of 7 RCTs, including 13,762 patients, revealed no significant difference between groups in the odds of composite outcome of death or non-fatal myocardial infarction at 30 day follow-up. Results revealed that patients who received delayed PCI had lower odds of repeat revascularisation than those who received early PCI. Conversely, the early PCI group had lower odds of bleeding than the delayed PCI group.	between groups at 10-year follow-up. Topic experts highlighted that there is an ongoing debate about whether angiography centres should have 24/7 capabilities for interventional procedures (angioplasty). 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. This may influence the health economic modelling performed in CG94. One topic expert suggested that patients with suspected NSTE-ACS are increasingly being offered coronary angiography (invasive strategy) and systematic use of risk stratification is not widely used. Another topic expert added that there is an issue about the quality and consistency of risk stratification. He stated that data from the GRACE registry suggests that cardiologists do not always select patients with NSTEMI who are at highest ischaemic risk and the evidence points to greatest benefit of early angiography in those at highest risk.	debate about whether angiography centres should have 24-hour capabilities to perform angioplasty. Experts also highlighted that early invasive confers improvements in other outcomes; including reduced radiation exposure, less renal nephropathy, reduced tariffs and shorter length of stay. This may influence the health economic modelling performed in CG94. As a result, this clinical question should be updated to clarify the role of early invasive investigation in patients with NSTEMI.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
bleeding in patients with UA/NSTEMI, compared with a conservative strategy. The review concluded that an invasive strategy may be particularly useful in those at high risk for recurrent events. A meta-analysis[75] was identified which evaluated the effect of age on long-term outcomes after a routine invasive or selective invasive strategy in patients with NSTE-ACS. Authors reported that the long-term benefit of a routine invasive strategy over a selective invasive strategy is attenuated in patients aged <65 years and in women by the increased risk of early events. A post-hoc analysis of 1 RCT[76] investigated the association between actual in-hospital revascularization and long-term outcome in patients with NSTE-ACS. Results revealed that in-hospital revascularization was independently associated with a reduction in 4 year mortality; however, no differences in cumulative event rates were observed between the early invasive and selective invasive strategies. A sub-group analysis of the ACUITY trial[77] evaluated the impact of arterial			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
access site on bleeding and ischaemic outcomes in patients with ACS managed with an early invasive strategy. In summary, several studies compared an early invasive strategy with a delayed invasive strategy in patients with NSTE-ACS. However, as the studies considered different time frames for early and delayed invasive strategies, further evidence is required to assess the choice of an early invasive versus a delayed invasive approach. In addition, from an assessment of the abstracts it was not possible to determine the risk score of the study population which may have an impact on whether to use an early invasive or delayed invasive strategy. As such, there is currently insufficient consistent new evidence which would change the direction of the current guideline recommendations. Furthermore, a Cochrane systematic review compared a conservative strategy with an invasive strategy. The review concluded that an invasive strategy may be particularly useful in those at high risk for recurrent events. As such, the identified new evidence supported the			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
guideline recommendation which states: Offer coronary angiography (with follow-on PCI if indicated) within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%) if they have no contraindications to angiography (such as active bleeding or comorbidity). Perform angiography as soon as possible for patients who are clinically unstable or at high ischaemic risk			
94 – 12 In adults with UA or non-ST elevation MI does CABG improve outcomes in comparison with PCI? (1.5.4, 1.5.5) **1.5.4 When advising patients about the choice of revascularisation strategy (PCI or CABG), take account of coronary angiographic findings, comorbidities, and the benefits and risks of each intervention.** **1.5.5 When the role of revascularisation or the revascularisation strategy is unclear, resolve this by discussion involving an interventional cardiologist, cardiac surgeon and other healthcare professionals relevant to the needs of the patient. Discuss the choice of revascularisation strategy with the patient.**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) A subgroup analysis of the ACUITY RCT[81] evaluated outcomes in patients	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
with ACS and multivessel coronary artery disease managed with PCI versus CABG. The results of the study indicated that 1-month and 1-year rates of mortality were comparable whilst patients treated with PCI more frequently developed recurrent ischaemia requiring repeat revascularization procedures during follow-up. In summary, the results of this subgroup analysis indicated that mortality rates between PCI and CABG were comparable for people with ACS. As such, this identified new evidence is unlikely to invalidate the current guideline recommendation which states: When advising patients about the choice of revascularization strategy (PCI or CABG), take account of coronary angiographic findings, comorbidities, and the benefits and risks of each intervention			
94 – 13 Does the use of Intra-Aortic Balloon Pump Counterpulsation affect the outcome of patients with non-ST elevation myocardial infarction or unstable angina? (Not linked to any guideline recommendation)			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.
94 – 14 In patients with UA/NSTEMI who do not undergo angiography, does investigation prior to hospital discharge for myocardial ischaemia affect outcome? (1.5.6)			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.
94 – 15 Does pre-discharge assessment of left ventricular function predict future risk in patients with UA/NSTEMI? (1.5.7-1.5.9) **1.5.7 Assessment of left ventricular function is recommended in all patients who have had an MI. (This recommendation is from 'MI – secondary prevention', NICE clinical guideline 172.)** **1.5.8 Consider assessing left ventricular function in all patients with unstable angina.** **1.5.9 Record measures of left ventricular function in the patient's care record and in correspondence with the primary healthcare team and the patient.**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.
94 – 16 Does management of inpatient care for people with unstable angina or NSTEMI by a specialist cardiology team vs non specialist team improve clinical outcomes? (Not linked to any guideline recommendation)			
Surveillance decision No new evidence was identified from systematic reviews in this 6-year surveillance review. Topic expert feedback suggested that this question should not be updated. This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	Topic experts stated that the question is unlikely to be answered by RCTs and systematic reviews. They stated that registry data is available; however, the available evidence may not be strong enough to make guideline recommendations.	No evidence was identified that would affect recommendations. No new evidence related to this clinical question was identified from literature searches. Topic expert feedback indicated that evidence from registries is available but may not be strong enough to make guideline recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
94 – 17 Do early psychosocial and educational interventions, mobilisation and discharge planning (cardiac rehabilitation – Phase 1) improve emotional and physical wellbeing and long-term outcomes in people with unstable angina or NSTEMI compared to deferred (cardiac rehabilitation Phase 2)? (1.5.10-1.5.12) **1.5.10 Before discharge offer patients advice and information about:** • **their diagnosis and arrangements for follow-up (in line with 'MI – secondary prevention', NICE clinical guideline 172)** • **cardiac rehabilitation (in line with 'MI – secondary prevention', NICE clinical guideline 172)** • **management of cardiovascular risk factors and drug therapy for secondary prevention (in line with 'MI – secondary prevention', NICE clinical guideline 172, and 'Lipid modification', NICE clinical guideline 67)** • **lifestyle changes (in line with 'MI – secondary prevention', NICE clinical guideline 172).** **1.5.11 Make cardiac rehabilitation equally accessible and relevant to all people after an MI, particularly people from groups that are less likely to access this service. These include people from black and minority ethnic groups, older people, people from lower socioeconomic groups, women, people from rural communities, people with a learning disability and people with mental and physical health conditions. (This recommendation is from MI – secondary prevention, NICE clinical guideline 172.)** **1.5.12 All patients who smoke should be advised to quit and be offered support and advice, and referral to an intensive support service (for example, the NHS Stop Smoking Services) in line with 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health guidance 1). (This recommendation is adapted from 'MI – secondary prevention', NICE clinical guideline 172.)**			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This review question should not be updated.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
Areas not currently covered in the guideline			
NQ – 01 What is the clinical and cost effectiveness of drug-eluting stents in patients with unstable angina or NSTEMI undergoing PCI? (New question derived from TA152 [Drug-eluting stents for the treatment of coronary artery disease] following discussions by Guidance Executive)			
Surveillance decision The identified new evidence (from 1 systematic review) is unlikely to impact on the guideline. New evidence was identified in the 2-year surveillance review of the clinical guideline on the acute management of ST-segment elevation myocardial infarction (CG167); prompting addition of a question on drug-eluting stents to the clinical guideline, It was proposed that CG94 and CG167 should be combined under 1 guideline. As a result, this clinical question should be added to ensure that recommendations in the combined guideline cover the use of drug-eluting stents for different types of acute coronary syndromes. This review question should be added.			
3-year surveillance (2012) No relevant evidence identified.	One systematic review[82] of 26 RCTs explored long-term outcomes of women who received PCI with drug eluting stents according to type of ACS. Analysis revealed that the 3-year crude mortality rate was 4.9% in women with stable angina, 6.1% for women with unstable angina or NSTEMI and 9.4% for women with STEMI (results were statistically significant). Conversely, no significant difference in crude mortality rates between 1 and 3 years across clinical presentations. After multivariable adjustment, STEMI was independently associated with greater risk of 3-year mortality, whereas no differences were observed between unstable angina or NSTEMI and stable angina.	In 2014, NICE Guidance Executive considered that it may be appropriate to update Technology Appraisals 71 (Guidance on the use of coronary artery stents) and 152 (Drug-eluting stents for the treatment of coronary artery disease) in any updates of the clinical guidelines on STEMI (CG167) and NSTEMI (CG94). During the 2-year surveillance review of CG167, which was performed concurrently with this 6-year review of CG97, evidence was identified which indicated that this clinical question should be added to the CG167. Topic experts suggested that the use of drug-eluting stents in patients with acute coronary syndromes has increased substantially in recent years due to	New evidence is unlikely to impact on the guideline The identified systematic review made no comparisons between drug-eluting stents and bare metal stents. Furthermore, no comparisons were made were made between different types of drug-eluting stents. New evidence was identified in the 2-year surveillance review of the clinical guideline on the acute management of STEMI (CG167), prompting addition of a question on drug-eluting stents to the guideline. It was proposed that CG94 should be combined with CG167 to form 1 clinical guideline. As a result, this clinical question should be added to

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
		evidence that newer generation drug-eluting stents are associated with favourable outcomes, compared to bare metal stents. Furthermore, topic experts highlighted that the costs of drug-eluting stents have fallen substantially in recent years.	ensure that NICE's recommendations on the use of stents will be brought together within the entire context of management of the conditions.
Research recommendations			
RR – 01 What is the clinical and cost effectiveness of the systematic use of risk scoring systems (in addition to clinical assessment) for ischaemic outcomes and bleeding complications in the management of unstable angina and NSTEMI (at all levels of risk) compared with clinical assessment alone?			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This research recommendation will be considered again at the next surveillance point.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect this research recommendation.
RR – 02 For patients with unstable angina and NSTEMI (at differing levels of risk), how do clinical outcome data (adverse cardiovascular events and bleeding complications) collected in cardiac registries compare with data derived from randomised clinical trials?			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This research recommendation will be considered again at the next surveillance point.			
3-year surveillance (2012)	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
No relevant evidence identified.			affect this research recommendation.
RR – 03 What is the efficacy and cost effectiveness of CABG versus PCI in the management of patients with NSTEACS?			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This research recommendation will be considered again at the next surveillance point.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect this research recommendation.
RR – 04 What is the efficacy and cost effectiveness of intra-aortic balloon counterpulsation (IABP) in the management of patients with non ST-segment elevation ACS?			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This research recommendation will be considered again at the next surveillance point.			
3-year surveillance (2012) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would affect this research recommendation.
RR – 05 What is the role of ischaemia testing in people after an acute coronary syndrome and what is the comparative efficacy and cost effectiveness of the different non-invasive tests (for example, stress ECG, echocardiography, radionuclide scanning and magnetic resonance imaging)?			
Surveillance decision The identified new evidence provides some evidence of the benefit of using specific non-invasive tests; however, no comparisons were made between non-invasive tests. This research recommendation will be considered again at the next surveillance point.			

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
3-year surveillance (2012) Topic experts also highlighted that imaging techniques such as, optical coherence tomography, magnetic resonance imaging, intravascular ultrasound, fractional flow reserve imaging and non-invasive perfusion imaging could assist in diagnosis of patients presenting with suspected ACSs.	A meta-analysis[83] of 12 studies, including 6,988 patients with NSTEMI, explored the diagnostic accuracy of combining cardiac troponin and copeptin assessments. Results revealed pooled sensitivity and specificity estimates of 0.95 (95% CI: 0.89 to 0.98) and 0.57 (95% CI: 0.49 to 0.65), respectively. One meta-analysis[84] of 5 randomised controlled trials aimed to "evaluate the potential of using B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) as surrogate markers to guide clinical interventional or conservative therapy decisions." Authors reported no significant difference in all-cause mortality rates of patients who received early invasive treatment or conservative treatment guided by BNP or NT-proBNP tests.	Topic experts suggested that CG94 could refer to a NICE guideline on highly specific troponin: Myocardial infarction (acute): early rule out using high-sensitivity troponin tests' (October 2014) DG15. One topic expert stated that the introduction of high sensitivity troponin assays is changing the management of patients with suspected acute coronary syndrome due to the ability to detect lower levels of elevated troponin earlier. As a consequence the prevalence of unstable angina may change and the relevance of this diagnosis is becoming unclear.	New evidence is unlikely to affect this research recommendation. The guideline states that blood tests, such as troponin tests, should be included in the formal risk assessment. The identified systematic reviews add further evidence supporting the guideline recommendation. However, more comparative studies are needed to establish which non-invasive tests are most beneficial in patients with STEMI.
RR – 06 What is the comparative efficacy and cost effectiveness of systems involving specialised care compared to non-specialised care?			
Surveillance decision Since the previous surveillance review, no new evidence was identified that would affect guideline recommendations. Furthermore, no comments related to this clinical question were provided by topic experts. This research recommendation will be considered again at the next surveillance point.			
3-year surveillance (2012)	No relevant evidence identified.	None identified relevant to this question.	No evidence was identified that would

Summary of evidence from previous surveillance	Summary of new evidence from 6-year surveillance	Summary of new intelligence from 6-year surveillance	Impact
No relevant evidence identified.			affect this research recommendation.

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