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All co-authors have no conflict of interest to declare.

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Abbreviations

CAD	Coronary artery disease
CPG	Clinical practice guideline
DM	Diabetes mellitus
DTB	Door to balloon time
DTN	Door to needle time
EMS	Emergency medical services
fPPCI	Facilitated primary percutaneous coronary intervention
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
IHD	Ischemic heart disease
KSA	Kingdom of Saudi Arabia
NICE	National Institute for Health and Care Excellence
QALY	Quality adjusted life year
RCT	Randomized controlled trial
ROSC	Return of spontaneous circulation
RR	Relative risk
STEMI	ST-elevation myocardial infarction
tPA	Tissue plasminogen activator
TNKase	Tenecteplase
PCI	Percutaneous coronary intervention
PPCI	Primary percutaneous coronary intervention
US	Unstable angina
WHO	World Health Organization

Contents

The Saudi Center for Evidence Based Health Care (EBHC)

The Saudi Centre for Evidence Based Health Care has managed and supported the coordination of the process of clinical practice guideline (CPG) development between the methodological team from McMaster University and the local clinical expert panel members in Saudi Arabia.

The EBHC staff members recruited local clinical experts through contacting Saudi specialist societies and also independent experts interested in developing reliable and most up-to-date CPGs to harmonize the treatment and provide the highest quality of health care in the kingdom of Saudi Arabia. These experts were health care professionals of multidisciplinary backgrounds. As much as possible, patient's representatives were also included in panels.

In an effort to make national recommendations, the participating experts were professionals from the Ministry of Health (MoH), National Guard Hospitals, King Faisal Specialist Hospital and Research Centre (KFSHRC), University Hospitals, Security Forces Hospitals, Prince Sultan Military Medical City (PSMMC) and from some private hospitals.

Based on a preselection of available evidence syntheses, the EBHC provided a list of potential topics to be addressed in CPGs after thorough consultations with the local stakeholders. These topics were further discussed with the McMaster team for important selection criteria and agreed on 12 topics for wave 2.

The guideline panel meetings were held in Riyadh on 15th-18th March 2015 where 96 local experts working in Saudi Arabia participated with the methodological support from 20 experts from McMaster University and its partners from the American University of Beirut, Lebanon, and the University of Freiburg, Germany, in providing high quality recommendations for common and important clinical conditions in the Kingdom.

The Saudi Centre for EBHC supports the efforts for dissemination of the CPGs by publishing online the full reports of the CPGs, facilitates writing concise versions of the CPGs for publication in peer reviewed medical journals, sending hard copies to hospitals and health care centers.
Finally, a mobile App has been introduced in KSA to facilitate the dissemination efforts of the completed practice guidelines.

The staff members at the Saudi Centre for EBHC:
***Dr Zulfa Al Rayess**, Consultant Family Medicine, Head of Saudi Center for EBHC*
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Executive Summary

Introduction

Ischemic heart disease (IHD) is the leading cause of morbidity and mortality around the world and its prevalence is expected to continue to increase in developing countries.[1] This is as a consequence of increasing prevalence of coronary artery disease (CAD) risk factors including hypertension, diabetes mellitus, dyslipidemia, obesity and smoking.[2] Acute presentations of IHD (Acute Coronary Syndrome – ACS) include ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarctions (NSTEMI) and unstable angina (US). STEMI is a clinical syndrome characterized by symptoms of myocardial ischemia in association with persistent ST segment elevation on the electrocardiogram (ECG), and subsequent release of biomarkers of cardiac necrosis.

The SPACE registry, a prospective registry of ACS in 17 hospitals in the Kingdom of Saudi Arabia (KSA), reported STEMI presentation in 41.5% of patients presenting with ACS.[3] Data from the registry suggest there is a high prevalence of CAD risk factors in the Saudi population including 58% of patients with diabetes mellitus (DM), the highest ever reported rate in an ACS population. Patients presenting with ACS were younger (mean age 58 years) compared with other populations. Among patients presenting with STEMI, only 14.8% received timely administration of thrombolytics (within 30 minutes of presentation) and 17.5% of patients received primary percutaneous coronary intervention (PPCI).

Given the importance of this topic, the Ministry of Health of the Kingdom of Saudi Arabia with the support of the McMaster University working group produced practice guidelines to assist health care providers in evidence-based decision-making on the management of ST-segment elevation myocardial infarction.

Methodology

This practice guideline is a part of the larger initiative of the Ministry of Health of the Kingdom of Saudi Arabia to establish a program of rigorous development of guidelines. The ultimate goals are to provide guidance for clinicians and other healthcare decision makers and reduce unnecessary variability in clinical practice across the Kingdom.

The Saudi expert guideline panel selected the topic of this guideline and all healthcare questions addressed herein using a formal prioritization process. For all selected questions we updated existing systematic reviews on myocardial infarction with ST-segment elevation published in July 2013 by the National Clinical Guideline Centre for the National Institute for Health and Care Excellence (NICE).[4] We also conducted systematic searches for information that was required to develop full guidelines for the KSA, including searches for information about patients' values and preferences, and costs and resource use specific to the Saudi context. Based on the systematic reviews we prepared summaries of available evidence supporting each recommendation following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach.[5] We used this information to prepare GRADE *evidence-to-decision* frameworks that served the guideline panel to follow the structured consensus process and transparently document all decisions made during the meeting (see Appendix 1). The guideline panel met in Riyadh on March 15 & 16, 2015 and formulated all recommendations during this meeting. Potential conflicts of interests of all panel members were managed according to the World Health Organization (WHO) rules.[6]

As a quality measure for any practice guideline prior to publication, the final report have been externally peer reviewed by a methodological expert who has not been involved in this guideline development.

How to use these guidelines

The guideline working group developed and graded the recommendations and assessed the quality of the supporting evidence according to the GRADE approach.[7] Quality of evidence (confidence in the estimates of effects) is categorized as: high, moderate, low, or very low based on consideration of risk of bias, indirectness, inconsistency, imprecision, and publication bias of the estimates as well as factors that lead to upgrading the quality of the evidence. High quality evidence indicates that we are very confident that the *true* effect lies close to that of the estimate of the effect. Moderate quality evidence indicates moderate confidence, and that the *true* effect is likely close to the estimate of the effect, but there is a possibility that it is substantially different. Low quality evidence indicates that our confidence in the effect estimate is limited, and that the *true* effect may be substantially different. Finally, very low quality evidence indicates that the estimate of effect of interventions is very uncertain, the *true* effect is likely to be substantially different from the effect estimate and further research is likely to have important potential for reducing the uncertainty.

The strength of recommendations is expressed as either strong ('guideline panel recommends…') or conditional ('guideline panel suggests…') and has explicit implications (see Table 1).[8] Understanding the interpretation of these two grades is essential for sagacious clinical decision making.

Table 1: Interpretation of strong and conditional (weak) recommendations

Implications	Strong recommendation	Conditional (weak) recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations	Policy making will require substantial debate and involvement of various stakeholders.

Key questions

1. Should fibrinolysis vs. delayed primary percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset to hospitals not capable of PPCI services?

2. Should facilitated primary percutaneous coronary intervention (fPPCI) ver-

sus PPCI alone be used in patients with STEMI?
3. Should routine thrombus extraction devices during PPCI versus PPCI alone be used for treatment of STEMI?
4. Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?
5. Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?
6. Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?
7. Should high volume centres versus low volume centres be used for PPCI services?
8. Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?
9. Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?

Recommendations

Recommendation 1:
The panel suggests using fibrinolytic therapy over delayed PPCI if there is a total time delay >120 minutes. (conditional recommendation, very low quality evidence)

Remarks:

- The total time delay of 120 minutes refers to the period from the first contact with the patient to the provision of PPCI.
- For patients presenting directly to a PCI-capable facility the suggested acceptable time delay to provision of PPCI is 90 minutes (i.e. door-to-balloon time).

Recommendation 2:
The panel suggests against using fPPCI in patients with STEMI. (conditional recommendation, very low quality evidence)

Remarks:

- Facilitated PPCI (fPPCI) should not be confused with a pharmacoinvasive PPCI strategy

Recommendation 3:
The panel recommends against routine use of aspiration or thrombus extraction devices in patients with STEMI. (strong recommendation, moderate quality evidence)

Recommendation 4:
The panel suggests multi-vessel PPCI over culprit-only PCI for patients with multi-vessel coronary artery disease undergoing PPCI. (conditional recommendation, low quality evidence)

Remarks:

- This recommendation is based on evidence with data predominantly from patients undergoing multi-vessel PCI during the index procedure, but the procedure may also be considered during the index hospitalization.
- This recommendation does not apply to patients with cardiogenic shock.

Recommendation 5:
The panel recommends early revascularization for patients with cardiogenic shock due to STEMI. (strong recommendation, moderate quality evidence)

Recommendation 6:
The panel suggests immediate angiography followed by PCI where indicated over usual care in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest. (conditional recommendation, very low quality evidence)

Remarks:

- For patients with unwitnessed out of hospital arrest, without documented time of arrest, the clinician may re-evaluate the patient for PCI with detailed assessment of the patient's neurological status before proceeding with a potentially futile intervention.

Recommendation 7:
The panel suggests prioritizing the management of patients with STEMI to high volume centres. (conditional recommendation, very low quality evidence)

Remarks:

- The implementation of this recommendation should not restrict care for patients who require PPCI in settings where only low-volume centres are available.

Recommendations 8, 9 and 10:
The panel suggests rescue PCI over conservative management (conditional recommendation, low quality evidence) **and suggests rescue PCI over repeated fibrinolysis** (conditional recommendation, low quality evidence) **in patients with STEMI who failed to reperfuse after fibrinolytic therapy. The panel suggests not offering repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy** (conditional recommendation, low quality evidence)**.**

Remarks:

- When there is no available immediate urgent access for the patient at a catheterization lab for the rescue PCI procedure, treating clinicians should determine with a lab if access to rescue PCI can become available for such patients.
- There should not be a repeated administration of streptokinase. The risk of adverse events with repeat administration of streptokinase is higher than the benefit.

Recommendation 11:
The panel suggests routine early angiography over routine deferred or selective angiography in patients with STEMI successfully treated by fibrinolysis. (conditional recommendation, moderate quality evidence)

Scope and purpose

The purpose of this document is to provide guidance about the management of ST-segment elevation myocardial infarction. The target audience of these guidelines includes primary care providers, cardiologists, interventional cardiologists, emergency medicine physicians, intensivists, hospital pharmacists, emergency medical services and paramedics, as well as policy makers in the Kingdom of Saudi Arabia (KSA). Other health care professionals may also benefit from these guidelines.

Given the importance of this topic, the Ministry of Health (MoH) of Saudi Arabia with the support of the McMaster University working group produced practice guidelines to assist health care providers in evidence-based decision-making. This practice guideline is a part of the larger initiative of the Ministry of Health of Saudi Arabia to establish a program of rigorous adaptation and de novo development of guidelines in the Kingdom; the ultimate goal being to provide guidance for clinicians and other healthcare decision makers and reduce unnecessary variability in clinical practice across the Kingdom.

Introduction

Ischemic heart disease (IHD) is the leading cause of morbidity and mortality worldwide and its prevalence is expected to increase in developing countries.[1] This is as a consequence of increasing prevalence of coronary artery disease (CAD) risk factors including hypertension, diabetes mellitus, dyslipidemia, obesity and smoking.[2] Acute presentations of IHD (Acute Coronary Syndrome – ACS) include ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarctions (NSTEMI) and unstable angina (US). STEMI is a clinical syndrome characterised by symptoms of myocardial ischemia in association with persistent ST segment elevation on the electrocardiogram (ECG), and subsequent release of biomarkers of cardiac necrosis.

The SPACE registry, a prospective registry of ACS in 17 hospitals in the Kingdom of Saudi Arabia (KSA) included hospitalized patients with ACS over a 24 month period. Of the 5055 patients included, 2096 (41.5%) presented with a STEMI.[3] The prevalence of CAD risk factors in the Saudi population is higher than that reported in European and US registries including 58% of patients with diabetes mellitus (DM), the highest ever reported rate in an ACS population. Patients presenting with ACS were younger (mean age 58 years) compared with populations reported in other registries. 41.5% of patients presenting with ACS had a STEMI; only 14.8% received timely administration of thrombolytics (within 30 minutes of presentation) and 17.5% of patients received primary percutaneous coronary intervention (PPCI). The Gulf RACE-2 registry, a multinational study included patients from KSA,[9] reported 45.6% patients presenting with ACS had STEMI with a mean age of 54 years and a high prevalence of risk factors. 79% of STEMI patients presented within 12 hours of symptom onset with a median time from symptom onset to hospital arrival of 178 minutes. In spite of the earlier age of presentation with STEMI, overall these patients had a 30 day mortality of 9.9% and 1 year mortality of 11.5%.

Although registry data with baseline characteristics, management practices and outcomes have been published for the KSA population, local studies of the interventions in this population addressed in the guideline are not available.

Methodology

To facilitate the interpretation of these guidelines; we briefly describe the methodology we used to develop and grade recommendations and quality of the supporting evidence.

The Saudi expert guideline panel selected the topic of this guideline and all healthcare questions addressed herein using a formal prioritization process. For the selected questions we updated existing systematic reviews on myocardial infarction with ST-segment elevation published in July 2013 by the National Clinical Guideline Centre (NCGC) for the National Institute for Health and Care Excellence (NICE).[4] For each question, the McMaster guideline working group updated the search strategy to identify new studies and/or new systematic reviews. When relevant, the meta-analyses were updated. We also conducted systematic searches for information that was required to develop full guidelines for the KSA, including searches for information about patients' values and preferences, and costs and resource use specific to the Saudi context (see **Appendix 2**).

Next, we developed for each question an evidence profile and an evidence-to-decision (EtD) table following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach and shared them with the panel members (see **Appendix 1**).[5,10] The guideline panel was invited to provide additional information, particularly when published evidence was lacking. The final step consisted of an in-person meeting of the guideline panel in Riyadh on March 15 & 16, 2015 to formulate the final recommendations. We used the GRADE evidence-to-decision frameworks to follow a structured consensus process and transparently document all decisions made during the meeting. Potential conflicts of interests of all panel members were managed according to the World Health Organization (WHO) rules.[6]

Grading of the quality of evidence

The GRADE working group defines the quality of evidence as the extent of our confidence that the estimate of an effect is adequate to support a particular decision or recommendation.[7] We assessed the quality of evidence using the GRADE approach.

Quality of evidence is classified as "high", "moderate", "low", or "very low" based on decisions about methodological characteristics of the available evidence for a specific health care problem. The definition of each category is as follows:

- *High*: We are very confident that the true effect lies close to that of the estimate of the effect.
- *Moderate*: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- *Low*: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- *Very low*: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Grading of the strength of recommendations

The GRADE working group defines the strength of recommendation as the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects. According to the GRADE approach, the strength of a recommendation is either strong or conditional (also known as or called weak) and has explicit implications.[8] Understanding the interpretation of these two grades – either strong or conditional – of the strength of recommendations is essential for sagacious clinical decision-making. (see **Table 1**)

As a quality measure for any practice guideline prior to publication, the final report have been externally peer reviewed by a methodological expert who has not been involved in this guideline development.

How to use these guidelines

The Ministry of Health of Saudi Arabia and McMaster University Practice Guidelines provide clinicians and their patients with a basis for rational decisions about the management of ST-segment elevation myocardial infarction. Clinicians, patients, third-party payers, institutional review committees, other stakeholders, or the courts should never view these recommendations as dictates. As described in other guidelines following the GRADE approach, no guideline or recommendation can take into account all of the often-compelling unique features of individual clinical circumstances. Therefore, no one charged with evaluating clinicians' actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion.

Statements about the underlying values and preferences, resources, feasibility, equity, acceptability as well as other qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate an accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines if they influence the strength or direction of the recommendation.

Key questions

The following is a list of the clinical questions selected by the panel and addressed in this guideline.

1. Should fibrinolysis vs. delayed primary percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset to hospitals not capable of PPCI services?
2. Should facilitated percutaneous coronary intervention (fPPCI) versus PPCI be used in patients with STEMI?
3. Should routine thrombus extraction devices during PPCI versus PPCI alone be used for treatment of STEMI?
4. Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?
5. Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?
6. Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?
7. Should high volume centres versus low volume centres be used for PPCI services?
8. Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?
9. Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?

Recommendations

For each of the recommendations below we describe the considerations and judgements made by the panel on the available evidence about the factors in the evidence-to-decision framework (i.e. benefits and harms of the options, resource use, feasibility, acceptability, balance of desirable and undesirable consequences, etc.). With respect to patients' values and preferences, unless otherwise noted for specific questions, the panel including the patient representative considered that there is no important variability or uncertainty in patients' values and preferences in the KSA setting for the outcomes considered across the questions addressed (i.e. mortality, stroke, reinfarction, heart failure, repeat revascularization, bleeding). The panel considered that patients would place a high value on benefits such as reduction in

mortality and lower value on potential adverse effects.

Question 1: Should fibrinolysis vs. delayed percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset to hospitals not capable of PPCI services?

Background: ST elevation myocardial infarction is caused by complete occlusion of a coronary artery by a thrombus causing cessation of downstream blood flow. This results in myocyte (heart muscle cell) death which rapidly progresses unless blood flow is restored. Timely intervention to restore flow is critical to myocardial salvage and restoring heart function.

Restoration of coronary blood flow (reperfusion) can occur by primary percutaneous coronary intervention (PPCI) using mechanical techniques in the cardiac catheterization laboratory or by thrombolytics (clot dissolving drugs that can be given intravenously). Due to ease of administration, thrombolytics can be initiated in any healthcare setting. In contrast, PPCI requires transfer to a facility that has a cardiac catheterization laboratory that is capable of performing PPCI, the time required to transfer the patient will add to the delay in reperfusion. Delay in reperfusion increases the risk of impaired left ventricular systolic function and death.[11,12]

Results of meta-analyses of randomized controlled trials (RCT) have demonstrated that timely PPCI is superior to thrombolysis with lower rates of mortality, re-infarction and stroke.[13,14] The advantage of PPCI over thrombolytics is diminished with increasing PPCI-related time delay (the additional time lost before reperfusion due to transfer of patient to a PPCI capable facility).

Timeliness of PPCI is assessed by the 'door to balloon time' (DTB), defined as the time from arrival at the hospital to inflation of the angioplasty balloon in the infarct related artery. For thrombolytics, this measure is the 'door to needle time' (DTN), defined as the time from arrival to the hospital to the administration of thrombolytics. In addition to the DTB time, the PPCI related time delay includes the additional time required for transport to a PPCI capable hospital. This incorporates the additional time required to transfer the patient to a PPCI capable facility instead of administering thrombolytics in the health care facility where the patient initially presents.

This question reviews the impact of delays to treatment on outcomes for 'PPCI after transfer' compared to thrombolytics administered at the presenting facility. The data were reviewed to determine if there is a PCI related time delay at which fibrinolysis becomes more effective in patients presenting with STEMI.

The preferred agents for fibrinolysis are tissue plasminogen activator (tPA) or tenecteplase (TNKase), while streptokinase should be used if tPA or TNKase are not available in a specific hospital or setting. Streptokinase is an antigenic thrombolytic agent; significant levels of antistreptokinase antibodies can form within a few days of administration and can persist for 4 years in up to 50% of patients. The antibodies may cause an allergic reaction or neutralize a further dose of streptokinase and render it ineffective [15]. Streptokinase is not recommended if a repeat dose of thromblytic is administered in a patient who has received a dose of streptokinase in the past.

Summary of Findings: The 2012 NICE systematic review included 6 meta-regression studies that addressed this question. A subsequent literature search for the time period from November 2012 to November 2014 did not identify any new meta-regression studies. Among the 6 meta-regressions included, 3 used study level data,[16,17,18] 2 used individual patient data compiled from randomized controlled trials[19,20] and one was based on a large registry.[21] The overall quality of evidence was judged as very low.

Benefits of the Option: PPCI and fibrinolysis are both accepted forms of reperfusion therapy in patients presenting with STEMI within 12 hours of symptom onset. Benefits of reperfusion therapy are closely related to the time

from symptom onset to delivery of reperfusion therapy; reperfusion therapy should be delivered as soon as possible after presentation. Although PPCI decreases adverse outcomes compared to thrombolytics, this benefit decreases with increasing delays. Based on all available evidence, the panel determined that if PPCI can be performed within a total delay of 120 minutes from first contact with the patient to the time of the procedure, it is superior to fibrinolysis with regard to 30 day mortality based on the very low quality evidence.

Harms of the Option: With longer duration of delay related to transfer for PPCI, the rate of adverse outcomes increased, if transfer to a PPCI capable hospital cannot be achieved within the specified timeframe, fibrinolysis is the preferred choice of treatment.

Resource Use: No KSA specific data was identified. From the 2012 NICE systematic review, two cost-utility analyses showed that PPCI was cost effective compared to in-hospital fibrinolysis, except at long PPCI-related time delays. Based on data from the study by Asseburg,[16] it was estimated that PPCI had a 90% probability of being cost effective (at threshold of £20,000 per QALY) based on average PPCI-related time delay of 64 minutes, which related to a median call-to-balloon time of 130 minutes. PPCI was less effective and more costly compared to fibrinolysis for patients transferred from hospital to a separate PPCI centre with time delays of 100 minutes (median call-to-balloon time of 167 minutes). The panel considered that up to the acceptable time delay the resources required would be small and that the incremental cost was small relative to the net benefits.

Acceptability: The panel considered that both intervention options are effective and acceptable to the patient population and to stakeholders including clinicians. If either intervention can be performed in a timely fashion, PPCI is superior to fibrinolysis. However in the absence of the ability for expedited transfer to a PPCI capable facility, fibrinolysis provides improved outcomes compared to no treatment.

Feasibility: Fibrinolysis is readily administered in many health care facilities. PPCI is available in limited hospitals. The panel considered both options feasible, but noted that rapid transfer to a PPCI capable hospital may pose logistical challenges in the KSA setting. The SPACE registry cited the infrequent use of ambulances (5.1% in 'own' patients), traffic congestion in major cities as potential reasons for delays in presentation and transfer of patients.

Balance between desirable and undesirable consequences: Based on the available evidence suggesting equipoise between the two treatment options at a time delay of approximately 120 minutes, the panel considered that below this threshold of total time delay the desirable consequences of delayed PPCI compared to fibrinolysis would outweigh the undesirable consequences. There is a decreasing benefit of PPCI with considerable PPCI-related time delay, but up to a delay of 120 minutes from first patient contact (including transport time to PCI-capable facility) PPCI was considered to result in better outcomes for patients as compared to fibrinolysis. The strength of recommendation was judged as conditional due to very low quality evidence.

Recommendation 1:

The panel suggests using fibrinolytic therapy over delayed PPCI if there is a total time delay >120 minutes. (conditional recommendation, very low quality evidence)

Remarks:

- The total time delay of 120 minutes refers to the period from the first contact with the patient to the provision of PPCI.
- For patients presenting directly to a PCI-capable facility the suggested acceptable time delay to provision of PPCI is 90 minutes (i.e. door-to-balloon time).

Implementation Considerations and Monitoring: The panel noted that in the KSA setting emergency medical services (EMS) are poorly developed, therefore resulting in poor results for transport of patients. In order to meet the desired threshold of <120 minutes in total delay time where PPCI results in better outcomes for patients than fibrinolysis, improvement in transport of patients to PPCI capable facilities is required. As another consideration, the panel also noted that EMS personnel in the KSA are currently not certified to administer fibrinolysis in transport, and therefore patients may also experience longer delay times for fibrinolysis. For this recommendation the preferred agents for fibrinolysis are tissue plasminogen activator (tPA) or tenecteplase (TNKase), while streptokinase should be used if tPA or TNKase are not available in a specific hospital or setting. In a patient with a prior history of administration of streptokinase, due to the possibility of neutralizing anitibody formation and allergic reaction, a repeat dose should not be used.

The SPACE registry [3] reported that of 1232 STEMI patients, 905 (73.5%) presented to hospital at <12 hours of symptom onset. Only 8.3% of patients arrived to hospital in an ambulance. Alshahrani et al [22] reported in a 2014 study that there was a significant difference in pre-hospital delay for male patients (median 5h) versus female patients (median 12.9h) in a sample of 311 STEMI patients presenting to 3 hospitals in Riyadh between March 2011 and August 2011. In a chart review of 536 patients who underwent PPCI at King Abdulaziz Cardiac Centre between September 2008 and September 2012, the average door-to-balloon time was 87.7 minutes, with the average time in 2012 reduced to 72 minutes.[23] The results of these studies support the panel's assertion that a focus on improvements in transport of patients to PPCI capable facilities is required to help meet the suggested threshold of time delay to improve patient outcomes.

Question 2: Should facilitated percutaneous coronary intervention (fPPCI) versus percutaneous coronary intervention (PPCI) be used in patients with STEMI?

Background: ST elevation myocardial infarction (STEMI) is usually caused by thrombotic occlusion of a coronary artery causing cessation of blood flow resulting in myocardial cell necrosis. The mainstay of treatment is restoration of blood flow by mechanical (PPCI) or pharmacological (thrombolytics) means. Pharmacologic agents can be administered in the field or the emergency room before PPCI to 'facilitate' restoration of flow or prevention of propagation of thrombus in the coronary artery. Facilitated PPCI is a strategy in which pharmacologic agents are given to the patient with STEMI before the patient arrives in the catheterization lab. The drugs that have been used for facilitated PPCI include fibrinolytics and glycoprotein 2b/3a inhibitors or a combination of these 2 agents. These agents may increase the success of PPCI but may also cause increased adverse effects in the form of bleeding.

The term 'pharmacoinvasive therapy' has been inconsistently used to refer to various pharmacologic interventions administered before PCI. These have included full dose fibrinolytics, reduced dose fibrinolytics and other agents to improve perfusion; a strategy of full dose fibrinolytics followed by rescue PCI[24] as needed and use of non-hematologic pharmacologic agents such as complement antibodies and caspase inhibitors.[25] To avoid misinterpretation, the term 'facilitated PPCI' is being used in this context – this question will address the use of fibrinolytic agents or glycoprotein 2b/3a inhibitors administered before arrival to the cardiac catheterization laboratory in patients undergoing PPCI.

Summary of Findings: Our literature review identified two new studies[26,27] that were added to our meta-analysis and that were not included in the NICE systematic review[28-49]. The quality of evidence for the outcomes was

low to very low, with the overall quality of evidence judged as very low.

Benefits of the Option: Although facilitated PPCI increased vessel patency of the infarct related artery in preliminary studies, this did not translate into improved patient important outcomes. Benefit of facilitated PPCI was noted for only the outcome of heart failure at 6 [38,36] to 12 [26] months. The relative risk of heart failure was 0.48 (95% confidence interval of 0.28-0.83) in patients randomized to a fPPCI strategy. The evidence was based on a total of 55 events among 745 patients enrolled in these 3 trials that reported long term heart failure outcome and was judged to be of low quality. No benefit was found for the outcome of long term mortality, long term stroke, long term reinfarction and long term repeat revascularization. The panel noted that in the absence of a significant reduction in mortality, the reduction in heart failure seems to be of lesser significance, and the panel determined that the desirable anticipated effects of fPPCI are probably not large.

Harms of the Option: The fPPCI group incurred significantly higher rates of both major (relative risk of 1.47; 95% confidence interval of 1.05-2.05) and minor (relative risk of 1.43; 95% confidence interval of 1.20-1.71)bleeding. The panel concluded that the undesirable anticipated effects of fPPCI are probably not small.

Patients' Values and Preferences: The panel noted that for the outcome of minor bleeding, there could possibly be some variability in how patients view the outcome in the KSA setting, but overall noted that there probably is no important uncertainty or variability in patients' values and preferences.

Resource Use: The panel noted that implementation of fPPCI requires well developed emergency medical services, and that resources would be required to implement EMS transfer procedures to allow fPPCI. Additional training of personnel would be required for the drugs were to be administered before hospital admission, and that the resources required for this would not be small for minimal benefit with increased harm to patients.

Acceptability: Given the minimal net benefit and the increase in harm for patients, as well as the additional resources required for fPPCI, this option was found by the panel as not acceptable to the key stakeholders.

Feasibility: The panel concluded that the option of fPPCI would not be feasible in the KSA setting due to the lack of EMS services to administer fibrinolytic agents or glycoprotein 2b/3a inhibitors before arrival to the cardiac catheterization laboratory and that training would be required.

Balance between desirable and undesirable consequences: The panel considered there was more harm than benefit when using fPPCI, in addition to the feasibility and resource use issues identified for the KSA setting (i.e. lack of EMS), and therefore the undesirable consequences outweighed desirable consequences. The strength of recommendation is conditional due to very low quality evidence.

Recommendation 2:

The panel suggests against using fPPCI in patients with STEMI. (conditional recommendation, very low quality evidence)

Remark:

- Facilitated PPCI (fPPCI) should not be confused with a pharmacoinvasive PPCI strategy

Implementation Considerations and Monitoring: In the KSA there are currently not many PPCI centres doing fPPCI procedures, and the panel considered that no specific implementation considerations or active monitoring for this recommendation are required.

Question 3: Should routine thrombus extraction devices during percutaneous coronary intervention (PPCI) versus percutaneous coronary intervention (PPCI) alone be used for treatment of STEMI?

Background: STEMI is usually caused by complete occlusion of a major coronary artery by a thrombus. The initial event leading to a STEMI is commonly rupture or erosion of an atheromatous plaque. This exposes the thrombogenic plaque contents to the circulating blood activating the coagulation cascade and platelets which leads to formation of the occlusive thrombus. This thrombus is loosely adherent to the vessel wall and while attempting to open the occluded artery during PPCI, the thrombus may get dislodged and migrate downstream occluding smaller vessels. The distal obstruction may continue to cause myocardial damage and negate the beneficial effects of reopening the coronary artery.

In an attempt to limit damage caused by distal embolization of the thrombus, devices to remove the thrombus during PPCI have been extensively studied. These range from simple hollow aspiration catheters to powered mechanical devices which can be used to fragment and aspirate the thrombus if the thrombus burden appears large. The disadvantage of using these devices is the added time to the procedure and the complications associated with the use of the device.

Several small studies have suggested better myocardial perfusion and decreased infarct size with thrombectomy. New trials evaluating the effect of thrombectomy on patient important outcomes have been published including 2 recent large trials which together enrolled more patients than all previous trials. The first of these is the TASTE trial published in 2013 [50] (1 year results published in 2014 [51]). This trial enrolled 7244 patients and randomized them to PPCI alone or PPCI with thrombus aspiration. Crossover from one group to the other was discouraged, 93.9% of the patients in the thrombus aspiration group underwent thrombus aspiration; in addition, 4.9% of patients in the PPCI alone group underwent thrombus aspiration. The second trial pulished in 2015 is the TOTAL[52] trial which enrolled 10,732 patients and randomly assigned them to PPCI alone or routine manual thrombectomy. In this trial, 'bailout thrombectomy' was allowed if there was failure of the initial PPCI alone strategy, defined as thrombolysis in myocardial infarction (TIMI) flow grade of 0 or with a large thrombus after predilation or the persistence of a large thrombus after stent deployment. The rate of crossover was 4.6% from thrombectomy to PPCI alone and 1.4% from PPCI to thrombectomy. Bailout thrombectomy was performed in 7.1% in the PPCI alone group. Prespecified subgroup analyses in this trial included comparisons based on thrombus burden, duration of symptoms, initial TIMI flow, age, center volume and type of MI (anterior versus nonanterior).

Summary of Findings: In addition to the studies included in the NICE systematic review [53-72], we identified 4 additional trials [50-52,73,74] that addressed the question of thrombus extraction during PPCI. One of them [74] compared rheolytic thrombectomy with manual thrombus aspiration, and was not included in the meta-analysis. The results of a large trial, the TOTAL [52] trial assessing thrombus aspiration, were published in March of 2015 and, given its importance, the entire literature search was updated to April 2015 for this recommendation.The outcomes were analyzed separately by subgroup for thrombus aspiration and mechanical thrombus extraction (see evidence profile in Appendix 1). The overall quality of evidence was rated as moderate.

Benefits of the Option: Target vessel revascularization in the long term (6 to 12 months) was performed less frequently (relative risk 0.85, 95% confidence interval 0.73 – 1.00) in the thrombus aspiration subgroup, with an absolute effect of 10 fewer per 1000 patients (95% confidence interval: from 0 fewer to 18 fewer). There was no difference in the mechanical thrombus extraction subgroup or the

overall group (relative risk 0.90, 95% confidence interval 0.80-1.01) for this outcome. No benefit was noted for any of the other outcomes including mortality and re-infarction, and the panel concluded that overall the desirable anticipated effects are probably not large.

Harms of the Option: There was increased risk of stroke within 30 days in the subgroup of patients that underwent mechanical thrombus extraction (relative risk 2.03, 95% confidence interval 1.19-3.47), translating to an absolute effect of 3 more strokes per 1000 patients (95% confidence interval: from 1 more to 8 more) and in the thrombectomy group overall (relative risk 1.50, 95% confidence interval 1.00-2.24), with an absolute effect of 2 more strokes per 1000 patients (95% confidence interval: from 0 fewer to 5 more). The risk of major bleeding was similar between the thrombectomy group overall and the control group undergoing PPCI alone.

Resource Use: Based on data from the NICE systematic review the panel discussed the cost difference between thrombus aspiration devices (£110–£125) and mechanical thrombus extraction devices (£1200) and noted that in the KSA setting there is a similar cost difference between the two types of devices. The panel considered that for mechanical thrombus extraction devices the resources required would not be small, and that for thrombus aspiration devices resources required may be small but total volume costs for routine use would need to be considered. However, it was determined that in consideration of the high cost of the primary PCI procedure (estimated at 20,000 SAR for Ministry of Health hospitals) the additional resources required for thrombus aspiration would likely be small. With respect to incremental cost relative to the net benefit, the panel concluded that the incremental cost would probably not be small relative to the net benefits of both types of devices.

Acceptability: The panel considered that for routine use, thrombus aspiration would probably be acceptable to key stakeholders including clinicians, but for mechanical thrombus extraction the option would probably not be acceptable due to the additional time required to conduct the procedure when using the device.

Feasibility: The panel considered that the use of both types of devices would be feasible in the KSA setting given current availability.

Balance between desirable and undesirable consequences: Given the lack of benefit of the options in the overall group on patient important outcomes, the increase in stroke within 30 days as an undesirable consequence outweighing the marginal benefit of decrease in long term revascularization in the thrombus aspiration subgroup, and the resource use required, the panel concluded that that the undesirable consequences of routine thrombectomy with either thrombus aspiration or mechanical thrombus extraction outweigh the desirable consequences.

Subgroup considerations: The panel considered whether the desirable consequences may outweigh the undesirable consequences in the group of patients with large visible clots and whether routine use of thrombus aspiration would be justified. The TOTAL trial provided preplanned subgroup analysis of the primary outcome (composite of cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or class IV heart failure) for the subgroups of patients with TIMI (Thrombolysis in Myocardial Infarction) grade >= 3 (largest dimension of thrombus 0.5 to 2.0 times the diameter of the vessel) and TIMI grade >=4 (largest dimension of thrombus more than 2.0 times the diameter of the vessel). The results in both subgroups were similar to the overall results suggesting no apparent benefit of thrombus aspiration in patients with TIMI thrombus grade >=3 (hazard ratio 0.96, 95% confidence interval 0.82-1.12) and >=4 (hazard ratio 0.97, 95% confidence interval: 0.82-1.14). (see table in Appendix 3 - Question 3)

Note that the recommendation is for routine use of thrombus aspiration in the treatment of STEMI, and does not preclude the use of thrombus aspiration as a bail out procedure when deemed necessary. Bailout thrombectomy was performed in the TOTAL trial for patients with a large thrombus burden if there was a failure of the PPCI strategy alone, which was defined as TIMI flow 0 or 1 with a large thrombus after balloon predilation or persistence of a large thrombus after stent deployment. In the trial, bailout thrombectomy was performed in 7.1% (355 patients) in the PPCI alone control group.

Recommendation 3:

The panel recommends against routine use of aspiration or thrombus extraction devices in patients with STEMI. (strong recommendation, moderate quality evidence)

Implementation Considerations and Monitoring: The panel noted there is little routine use of thrombus aspiration or mechanical thrombus extraction devices in the KSA, and that there are probably no additional requirements for implementation of this recommendation.

Question 4: Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?

Background: In patients undergoing PPCI for STEMI, significant stenosis may be identified in non-infarct related arteries. Many patients have multi vessel disease with significant stenosis in arteries other than the culprit vessel. The management of the additional lesions at the time of PPCI is controversial.

The strategy of treating all significant lesions at the time of PPCI has the advantage of complete revascularization thus potentially decreasing future cardiac events. The disadvantage is the additional time and contrast used for the additional PCIs and the potential complications associated with the longer procedure.

Until recently most of the evidence available to answer this question was based on observational studies. More recently, RCTs have been published addressing this question. In these trials, the timing of the non- infarct related artery intervention varies from index procedure, repeat procedure during index hospitalization and within 3-4 weeks of the STEMI. For the purpose of this question, trials evaluating multi-vessel PCI during index procedure were considered.

Summary of Findings: The previous NICE systematic review identified several observational studies and 2 RCTs[75,76]. The data from observational studies were heterogeneous and overall there was no clear indication of benefit from either strategy.

Since the publication of the NICE systematic review, 2 more RCTs [77,78] have been published. One of these trials[77] was presented at the European Society of Cardiology meeting in September of 2014 and was published in March of 2015 prior to the panel meeting. The literature search for this recommendation was updated to March 2015. A large multicenter trial (COMPLETE trial, ClinicalTrials.gov Identifier: NCT01740479) is currently enrolling patients with a projected recruitment of 3900 and an estimated study completion date of December 2018.

Due to inconclusive evidence based on observational studies and additional RCT results available since the NICE publication, the studies included to address this question in these guidelines were limited to RCTs. 4 RCTs were included, 2 of these trials performed the multi-vessel PCI exclusively during the index procedure [75,78], the third trial compared three groups; a group with intervention during index procedure and a group with staged revascularization in addition to a control group (the data for the groups randomized to complete revascularization during the index procedure

and control were used in the meta analysis; staged revascularization group was not included) and in the fourth trial, 64% of patients in the multi-vessel intervention group received complete revascularization during index procedure and the remaining during the index hospitalization - the decision to stage the procedure was based on clinical reasons made by the operator performing the PCI; the outcomes were not separated based on complete revascularization performed during index procedure versus index hospitalization.

Benefits of the Option: There meta-analysis showed for long term (>1 year follow up) mortality a relative risk of 0.63 for multi-vessel PCI, but with a wide confidence interval of 0.37 to 1.05, translating to an absolute effect of 27 fewer deaths per 1000 patients with multi-vessel PCI (95% confidence interval: from 46 fewer to 4 more). The relative risk of reinfarction was significantly lower (relative risk 0.37, 95% confidence interval 0.19-0.71) in the multi-vessel PCI group. As expected, due to complete revascularization during the index procedure, rate of revascularization was significantly lower (relative risk 0.37, 95% confidence interval of 0.26-0.53) in the multi-vessel PCI group.

Harms of the Option: No specific harm was identified with multi-vessel PCI based on the meta-analysis. Contrast induced nephropathy was variably reported, there was no significant difference in this outcome in the 2 groups based on available data (limited data available in 3 of the 4 published studies, relative risk of 0.55 in favour of multi-vessel PCI; 95% confidence interval 0.16-1.89). The panel additionally noted that every PCI procedure carries risk, and that with multi-vessel PCI the time of the procedure is extended.

Resource Use: Resource use with multi-vessel PCI would be increased due to increased use of lab time, and more stents, contrast and other supplies required. This, however, is offset by lower resource use during follow up due to decreased incidence of myocardial infarctions and revascularization. No data specific for the KSA setting were available, but one cost-consequence analysis [75] identified in the NICE systematic review reported that culprit only PCI was more costly over 12 months as compared to immediate multi-vessel PCI based on a sample of 69 patients. The panel considered that the incremental cost of multi-vessel PCI was probably small relative to the net benefits.

Acceptability: The panel noted that there may be reluctance to accept multi-vessel PCI in patients with STEMI as some providers may question the reason for the procedure (i.e. as compared to CABG procedure for the patient) and payers and hospital administrators may also be reluctant to accept the procedure given the resource use.

Feasibility: Multi-vessel PCI was viewed as a feasible option to implement. Consideration should be given to the increased procedure time in the cardiac catheterization laboratory to perform multi-vessel PCI, with scheduling constrains that may occur.

Balance between desirable and undesirable consequences: The panel considered that multi-vessel PCI as compared to culprit-only PCI was shown to probably have large desirable effects relative to undesirable effects with overall net benefit for the patient. The strength of recommendation was conditional based on the low quality evidence as well as some uncertainty about the resource use in the local healthcare setting and acceptability from providers and administrators.

Recommendation 4:

The panel suggests multi-vessel PPCI over culprit-only PCI for patients with multi-vessel coronary artery disease undergoing PPCI. (conditional recommendation, low quality evidence)

Remarks:

- This recommendation is based on evidence with data predominantly from patients undergoing multi-vessel PCI during the index procedure, but the procedure may also be considered during the index hospitalization.
- This recommendation does not apply to patients with cardiogenic shock.

Implementation Considerations and Monitoring: As the results of the COMPLETE trial will be available in December of 2018, the panel has set this as the expiration date for this recommendation. The recommendation will be reviewed and revised as necessary at that time.

Given the considerations around acceptability of multi-vessel PCI by the providers the panel recommends that a policy be developed to outline how interaction between surgeons and cardiologists in hospitals should be dealt with as part of the care pathway for ACS and STEMI patients, where considerations such as availability and providing procedures such as CABG can be outlined.

Question 5: Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?

Background: Around 5% to 8% of patients admitted to hospitals with STEMI are in cardiogenic shock at the time of presentation. A state of decreased end organ perfusion due to low cardiac output is termed cardiogenic shock. In patients with STEMI, this can be due to pump failure due to myocardial dysfunction from the STEMI; due to mechanical complications including acute mitral regurgitation or septal or free wall rupture or due to malignant arrhythmias. These patients have a high mortality with greater than 50% in hospital mortality.[79,80]

In patients with STEMI, early revascularization is the cornerstone of treatment to improve perfusion and limit myocardial damage. However, patients in cariogenic shock may be too unstable and may benefit from early medical stabilization.

Summary of Findings: The NICE systematic review identified 2 RCTs with results included in 10 [79,81-89] publications. We identified no new trials were identified in our updated systematic review. The overall quality of evidence was moderate.

Benefits of the Option: The analysis showed that mortality at one year was significantly lower in the intervention group with early revascularization as compared to medical stabilization (relative risk 0.80, 95% confidence interval 0.67-0.97) based on one study, translating to an absolute effect of 134 fewer deaths per 1000 patients (95% confidence interval: from 221 fewer to 20 fewer). Short term mortality based on two studies was also lower in the early revascularization group but with a wide confidence interval (relative risk 0.84, 95% confidence interval 0.70-1.02), as was class III or IV heart failure at 2 weeks follow-up (relative risk 0.64, 95% confidence interval 0.36-1.15).

Harms of the Option: There were no harms identified for early revascularization based on the outcomes reported in these studies.

Resource Use: No data specific to the KSA setting were available for costs and cost-effectiveness. The panel considered that the resources required for early revascularization are probably not small, considering all costs including downstream costs. However, the incremental cost was considered probably

small relative to the net benefit, in consideration of the significant improvement in morality at 1 year.

Acceptability and Feasibility: The option of early revascularization was viewed as acceptable to all key stakeholders. However, given that patients with cardiogenic shock would require to be transferred to a PCI capable facility if the hospital they present to does not offer the procedure, and that there are difficulties with universal access to PCI in the KSA the option was viewed as probably not feasible for all patients in all settings.

Balance between desirable and undesirable consequences: A high weight was placed on the benefits of the intervention for patients and the panel concluded that desirable consequences clearly outweigh undesirable consequences. The panel considered that patients with cardiogenic shock are already at high risk, supporting intervention with early revascularization.

Recommendation 5:

The panel recommends early revascularization for patients with cardiogenic shock due to STEMI. (strong recommendation, moderate quality evidence)

Subgroup Considerations: When a significant delay is expected for patients for early revascularization with PPCI, full conventional therapy, including fibrinolytics, may be considered.

Implementation Considerations and Monitoring: The feasibility issues outlined above need to be addressed to allow full implementation of this recommendation. As there are issues in the KSA healthcare setting with universal access to PCI, particularly in hospitals in areas peripheral to large urban centres where catheterization labs and PCI-capable facilities are available, focus should be placed on developing PCI services to improve access. The development of catheterization labs and training of personnel is desirable in peripheral hospitals.

Question 6: Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?

Background: A considerable proportion of patients with STEMI present as out-of-hospital cardiac arrest; one study estimated that a third of patients with STEMI present as sudden cardiac death [90]. Emergency medical personnel attempt resuscitation in the majority of out of hospital cardiac arrests, however only a minority of these patients achieve return of spontaneous circulation (ROSC) [90]. Of the patients who are admitted to a hospital with ROSC, most are unconscious in the immediate period following the resuscitation. During this time, a variety of treatments may be indicated and providers may need to prioritize treatment options based on the condition of the patient and availability of treatment options. It is not clear if immediate PPCI is beneficial compared to stabilization in the intensive care unit prior to PPCI.

Overall, in the KSA emergency medical services are poorly developed, and particularly in non-urban areas in the KSA there may not be extensive EMS and resuscitation may not be attempted on many patients with cardiac arrest. This question addresses management of patients who have been successfully resuscitated from a cardiac arrest with ROSC.

Summary of Findings: Three studies [91-93] were identified based on the literature search in the previously published NICE systematic review. We did not identify additional studies in our update of the systematic review. The meta-analysis included observational studies and the overall quality of evidence was judged as very low.

Benefits of the Option: Mortality at 30 days was significantly lower (relative risk 0.51, 95%

confidence interval 0.38-0.69) in patients treated with immediate angiography and PCI. Incidence of stroke at 30 days was reported only in one study and this was significantly lower in the patients treated with immediate angiography and PCI (relative risk 0.5, 95% confidence interval 0.28-0.88)

Harms of the Option: No harms were identified based on the outcomes reported in these studies.

Resource Use: The resource use required for immediate angiography followed by PCI was judged as not small, taking into consideration the costs for the procedure and in particular if transfer of the patient is required. However, the panel noted that the incremental cost relative to the net benefit is probably small given the large benefit for patients shown in the meta-analysis.

Acceptability: The option of immediate angiography followed by PCI for patients with cardiac arrest was viewed as probably not acceptable to key stakeholders in the KSA setting as the panel noted that at arrival to hospital providers may not want to accept the patient and that these patients with out of hospital arrest may be rejected. For patients with in-hospital cardiac arrest, this would not be applicable and patients would receive treatment immediately.

Feasibility: The panel noted that the option of immediate angiography followed by PCI is also probably not feasible in the KSA setting. It is difficult for patients with out of hospital cardiac arrest to make it to the hospital due to poorly developed EMS. Cases of patients who suffer an out of hospital cardiac arrest and are resuscitated, achieving return of spontaneous circulation, are infrequent. Additionally, as previously noted there is a lack of access to PCI services for the overall population in the KSA, with 48 cardiac centres with catheterization labs currently operating, but due to the geographical distribution and concentration of these centres in urban areas, a large portion of the population is left without access. Therefore, patients with out of hospital arrest with poor prognosis would be competing for limited spaces for PCI.

Balance between desirable and undesirable consequences: The desirable consequences probably outweigh undesirable consequences for immediate angiography followed by PCI for patients with cardiac arrest who are resuscitated but remain unconscious. In consideration of the probably large benefit for patients with reduction in morality, but issues of feasibility and acceptability in the KSA healthcare setting, as well as overall very low quality evidence based on observational studies, the strength of the recommendation is conditional.

Recommendation 6:

The panel suggests immediate angiography followed by PCI where indicated over usual care in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest. (conditional recommendation, very low quality evidence)

Remarks:

- For patients with unwitnessed out of hospital arrest, without documented time of arrest, the clinician may re-evaluate the patient for PCI with detailed assessment of the patient's neurological status before proceeding with a potentially futile intervention.

Subgroup Considerations: A subgroup consideration was made for in-hospital versus out of hospital cardiac arrest, and in the latter for witnessed versus unwitnessed arrest. The panel noted that for patients with unwitnessed out of hospital cardiac arrest, without documented time of arrest, the patient may be re-evaluated and assessed by a clinician, with detailed assessment of the patient's neurological status before proceeding with a potentially futuile intervention.[94]

It may be difficult to establish STEMI in patients with out of hospital arrest who remain unconscious, particularly in the case of unwitnessed arrest where there will be further uncertainty for the patient's prognosis. This consideration was made in the context of the discussion about feasibility and difficulties with access to PCI services for the KSA population.

Research possibilities: Given the infrequent occurrence of cardiac arrest patients arriving to hospital with ROSC, the panel suggests a registry study and auditing to determine how many patients with cardiac arrest with presumed STEMI make it to a catheterization lab and what their outcomes are in the KSA setting.

Question 7: Should high volume centres versus low volume centres be used for PPCI services?

Background: Success of percutaneous coronary intervention (PCI) depends on individual expertise of the operator and the quality of supporting staff and infrastructure. These include appropriate facilities, trained staff and an ongoing volume of procedures to attain and sustain excellent procedural outcomes. Over time staff attain a level of expertise which leads to lower complications and better outcomes. In addition, primary percutaneous coronary intervention is a more complex process that requires communication and collaboration between the ambulance services, emergency department, clinical and interventional cardiology and other clinical and non-clinical services at the hospital. Furthermore, the cardiac catheterization laboratory team must be available to perform the procedure at any time of day or night to deliver timely and efficient PPCI.

Several studies have identified an inverse relationship between hospital volumes and adverse outcomes for PPCI. Addressing this question is a healthcare systems issue. Preferential referral of PPCI procedures to high volume centers needs to be balanced with the need for centers in remote locations that can provide timely access to PPCI for the population. This question addresses the extent to which procedural volumes influence patient outcomes.

Summary of Findings: Five publications [95-99] were identified in the previously published NICE systematic review. Our updated systematic review included one additional publication.[100] The studies identified were observational registry studies reporting on the outcome of in-hospital mortality. One study reported on in-hospital stroke and major bleeding. Data is reported for in-hospital mortality only from five registry studies, and the data was not pooled across studies due to differences in reporting of the outcomes and definition of high-, medium- and low-volume centres. The overall quality of evidence was very low.

Benefits of the Option: Each of the 5 registry studies showed a trend for decreasing in-hospital mortality with higher volume of PPCI procedures performed per year (see evidence profile in Appendix 1). The number of procedures per year defining a low-, medium-, and high-volume centre varied between the studies. The trend in decreasing in-hospital mortality was observed when comparing low-volume versus medium-volume centres, as well as medium-volume versus high-volume centres. Higher volume centers were therefore shown to have a lower risk for the outcome of in-hospital mortality after PPCI for a STEMI.

Harms of the Option: No data were available on harms with respect to patient-important outcomes for low-volume vs. high-volume centres. The panel noted that limiting PPCI services to high volume centers would likely result in an increase in the time taken to transfer patients with STEMI to a PPCI-capable facility.

Resource Use: No data was available on resource use or cost-effectiveness of high-volume versus low-volume centres. The panel

considered that the resources required for prioritizing PPCI to high-volume centres would probably be small and incremental cost would probably be small relative to the net benefit of reduction in in-hospital mortality.

Impact on Health Equity: The panel noted that prioritizing high-volume centres for PPCI services would improve patient outcomes and that in general increasing volume at existing low-volume centres would improve access for patients to PPCI services, thereby probably reducing health inequity in the KSA setting.

Acceptability: Prioritizing high-volume centres for PPCI services was found as probably acceptable to key stakeholders. However, the panel noted that patients' access to PPCI would be reduced if PPCI services were to be restricted to high volume centers only.

Feasibility: The feasibility of prioritizing high-volume centres for PPCI services was uncertain as it is a healthcare system issue that will require input and debate from policy makers. The recommendation needs to be addressed as a health systems issue with logistical support and planning to improve centre volumes and patient access overall in the KSA setting.

Balance between desirable and undesirable consequences: The desirable consequences of prioritizing high-volume centres for PPCI services probably outweigh the undesirable consequences if healthcare system changes are implemented to improve timely access to high volume centers. Higher volume centres were shown to improve patient outcomes and have a lower risk of in-hospital mortality. There is no restriction set on centre size so as to not further reduce access for patients in the KSA setting, and expansion of PCI services to increase volume should be prioritized. The strength of recommendation is conditional due to uncertainty about feasibility as well as very low quality evidence.

Recommendation 7:

The panel suggests prioritizing the management of patients with STEMI to high volume centres. (conditional recommendation, very low quality evidence)

Remark:

- The implementation of this recommendation should not restrict care for patients who require PPCI in settings where only low-volume centres are available.

Implementation Considerations and Monitoring: Implementation of this recommendation should focus on prioritizing expansion of PPCI services to increase volume, in particular in existing low-volume centres. The goal for the KSA healthcare system is to improve access for patients to PPCI services, where there is currently lack of access, which should not involve restricting access from current low-volume centres. The consideration for increasing volume at existing centres is a healthcare system issue that is in concordance with the previously discussed need for improvement in transport and transfer of patients to PPCI-capable facilities to improve access for patients across the KSA.

Research possibilities: Based on the considerations for the KSA healthcare setting and current levels of access to PPCI services for STEMI patients, the panel suggests research to assess outcomes for patients receiving PPCI at low-volume centres versus treatment with thrombolytics.

Question 8: Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?

Background: STEMI is usually caused by thrombotic occlusion of a major coronary artery. Fibrinolytic therapy restores flow in the coronary artery by lysing the thrombus leading to preserved myocardial function and de-

creased mortality. Complete reperfusion with normal flow in the infarct related artery is found only in approximately 50% of the patients who receive fibrinolytic therapy. In some patients, delayed, sluggish flow is restored with complete filling of the distal coronary territory. Fibrinolysis fails to reperfuse the distal myocardium in approximately 40% of patients[101]. This is identified clinically by persistent ST elevation (<50% ST segment resolution on a follow up electrocardiogram 60-90 minutes after administration of fibrinolytics). Incomplete restoration of distal flow does not improve survival. These patients may benefit from additional interventions to reperfuse the myocardium[102].

Options for further revascularization include repeat fibrinolysis and immediate referral for coronary angiography and PCI (rescue PCI) to restore distal flow. Rescue PCI requires emergency transfer of the patient to a hospital with a cardiac catheterization laboratory with PCI capabilities. A third alternative is conservative therapy without repeat fibrinolysis or rescue PCI.

Summary of Findings: The previously published NICE systematic review identified 10 studies [103-112] that were included in our meta-analysis. We did not identify additional studies in our updated systematic review. We analyzed and presented the comparisons for the 3 options (rescue PCI, repeat fibrinolysis and conservative therapy) separately and prepared evidence profiles for each comparison – rescue PCI versus conservative therapy, repeat fibrinolysis versus conservative therapy and rescue PCI versus repeat fibrinolysis. Overall the quality of evidence was low for each of the 3 comparisons. One of the studies [110] included in the repeat fibrinolysis versus conservative management had a higher than expected mortality in the conservative management arm (29%) and a higher rate of angina (40% versus 6.6%) and urgent revascularization (31% versus 2.2%) in the repeat fibrinolysis arm compared to the conservative management arm - successful thrombolysis should decrease the incidence of angina and need for urgent revascularization. This was a small study (total 90 patients) and although labelled as a randomized double blind study, there were significant unexplained differences between the two groups (45 patients each).

Benefits of the Option: In the comparison between rescue PCI and conservative management, the rate of reinfarction within 6 months was significantly lower in the rescue PCI group (relative risk 0.47, 95% confidence interval 0.26-0.84). Unplanned revascularization at 6 to 12 months was lower in the rescue PCI group (relative risk 0.55, 95% confidence interval 0.38-0.78). The meta-analysis also showed lower mortality at 6 months (relative risk 0.71, 95% confidence interval 0.44-1.13) and lower rate of heart failure at 6 months (relative risk 0.78, 95% confidence interval 0.56-1.09) in the rescue PCI group, but with wide confidence intervals, translating to 57 fewer deaths per 1000 patients (95% confidence interval: from 69 fewer to 16 more) and 44 fewer heart failures per 1000 patients (95% confidence interval: from 88 fewer to 18 more). The panel concluded that the anticipated desirable effects of rescue PCI are probably large compared to conservative therapy.

The comparison between repeat fibrinolysis and conservative management suggested lower mortality at 6 weeks in the repeat fibrinolysis group (relative risk 0.28, 95% confidence interval 0.10-0.81). The meta-analysis for the mortality outcome included 2 studies with a total of 127 patients (64 in the repeat fibrinolysis arm and 63 in the conservative arm), and the result appears to be driven by events in the one study with an unexpectedly high mortality (29%) in the control group[110]. Another RCT, the REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Fibrinolysis) Trial recruited 142 patients to repeat fibrinolysis and 141 to conservative therapy, and reported mortality as time to event , with no difference in outcomes between the 2 groups including in longer term follow-up of patients (median of 4.4 years of follow up). Mortality at 6 months was 12.7% in repeat

fibrinolysis group and 12.8% in the conservative group and mortality at 4.4 years was 22.3% in the repeat fibrinolysis group and 22.4% in the conservative group. Repeat fibrinolysis did show a reduction in reinfarction at 6 months, heart failure at 6 months, or unplanned revascularization before discharge. The panel concluded that the desirable effects of repeat fibrinolysis are probably not large relative to the undesirable effects when compared to conservative management.

Only one trial evaluated rescue PCI versus repeat fibrinolysis and assessing outcomes of heart failure (relative risk 0.69, 95% confidence interval 0.27-1.76), stroke (relative risk 2.96, 95% confidence interval 0.31-28.10), and major bleeding (relative risk 0.56, 95% confidence interval 0.17-1.88), with overall low quality of evidence and uncertainty in the estimates of effects.

Harms of the Option: Rescue PCI was not associated with reported adverse events in these trials. In the one study [110] of repeat fibrinolysis compared to conservative management, unexpectedly, the rate of unplanned revascularization was higher in the repeat fibrinolysis group. There was uncertainty about the estimates of effects for the major bleeding outcome with wide confidence intervals when comparing repeat fibrinolysis versus conservative management (relative risk 1.33, 95% confidence interval 0.47-3.74) and rescue PCI versus repeat fibrinolysis (relative risk 0.56, 95% confidence interval 0.17-1.88). As an important note, the panel noted that the risk of bleeding would be much higher if using streptokinase versus for example tissue plasminogen activator (tPA) or tenecteplase (TNKase).

Resource Use: When compared to repeat fibrinolysis and conservative management, rescue PCI may require significant resources that include the high cost of the procedure as well as cost of transfer of the patient, which will vary by geographical region across the KSA. Although resources required are not small, the incremental cost of rescue PCI was considered probably small relative to the benefit as there is a net benefit for patients, with lower likelihood of future events requiring additional resource use for treatment. The panel similarly noted the increased resource use with repeat fibrinolysis, particularly considering the high cost of tPA and TNKase (estimated at 5000 SAR), and incremental cost that is probably not small relative to the net benefit as a result of probably no large benefit shown in the analysis for repeat fibrinolysis.

Impact on Health Equity:
The panel noted that the option of rescue PCI would increase health inequities in the KSA setting, as outlined in the previous questions, because of lack of universal access to PCI services, particularly in peripheral geographic areas. Patients would be treated differentially depending on geographical location, with some patients still denied access to the procedure. Repeat fibrinolysis may similarly increase health inequity due to the high cost of the drugs.

Acceptability: Rescue PCI was viewed as acceptable to key stakeholders including clinicians. Repeat fibrinolysis was viewed as probably not acceptable to key stakeholders as the panel noted that most clinicians would not provide repeat fibrinolysis.

Feasibility: Given current levels of access to PCI services, rescue PCI may be difficult to implement universally. Patients require transfer to a PCI capable facility. The option may not be feasible, particularly in geographical areas in the KSA lacking PCI-capable facilities. There are, however, geographical locations where rescue PCI is already routinely performed. The option of repeat fibrinolysis was viewed as probably feasible, given availability of tPA and TNKase.

Balance between desirable and undesirable consequences: The desirable consequences of rescue PCI probably outweigh undesirable consequences when compared to both conservative management and repeat fibrinolysis for patients with STEMI who fail to reperfuse

after fibrinolytic therapy. For repeat fibrinolysis, the benefit is less clear based on limited data, and repeat fibrinolysis should not involve repeat administration of streptokinase due to risk of adverse events and higher risk of bleeding. Implementation of rescue PCI as the treatment option for patients who fail to reperfuse after fibrinolytic therapy requires that feasibility issues around the lack of universal access to PCI services be addressed in the KSA setting. The strength of recommendation is conditional due to uncertainty about the feasibility, impact on health inequity, and low quality of evidence.

Recommendations 8, 9, 10:

The panel suggests rescue PCI over conservative management (conditional recommendation, low quality evidence) and suggests rescue PCI over repeated fibrinolysis (conditional recommendation, low quality evidence) in patients with STEMI who failed to reperfuse after fibrinolytic therapy. The panel suggests not offering repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy (conditional recommendation, low quality evidence).

Remarks:

- When there is no available immediate urgent access for the patient at a catheterization lab for the rescue PCI procedure, treating clinicians should determine with a lab if access to rescue PCI can become available for such patients.
- There should not be a repeated administration of streptokinase. The risk of adverse events with repeat administration of streptokinase is higher than the benefit.

Implementation Considerations and Monitoring: In order to implement the recommendation for rescue PCI the feasibility issues regarding lack of universal access to PCI services in specific geographical regions of the KSA need to be addressed.

Research possibilities: The panel suggests future research that will inform the implementation issues including a registry study to provide information regarding the number of patients eligible for rescue PCI who currently do not receive rescue PCI. Keeping track of patients who do not have access to PCI services and do not get treatment is intended to provide support for policymakers to improve access across the KSA.

Question 9: Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?

Background: STEMI is usually caused by thrombotic occlusion of a major coronary artery. Fibrinolytic therapy restores flow in the coronary artery by lysing the thrombus leading to preserved myocardial function and decreased mortality. Complete reperfusion with normal flow in the infarct related artery is found only in half the patients who receive fibrinolytic therapy. Following clinically successful thrombolysis there may be residual coronary stenosis at the site of the lesion which may predispose to worsening coronary stenosis and clinical events. Additionally patients with STEMI frequently have multi vessel disease which may be responsible for symptoms and clinical events.

To evaluate the coronary anatomy and prescribe the most appropriate mode of treatment for patients with STEMI who are treated with fibrinolysis, coronary angiography may be recommended. The role and optimal timing of angiography has been studied in clinical trials. This question addresses whether routine early versus routine deferred or selective angiography should be used for management of patients with STEMI successfully treated by fibrinolysis.

Summary of Findings: The previously published NICE systematic review identified 8 publications [113-120] relevant to this question. Our literature search update identified one

additional study.[121] The overall quality of evidence was judged as moderate on the basis of the reinfarction at 6 to 12 months outcome and the estimates of effects for all critical outcomes being in the same direction in favour of early angiography.

Benefits of the Option: There was a large reduction in reinfarction at 6 to 12 months (relative risk 0.58, 95% confidence interval 0.41-0.83) in patients receiving routine early angiography, with an absolute effect of 28 fewer patients with reinfarction per 1000 patients (95% confidence interval; from 11 fewer to 39 fewer). The relative risk for mortality at 6 to 12 months with early angiography was 0.88 with a wide 95% confidence interval from 0.61 to 1.27, translating to 6 fewer deaths per 1000 patients (95% confidence interval: from 19 fewer to 13 more). There was also a reduction in recurrent ischemia at 6-12 months (relative risk 0.52, 95% confidence interval 0.41-0.66) and unplanned revascularization (relative risk 0.33, 95% confidence interval 0.25-0.44) with early angiography when compared to the selective or deferred angiography. Based on one study [118], the length of hospital stay was also lower in the routine angiography group (mean difference of 3.4 fewer days, 95% confidence interval of 2.41 fewer days to 4.39 fewer days)

Harms of the Option: There were no harms identified for early angiography based on the outcomes reported in these trials.

Resource Use: One pilot trial [122] was identified in the literature search that performed a cost-analysis comparing routine early angiography versus a conservative strategy with risk stratification based on stress myocardial perfusion imaging. The cost analysis including total hospital costs, costs of therapy, subsequent hospitalization, subsequent noninvasive tests, or repeat revascularization showed overall higher cost for routine early angiography versus the conservative strategy at 6-month follow-up with a cost of $4953.5 ± 3108.5 versus $2764.6 ± 2636.7, respectively. The previously published NICE systematic review included one published cost-utility analysis [115,116] reporting an incremental cost-effectiveness ratio (ICER) of £62,648 per QALY (quality-adjusted life-year) gained for routine early angiography compared to routine deferred angiography (angiography where clinically indicated or otherwise within 2 weeks of hospital discharge) following STEMI successfully treated by fibrinolysis. The cost-utility analysis had two important limitations of high cost of transfer due to helicopter ambulance costs as well as a study population mortality rate lower than the general STEMI population potentially underestimating benefits of early angiography.

For the KSA setting, the incremental cost was considered probably small relative to the net benefits, given probably large benefit, and resources required for routine early angiography and transfer. Compared to the evidence reviewed the panel considered that the cost per QALY in the KSA would be lower.

Acceptability and Feasibility: The option of early angiography was viewed as acceptable to all key stakeholders. The availability of catheterization lab time during the index hospitalization for early angiography may be difficult in busy catheterization labs, and patients treated in hospitals without a catheterization lab would require transfer to a lab. Given the issues of lack of universal access to catheterization labs in the KSA setting that were discussed in the previous questions, with the panel noting that approximately 25% of the population in the KSA does not have good access to a catheterization lab, the option of early angiography may not be feasible for all patients. For patients in geographical regions with access to catheterization labs the option would be feasible.

Balance between desirable and undesirable consequences: The desirable consequences of routine early angiography compared to deferred or selective angiography probably outweigh the undesirable consequences. A high weight was placed on the benefit of early angiography on patient important outcomes and

in consideration of the feasibility issues in the KSA setting the strength of recommendation is conditional.

Recommendation 11:

The panel suggests routine early angiography over routine deferred or selective angiography in patients with STEMI successfully treated by fibrinolysis. (conditional recommendation, moderate quality evidence)

Implementation Considerations and Monitoring: As outlined in questions 7 and 8 above, implementation of this recommendation requires addressing the feasibility issues regarding lack of universal access to catheterization labs, particularly in geographical regions peripheral to the urban centres in the KSA that currently have catheterization labs.

Overall Research Priorities Identified for the KSA

In formulating the above recommendations the panel considered research priorities for the KSA healthcare setting with respect to the treatment of patients with STEMI. As discussed in the context of the recommendations made, current issues for the management of patients with STEMI in the KSA center around poorly developed emergency medical services, resulting in delays in presentation to hospitals and difficulties with transport and transfer or patients, and lack of universal access to catheterization labs with PCI services for a significant portion of the population, specifically in regions peripheral to urban centres. The feasibility issues have a particularly strong impact on specific cases and groups of patients receiving the most appropriate treatment such as those who have failed to be treated successfully with fibrinolytic therapy (i.e. question 8), those who have been successfully treated with fibrinolytic therapy (i.e. question 9), and those who have suffered out-of-hospital cardiac arrest (i.e. question 6) or cardiogenic shock (i.e. question 5).

The main research priority outlined by the panel involves conducting audits and high quality registry studies with representation of all geographical regions, which the panel had identified as a potential limitation of existing registry studies, to assess the current state of practice and patients' outcomes in the KSA healthcare setting. The registry studies would provide information about the number of patients eligible for PCI who currently do not receive treatment with PCI (i.e. question 9), and address queries previously outlined such as how many patients with cardiac arrest arrive to hospitals and are treated in the catheterization lab and what their outcomes are (i.e. question 6). The suggested research is intended to inform policymakers to address the implementation issues outlined with each of the recommendations and to develop a plan for improved and coordinated access to the treatments that are most beneficial for patients with STEMI.

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Appendices

1. Appendix 1: Evidence-to-Decision Frameworks
2. Appendix 2: Search Strategies and Results
3. Appendix 3: Forest plots from meta-analyses

Appendix 1: Evidence to Decision Frameworks

Guideline Question 1: Should fibrinolysis vs. delayed percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset to hospitals not capable of PPCI services?

Problem: STEMI
Option: fibrinolysis
Comparison: delayed PPCI
Setting: hospitals not capable of PPCI services
Perspective: KSA MoH

Background and Objective: Timely PPCI is superior to fibrinolysis with lower rates of mortality, re-infarction and stroke. The advantage of PPCI over fibrinolysis is diminished with increasing PPCI-related time delay. This question reviews the impact of delays to treatment on outcomes of PPCI and fibrinolysis.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td>The panel noted that currently in the KSA, EMS services are poorly developed and that most patients transport themselves to the hospital emergency department.</td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
● Very low
○ Low</td><td>The relative importance or values of the main outcomes of interest:<table><tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr></table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no im-</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td></td>
<td>○ Moderate
○ High</td>
<td rowspan="3">
<table>
<tr><td>Mortality - Kent 2001</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
<tr><td>Mortality - Zijlstra 2002</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
<tr><td>Mortality - Pinto 2006</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
<tr><td>Mortality - Boersma 2006</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
<tr><td>Mortality - Assebburg 2007</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
<tr><td>Mortality - Tarantini 2010</td><td>CRITICAL</td><td>⊕◯◯◯
VERY LOW</td></tr>
</table>
Summary of findings: Fibrinolysis compared to delayed percutaneous coronary intervention (PPCI) for treatment of STEMI in patients who present within 12 hours of symptom onset
<table>
<tr><th>Outcome</th><th>Impact</th></tr>
<tr><td>Mortality - Kent 2001</td><td>Equipoise: 50 minutes **Kent 2001 and Zijlstra 2002 used the same 10 studies for their meta-regression / analysis</td></tr>
<tr><td>Mortality - Zijlstra 2002</td><td>Fibrinolysis all-cause long term (6 months) mortality (%) < 2 hours: 5.4; 2-4 hours 7.3; >4 hours 14.6 PPCI all-cause long term mortality (%) < 2 hours: 5.1; 2-4 hours 6.1; >4 hours 6.7%</td></tr>
</table>
</td>
<td rowspan="3">portant variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.</td>
</tr>
<tr>
<td></td>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td>
</tr>
<tr>
<td></td>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
</tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td rowspan="2"></td><td>Are the undesirable anticipated effects small?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td><td rowspan="2"><table>
<tr><td>Mortality - Pinto 2006</td><td>Equipoise: 114 minutes (95% CI 96, 132)</td></tr>
<tr><td>Mortality - Boersma 2006</td><td>Based on multilevel logistic regression of individual patient data of 22 RCTs. Fibrinolysis all-cause mortality (%) <35 min 8.2; 36-50 min 6.8; 51 - 62 min 5.4; 63-79 min 9.5; 80-120 min 9.6. PPCI all-cause mortality (%) < 35 min 2.8; 36-50 min 5.4; 51-62 min 4.8; 63-79 min 6.9; 80-120 min 6.6</td></tr>
<tr><td>Mortality - Asseburg 2007</td><td>Equipoise for long-term (6 months) all-cause mortality 90 minutes odds ratio 0.7 (0.42-1.18)</td></tr>
<tr><td>Mortality - Tarantini 2010</td><td>Equipoise between PPCI and fibrinolysis influenced by baseline all-cause mortality, regression analysis shows that an acceptable PPCI related time delay has a wide range based mainly on different risk profiles.</td></tr>
</table></td><td rowspan="2"></td></tr>
<tr><td>Are the desirable effects large relative to undesirable effects?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>No evidence identified specific to KSA – Panel members considered costs and resource use when comparing fibrinolysis vs. delayed PPCI.

From NICE systematic review, two cost-utility analyses showed that PPCI was cost effective compared to in-hospital fibrinolysis, except at long PPCI-related time delays. Based on data from Asseburg study (ref #5), it was estimated that PPCI had a 90% probability of being cost effective (at threshold of £20,000 per QALY) based on average PPCI-related time delay of 64 minutes, which related to a median call-to-balloon time of 130 minutes. PPCI was less effective and more costly compared to fibrinolysis for patients transferred from hospital to a separate PPCI centre with time delays of 100 minutes (median call-to-balloon time of 167 minutes). It was similarly noted that that if based on data from Boersma study (ref #4), PPCI may be cost effective up to</td><td></td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
			time delays of 120 minutes.	
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing delated PPCI vs. fibrinolysis) are small relative to benefits. See note above.	
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ○ Uncertain ● Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA (see note about pre-hospital delay for female vs. male patients under feasibility). Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending fibrinolysis vs. delayed PPCI.	
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find fibrinolysis an acceptable option over delayed PPCI.	

	Criteria	Judgements	Research evidence	Additional considerations
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	The SPACE registry (AlHabib et al 2011) reported that of 1232 STEMI patients, 905 (73.5%) presented at <12 hours of symptom onset. 102 patients (8.3%) arrived at hospital in an ambulance, and time from symptom onset to hospital arrival was 150 min (IQR: 223). 625 patients (69.1%) were treated with thrombolytic therapy, 93 (14.8%) received thrombolytic therapy at less than 30 minutes of hospital arrival, with median door-to-needle time of 52 min (IQR: 55). The most commonly used therapy was streptokinase (46%), followed by retaplase (32.2 %). 158 (17.5%) patients had primary PCI. A chart review of 536 patients at King Abdulaziz Cardiac Centre who underwent primary PCI between Sept. 2008 and Sept 2012 reported average door-to-balloon time of 87.7 (STD +35.5) minutes for all patients, with average time reduced from 105 min in 2008 to 72 min in 2012. 64.2% of the patients met <90 minute door-to-balloon time. (Alghamdi 2013 Abstract) Alshahrani et al (2014) also reported a significant difference in pre-hospital delay for male patients (median 5h) versus female patients (median 12.9h) in a sample of 311 patients presenting with STEMI in 3 hospitals in Riyadh between March 2011 and August 2011. Female gender was the strongest predictor of total delay in this sample.	Panel noted the local data available on how poor transport is, and data on door to balloon time. Panel noted that for EMS services, all personnel are EMT Class 1, not certified to administer fibrinolysis in transport.

Recommendation **Should fibrinolysis vs. delayed percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests using fibrinolytic therapy over delayed PPCI if there is a total time delay >120 minutes. (conditional recommendation, very low quality evidence) Remarks: - The total time delay of 120 minutes refers to the period from the first contact with the patient to the provision of PPCI - For patients presenting directly to a PCI-capable facility the suggested acceptable time delay to provision of PPCI is 90 minutes (i.e. door-to-balloon time)
Justification	There is a decreasing benefit of PPCI with considerable PPCI-related time delay, but up to a delay of 120 minutes from first patient contact (including transport time to PCI-capable facility) PPCI was considered to result in better outcomes for patients as compared to fibrinolysis, based on evidence rated as very low quality.
Subgroup considerations	None
Implementation considerations	None
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Fibrinolysis compared to delayed percutaneous coronary intervention (PPCI) for treatment of STEMI in patients who present late after symptom onset

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15

Quality assessment							№ of patients		Impact	Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consid-erations	fibrinolysis	delayed percutaneous coronary intervention (PPCI)			
Mortality - Kent 2001											
10	observational studies [1]	very seri-ous [2 3 4]	not serious	serious [3]	not serious	none			Equipoise: 50 minutes **Kent 2001 and Zijlstra 2002 used the same 10 studies for their meta-regression / analysis	⊕◯◯◯ VERY LOW	CRITICAL
Mortality - Zijlstra 2002											
10	observational studies [5]	very seri-ous [2 3 4]	not serious	serious [3]	not serious	none			Fibrinolysis all-cause long term (6 months) mortality (%) < 2 hours: 5.4; 2-4 hours 7.3; >4 hours 14.6 PPCI all-cause long term mortality (%) < 2 hours: 5.1; 2-4 hours 6.1; >4 hours 6.7%	⊕◯◯◯ VERY LOW	CRITICAL
Mortality - Pinto 2006											
1	observational studies [6]	very seri-ous [7]	not serious	not serious	not serious	none			Equipoise: 114 minutes (95% CI 96, 132)	⊕◯◯◯ VERY LOW	CRITICAL
Mortality - Boersma 2006											
22	observational studies [5]	serious [8 9]	not serious	not serious	serious [10]	none			Based on multilevel logistic regression of individual patient data of 22 RCTs. Fibrinolysis all-cause mortality (%) <35 min 8.2; 36-50 min 6.8; 51 - 62 min 5.4; 63-79 min 9.5; 80-120 min 9.6. PPCI all-cause mortality (%) < 35 min 2.8; 36-50 min 5.4; 51-62 min 4.8; 63-79 min 6.9; 80-120 min 6.6	⊕◯◯◯ VERY LOW	CRITICAL

Mortality - Asseburg 2007											
9	observational studies [1]	very serious [2,3,4]	not serious	not serious	not serious	none			Equipoise for long-term (6 months) all-cause mortality 90 minutes odds ratio 0.7 (0.42-1.18)	⊕◯◯◯ VERY LOW	CRITICAL
Mortality - Tarantini 2010											
16	observational studies [1]	serious [2]	not serious	not serious	not serious	none			Equipoise between PPCI and fibrinolysis influenced by baseline all-cause mortality, regression analysis shows that an acceptable PPCI related time delay has a wide range based mainly on different risk profiles.	⊕◯◯◯ VERY LOW	CRITICAL

1. Study level of randomized trials
2. Study-level data is subject to ecological fallacy, which assumes that individual members have the average characteristics of the group as a whole. Statistics using group characteristics do not necessarily apply to individuals within the group and do not account for greater variability in individuals than the variability of the group mean.
3. Includes older studies (RCTs) that are less reflective of current practice; none of the studies used stents in PPCI arm.
4. < 20 RCTs
5. Individual patient data from RCTs
6. Registry cohort
7. Registry data with high risk of bias
8. Unclear allocation concealment in many of the included RCTs
9. Wide variation in individual trial characteristics and outcome (for example 30 day mortality varied from 0 to 22%)
10. Wide confidence interval at equipoise

Guideline Question 2: Should facilitated percutaneous coronary intervention (fPPCI) versus percutaneous coronary intervention (PPCI) be used in patients with STEMI?

Problem: STEMI
Option: fPPCI
Comparison: PPCI
Setting: in hospital
Perspective: KSA MoH

Background and Objective: Facilitated PPCI (fPPCI) is a strategy in which pharmacologic agents are given to the patient with STEMI before the patient arrives in the catheterization lab. The drugs that have been used for facilitated PPCI include fibrinolytics and glycoprotein 2b/3a inhibitors or a combination of these 2 agents. These agents may increase the success of PPCI but may also cause increased adverse effects. This question addresses whether fPPCI should be used in patients with STEMI

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
● Very low
○ Low
○ Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality - longer term</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
<tr><td>Stroke - longer term</td><td>CRITICAL</td><td>⨁◯◯◯</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no important variability or</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
● Probably no important uncertainty of variability
○ No important uncertainty of variability
○ No known undesirable</td>
<td>
<table>
<tr><td></td><td></td><td>VERY LOW</td></tr>
<tr><td>Reinfarction - longer term</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
<tr><td>Major bleeding - in hospital</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Minor bleeding - in hospital</td><td>IMPORTANT</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Heart failure - longer term</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Repeat revascularization - longer term</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
</table>
Summary of findings: Facilitated percutaneous coronary intervention (fPPCI) compared to percutaneous coronary intervention (PPCI) in patients with STEMI
<table>
<tr><th>Outcome</th><th>Without facilitated percutaneous coronary intervention (fPPCI)</th><th>With facilitated percutaneous coronary intervention (fPPCI)</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality - longer term</td><td>43 per 1000</td><td>41 per 1000 (30 to 57)</td><td>2 fewer per 1000 (from 13 fewer to 14 more)</td><td>RR 0.95 (0.69 to 1.32)</td></tr>
<tr><td>Stroke - longer term</td><td>8 per 1000</td><td>5 per 1000 (1 to 20)</td><td>3 fewer per 1000 (from 7 fewer to 12 more)</td><td>RR 0.63 (0.17 to 2.40)</td></tr>
<tr><td>Reinfarction - longer term</td><td>24 per 1000</td><td>23 per 1000 (14 to 40)</td><td>1 fewer per 1000 (from</td><td>RR 0.96 (0.56 to</td></tr>
</table>
</td>
<td>uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.

The panel noted that for the outcome minor bleeding, there could possibly be some variability in how patients view that outcome.

There was discussion about whether the desirable anticipated effects were probably not large or uncertain. Vote of 5 for 'probably no' and 1 vote for 'uncertain'.

In the absence of a significant reduction in mortality, the reduction in heart failure seems to be of lesser significance. Therefore the panel concluded that the desirable anticipated effects are probably not large.</td>
</tr>
<tr>
<td></td>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are the undesirable anticipated effects small?</td>
<td>○ No
● Probably no</td>
<td></td>
<td></td>
</tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considera-tions</th></tr>
<tr><td></td><td></td><td>○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td rowspan="2"><table>
<tr><td></td><td></td><td></td><td>11 fewer to 16 more)</td><td>1.64)</td></tr>
<tr><td>Major bleeding - in hospital</td><td>36 per 1000</td><td>54 per 1000 (38 to 75)</td><td>17 more per 1000 (from 2 more to 38 more)</td><td>RR 1.48 (1.06 to 2.06)</td></tr>
<tr><td>Minor bleeding - in hospital</td><td>148 per 1000</td><td>212 per 1000 (178 to 253)</td><td>64 more per 1000 (from 30 more to 105 more)</td><td>RR 1.43 (1.20 to 1.71)</td></tr>
<tr><td>Heart failure - longer term</td><td>101 per 1000</td><td>49 per 1000 (28 to 84)</td><td>53 fewer per 1000 (from 17 fewer to 73 fewer)</td><td>RR 0.48 (0.28 to 0.83)</td></tr>
<tr><td>Repeat revascu-larization - longer term</td><td>41 per 1000</td><td>40 per 1000 (18 to 88)</td><td>0 fewer per 1000 (from 22 fewer to 47 more)</td><td>RR 0.99 (0.45 to 2.16)</td></tr>
</table></td><td></td></tr>
<tr><td></td><td>Are the desirable effects large relative to undesirable effects?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td></td><td></td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>● No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td>No evidence identified specific to KSA – Panel members considered costs and resource use when comparing fPPCI vs. PPCI. Use of GPIs and fibrinolytic agents before arrival to catheterization lab would be associated with additional costs.</td><td>To implement fPPCI well developed EMS are needed. Resources would be required to implement EMS transfer procedures.</td></tr>
<tr><td></td><td>Is the incremental cost small relative to the</td><td>● No</td><td>No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing fPPCI vs. PPCI) are small relative to benefits of fPPCI.</td><td>There is no cost-benefit.</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considera-tions
	net benefits?	○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies		
Equity	**What would be the impact on health inequi-ties?**	○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending fPPCI vs. PPCI.	
Acceptability	**Is the option acceptable to key stakehold-ers?**	● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find fPPCI an acceptable option over PPCI.	Based on no benefit, harm, and additional re-sources, stakeholders would not find fPPCI ac-ceptable.

	Criteria	Judgements	Research evidence	Additional considera-tions
Feasibility	**Is the option feasible to im-plement?**	● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. fPPCI).	Panel noted that there is no net benefit, and that fPPCI cannot be provided in KSA due to lack of EMS and that training would be required.

Recommendation **Should facilitated percutaneous coronary intervention (fPPCI) vs. percutaneous coronary intervention (PPCI) be used in patients with STEMI?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	●	○	○	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	●	○	○

Recommendation	The panel suggests against using fPPCI in patients with STEMI. (conditional recommendation; very low quality evidence) Remark: - Facilitated PPCI (fPPCI) should not be confused with a pharmacoinvasive PPCI strategy
Justification	The panel considered there was more harm than benefit when using fPPCI, in addition to feasibility and resource use considerations for the KSA setting (i.e. lack of EMS)
Subgroup considerations	None
Implementation considerations	Not many (or any) centres in KSA are currently doing fPPCI.
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Facilitated percutaneous coronary intervention (fPPCI) compared to percutaneous coronary intervention (PPCI) in patients with STEMI

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliography: Bellandi 2006, BRAVE-3 2009, Schulz 2010 (BRAVE-3), Dudek 2010, Emre 2006, Gabrial 2006 (ERAMI), Elli 2008 (FINESSE), Han 2012, Zeymer (INTAMI-pilot), van't Hof 2004 (On-TIME), van't Hof 2008 (On-TIME), van't Hof 2010 (On-TIME), Maioli 2007 (RELAx-AMI), 2006 (ASSENT-4 PCI), Kim 2012 (ECLAT-STEMI), Le May 2009 (ASSIST), Liu 2012, Ohlmann 2012 (MISTRAL), Zorman 2002

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**facilitated percutaneous coronary intervention (fPPCI)**	**percutaneous coronary intervention (PPCI)**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality - longer term												
8	randomised trials	very serious [1]	not serious	not serious	serious [2]	none	68/1666 (4.1%)	71/1658 (4.3%)	**RR 0.95** (0.69 to 1.32)	2 fewer per 1000 (from 13 fewer to 14 more)	⊕◯◯◯ VERY LOW	CRITICAL
Stroke - longer term												
2	randomised trials	very serious [1]	serious [3]	not serious	very serious [2]	none	3/602 (0.5%)	5/598 (0.8%)	**RR 0.63** (0.17 to 2.40)	3 fewer per 1000 (from 7 fewer to 12 more)	⊕◯◯◯ VERY LOW	CRITICAL
Reinfarction - longer term												
5	randomised trials	very serious [1]	not serious	not serious	very serious [2]	none	25/1071 (2.3%)	26/1066 (2.4%)	**RR 0.96** (0.56 to 1.64)	1 fewer per 1000 (from 11 fewer to 16 more)	⊕◯◯◯ VERY LOW	CRITICAL
Major bleeding - in hospital												
5	randomised trials	very serious [1]	not serious	not serious	not serious	none	78/1449 (5.4%)	54/1490 (3.6%)	**RR 1.48** (1.06 to 2.06)	17 more per 1000 (from 2 more to 38 more)	⊕⊕◯◯ LOW	CRITICAL
Minor bleeding - in hospital												

2	randomised trials	very serious [1]	not serious	not serious	not serious	none	228/1094 (20.8%)	168/1134 (14.8%)	**RR 1.43** (1.20 to 1.71)	64 more per 1000 (from 30 more to 105 more)	⊕⊕◯◯ LOW	IMPORTANT
Heart failure - longer term												
3	randomised trials	very serious [1]	not serious	not serious	not serious	none	18/370 (4.9%)	37/365 (10.1%)	**RR 0.48** (0.28 to 0.83)	53 fewer per 1000 (from 17 fewer to 73 fewer)	⊕⊕◯◯ LOW	CRITICAL
Repeat revascularization - longer term [4]												
2	randomised trials	very serious [1]	not serious	not serious	very serious [2]	none	12/298 (4.0%)	12/294 (4.1%)	**RR 0.99** (0.45 to 2.16)	0 fewer per 1000 (from 22 fewer to 47 more)	⊕◯◯◯ VERY LOW	CRITICAL

1. Poor unclear randomization, poor unclear allocation concealment, not blinded, unclear ITT analysis
2. Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect.
3. Unexplained heterogeneity that was considered substantial and informed by an I square of 69%.
4. Pooled results of studies that reported short term outcomes for fPPCI vs. PPCI (RR, 95%CI) showed that fPPCI was not favoured for all but one of the outcomes (RR>1): Mortality – in hospital: 1.22 (0.76, 1.96) Mortality – short term: 1.19 (0.92, 1.54) Stroke – in hospital: 3.42 (1.32, 8.86) Stroke – short term: 0.83 (0.46, 1.49) Reinfarction – short term: 1.08 (0.86, 1.37) Heart failure – short term: 1.20 (0.93, 1.54) Repeat revascularization – short term: 1.86 (1.23, 2.80)

Guideline Question 3: Should routine thrombus extraction devices during percutaneous coronary intervention (PPCI) versus percutaneous coronary intervention (PPCI) alone be used for treatment of STEMI?

Problem: STEMI
Option: routine use of thrombus extraction devices
Comparison: PPCI alone (no routine use of thrombus extraction devices)
Setting: in hospital
Perspective: KSA MoH

Background and Objective: In an attempt to limit damage caused by distal embolization of the thrombus, devices to remove the thrombus during PPCI have been extensively studied. These range from simple hollow aspiration catheters to powered mechanical devices which can be used to fragment and aspirate the thrombus if the thrombus burden appears large. This question addresses whether thrombus extraction devices (thrombus aspiration and mechanical thrombus extraction) should be used routinely for treatment of STEMI.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low</td><td>The relative importance or values of the main outcomes of interest:<table><tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr></table></td><td>No evidence specific to KSA identified in literature search for patients’ values and preferences.</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td rowspan="3"></td><td></td><td>○ Low
● Moderate
○ High</td><td rowspan="3"><table>
<tr><td>Mortality - long term</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Re-infarction long term</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Stroke at 30 days</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Heart Failure within 30 days</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Target Vessel Revascularization - long term</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Major Bleeding</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
</table>
Summary of findings: Routine thrombus extraction devices during percutaneous coronary intervention (PPCI) compared to percutaneous coronary intervention (PPCI) alone for treatment of STEMI
<table>
<tr><th>Outcome</th><th>Without routine thrombus extraction devices during percutaneous coronary intervention (PPCI)</th><th>With routine thrombus extraction devices during percutaneous coronary intervention (PPCI)</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality - long term</td><td>45 per 1000</td><td>40 per 1000 (35 to 45)</td><td>5 fewer per 1000 (from 1 more to 10 fewer)</td><td>RR 0.89 (0.78 to 1.02)</td></tr>
<tr><td>Re-infarction long term</td><td>23 per 1000</td><td>22 per 1000 (18 to 26)</td><td>1 fewer per 1000 (from</td><td>RR 0.94 (0.79 to</td></tr>
</table></td><td rowspan="3">Panel members, including patient representative noted that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.</td></tr>
<tr><td>Is there important uncertainty about how much people value the main outcomes?</td><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td></tr>
<tr><td>Are the desirable anticipated effects large?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td></td><td></td><td>○ Yes
○ Varies</td><td rowspan="3"><table>
<tr><td></td><td></td><td></td><td>3 more to 5 fewer)</td><td>1.13)</td></tr>
<tr><td>Stroke at 30 days</td><td>4 per 1000</td><td>6 per 1000 (4 to 9)</td><td>2 more per 1000 (from 0 fewer to 5 more)</td><td>RR 1.50 (1.00 to 2.24)</td></tr>
<tr><td>Heart Failure within 30 days</td><td>66 per 1000</td><td>57 per 1000 (41 to 81)</td><td>9 fewer per 1000 (from 15 more to 26 fewer)</td><td>RR 0.86 (0.61 to 1.22)</td></tr>
<tr><td>Target Vessel Revascularization - long term</td><td>55 per 1000</td><td>50 per 1000 (44 to 56)</td><td>6 fewer per 1000 (from 1 more to 11 fewer)</td><td>RR 0.90 (0.80 to 1.01)</td></tr>
<tr><td>Major Bleeding</td><td>17 per 1000</td><td>18 per 1000 (14 to 24)</td><td>1 more per 1000 (from 3 fewer to 7 more)</td><td>RR 1.08 (0.83 to 1.42)</td></tr>
</table></td><td rowspan="3"></td></tr>
<tr><td></td><td>Are the undesirable anticipated effects small?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td></tr>
<tr><td></td><td>Are the desirable effects large relative to undesirable effects?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>○ No
○ Probably no
○ Uncertain</td><td>No evidence identified specific to KSA on resource use with thrombus extraction devices – Panel members considered costs and resource use when comparing PPCI with thrombus extraction vs. PPCI alone.

One cost analysis included in the NICE systematic review found that “PPCI carried out using a thrombus extraction device was more costly than PPCI carried out without a throm-</td><td>More than 70% of patients are being served by MoH. The panel noted that in the KSA there is a similar cost difference between the two types of devices.</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
		○ Probably yes ○ Yes ● Varies	bus extraction device (cost difference: £110–£125 for PPCI using a thrombus aspiration device, £1200 for PPCI using a mechanical thrombus extraction device)".	The panel considered that for thrombus extraction device the resources required would not be small. The panel considered that for thrombus aspiration devices the resources required may be small but there was some difference in opinion across the panel, considering overall and total volume costs for routine use. Additionally it was noted when using thrombus aspiration balloon use may not be required allowing direct stenting, thereby reducing the cost (or not adding cost). The panel also took into consideration the already large cost of the primary PCI procedure (estimated at 20,000 SAR for the MoH).
	Is the incremental cost small relative to the net benefits?	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing PPCI with thrombus extraction vs. PPCI alone) are small relative to benefits.	

	Criteria	Judgements	Research evidence	Additional considerations
		○ Varies		
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ● Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending PPCI with thrombus extraction vs. PPCI alone.	When considering routine use, every patient would have the intervention available.
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ● Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find fPPCI with thrombus extraction an acceptable option over PPCI alone?	The panel considered that for routine use, thrombus aspiration would likely be acceptable to key stakeholders: 'probably yes'. For mechanical thrombus extraction it would probably not be acceptable given the extra time required: 'probably no'.

	Criteria	Judgements	Research evidence	Additional considera-tions
Feasibility	**Is the option feasible to im-plement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. PPCI with thrombus extraction).	For both types of devices it would be feasible. They are available in the KSA healthcare setting.

Recommendation **Should routine thrombus extraction devices during percutaneous coronary intervention (PPCI) vs. percutaneous coronary intervention (PPCI) alone be used for treatment of STEMI?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	●	○	○	○	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	●	○	○	○

Recommendation	The panel recommends against routine use of aspiration or thrombus extraction devices in patients with STEMI. (strong recommendation; very low quality evidence)
Justification	There is lack of benefit for routine use, and resources required with use of thrombectomy devices.
Subgroup considerations	Consideration for subgroup of patients with large visible clot where interventional cardiologist feels they cannot proceed without removing the thrombus.
Implementation considerations	Recommendation is likey consistent with current practice. There are probably no additional requirements for implementation.
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Thrombus extraction devices during percutaneous coronary intervention (PPCI) compared to percutaneous coronary intervention (PPCI) alone for treatment of STEMI

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2015-03-23
Bibliography: Bulum 2012, DeLuca 2008, Sardella 2010 (EXPIRA), Liu 2012 (ITTI), Migliorini 2010 (JETSTENT), Jolly 2015, Lagerqvist 2014, De Carlo 2012 (MUSTELA), Dudek 2010 (PIHRATE), Vlaar 2008 (TAPAS), Ikari 2008 (VAMPIRE), Lefevre 2005 (X AMINE), Lilstro 2009, AIMI 2006, Antoniucci 2004, Frobert 2013, Stone 2012 (INFUSE-AMI), Napadano 2003, Burzotta 2005 (REMEDIA)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**routine thrombus extraction devices during percutaneous coronary intervention (PPCI)**	**percutaneous coronary intervention (PPCI) alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality - long term												
12	randomised trials	serious [1]	not serious	not serious	not serious	none	398/10096 (3.9%)	449/10070 (4.5%)	**RR 0.89** (0.78 to 1.02)	5 fewer per 1000 (from 1 more to 10 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality - long term - Thrombus aspiration												
8	randomised trials	serious [2]	not serious	not serious	not serious	none	223/4603 (4.8%)	255/4591 (5.6%)	**RR 0.82** (0.58 to 1.16)	10 fewer per 1000 (from 9 more to 23 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality - long term - Mechanical thrombus extraction												
4	randomised trials	serious [3]	not serious	not serious	not serious	none	175/5493 (3.2%)	194/5479 (3.5%)	**RR 0.90** (0.74 to 1.10)	4 fewer per 1000 (from 4 more to 9 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Re-infarction long term												
13	randomised trials	serious [1]	not serious	not serious	not serious	none	219/10159 (2.2%)	234/10131 (2.3%)	**RR 0.94** (0.79 to 1.13)	1 fewer per 1000 (from 3 more to 5 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

Re-infarction long term - Thrombus aspiration											
9	randomised trials	serious [2]	not serious	not serious	not serious	none	114/4666 (2.4%)	133/4652 (2.9%)	**RR 0.87** (0.68 to 1.12)	4 fewer per 1000 (from 3 more to 9 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Re-infarction long term - Mechanical thrombus extraction											
4	randomised trials	serious [3]	not serious	not serious	not serious	none	105/5493 (1.9%)	101/5479 (1.8%)	**RR 1.04** (0.79 to 1.36)	1 more per 1000 (from 4 fewer to 7 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Stroke at 30 days											
9	randomised trials	serious [1]	not serious	not serious	not serious	none	60/9623 (0.6%)	39/9605 (0.4%)	**RR 1.50** (1.00 to 2.24)	2 more per 1000 (from 0 fewer to 5 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Stroke at 30 days - Thrombus aspiration											
3	randomised trials	serious [2]	not serious	not serious	not serious	none	20/3898 (0.5%)	20/3894 (0.5%)	**RR 1.01** (0.55 to 1.86)	0 fewer per 1000 (from 2 fewer to 4 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Stroke at 30 days - Mechanical thrombus extraction											
6	randomised trials	serious [3]	not serious	not serious	not serious	none	40/5725 (0.7%)	19/5711 (0.3%)	**RR 2.03** (1.19 to 3.47)	3 more per 1000 (from 1 more to 8 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Heart Failure within 30 days											
4	randomised trials	serious [1]	not serious	not serious	not serious	none	264/3996 (6.6%)	265/3988 (6.6%)	**RR 0.86** (0.61 to 1.22)	9 fewer per 1000 (from 15 more to 26 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Heart Failure within 30 days - Thrombus aspiration											
3	randomised trials	serious [2]	not serious	not serious	not serious	none	259/3950 (6.6%)	255/3942 (6.5%)	**RR 1.00** (0.82 to 1.22)	0 fewer per 1000 (from 12 fewer to 14 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Heart Failure within 30 days - Mechanical thrombus extraction											
1	randomised	very	not serious	not serious	not serious	none	5/46 (10.9%)	10/46 (21.7%)	**RR 0.50**	109 fewer per 1000 (from	⊕⊕◯◯	CRITICAL

	trials	serious [4]							(0.19 to 1.35)	76 more to 176 fewer)	LOW	
Target Vessel Revascularization - long term												
10	randomised trials	serious [1]	not serious	not serious	not serious	none	500/9994 (5.0%)	551/9976 (5.5%)	**RR 0.90** (0.80 to 1.01)	6 fewer per 1000 (from 1 more to 11 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Target Vessel Revascularization - long term - Thrombus aspiration												
6	randomised trials	serious [2]	not serious	not serious	not serious	none	253/4507 (5.6%)	295/4504 (6.5%)	**RR 0.85** (0.73 to 1.00)	10 fewer per 1000 (from 0 fewer to 18 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Target Vessel Revascularization - long term - Mechanical thrombus extraction												
4	randomised trials	serious [3]	serious [5]	not serious	not serious	none	247/5487 (4.5%)	256/5472 (4.7%)	**RR 0.80** (0.51 to 1.25)	9 fewer per 1000 (from 12 more to 23 fewer)	⊕⊕◯◯ LOW	CRITICAL
Major Bleeding												
5	randomised trials	serious [1]	not serious	not serious	not serious	none	110/5914 (1.9%)	101/5905 (1.7%)	**RR 1.08** (0.83 to 1.42)	1 more per 1000 (from 3 fewer to 7 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Major Bleeding - Thrombus aspiration												
1	randomised trials	serious [6]	not serious	not serious	not serious	none	20/529 (3.8%)	18/531 (3.4%)	**RR 1.12** (0.60 to 2.08)	4 more per 1000 (from 14 fewer to 37 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Major Bleeding - Mechanical thrombus extraction												
4	randomised trials	serious [3]	not serious	not serious	not serious	none	90/5385 (1.7%)	83/5374 (1.5%)	**RR 1.08** (0.80 to 1.45)	1 more per 1000 (from 3 fewer to 7 more)	⊕⊕⊕◯ MODERATE	CRITICAL

1. Not blinded, smaller trials unclear allocation concealment, randomization.
2. Not blinded. TASTE was the largest trial in this subgroup with low risk of bias. Some of the other trials had unclear randomization and allocation concealment.
3. Not blinded. TOTAL was the largest trial in this subgroup and had a low risk of bias. Some of the other trials had unclear randomization and allocation concealment.

4. Only one trial reported this data, unclear randomization, allocation concealment. Small trial, n=92
5. I square >50%
6. Not blinded. Only one trial reported this outcome. TAPAS enrolled 1071 patients.

Guideline Question 4: Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?

Problem: STEMI
Option: multi-vessel PPCI
Comparison: culprit-only PPCI
Setting: in hospital
Perspective: KSA MoH

Background and Objective: Many patients with STEMI have multi vessel disease with significant stenosis in arteries other than the culprit vessel. The strategy of treating all significant lesions at the time of PPCI has the advantage of complete revascularization thus potentially decreasing future cardiac events. The management of the additional lesions at the time of PPCI is controversial. This question addresses whether multi-vessel PPCI versus culprit only PPCI should be performed in patients with STEMI and multi-vessel coronary artery disease.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td rowspan="2">Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
● Low
○ Moderate
○ High</td><td rowspan="2">The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality - long term</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Reinfarction</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
</table></td><td rowspan="2">No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a</td></tr>
<tr><td>Is there important</td><td>○ Important</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td>uncertainty about how much people value the main outcomes?</td>
<td>uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td>
<td>
<table>
<tr><td>Revascularization</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Contrast Induced Nephropathy</td><td>IMPORTANT</td><td>⊕⊕◯◯
LOW</td></tr>
</table>
Summary of findings: multi-vessel PPCI compared to culprit only PPCI in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI
<table>
<tr><th>Outcome</th><th>Without multi-vessel PPCI</th><th>With multi-vessel PPCI</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality - long term</td><td>73 per 1000</td><td>46 per 1000 (27 to 77)</td><td>27 fewer per 1000 (from 4 more to 46 fewer)</td><td>RR 0.63 (0.37 to 1.05)</td></tr>
<tr><td>Reinfarction</td><td>67 per 1000</td><td>25 per 1000 (13 to 48)</td><td>42 fewer per 1000 (from 19 fewer to 54 fewer)</td><td>RR 0.37 (0.19 to 0.71)</td></tr>
<tr><td>Revascularization</td><td>192 per 1000</td><td>71 per 1000 (50 to 102)</td><td>121 fewer per 1000 (from 90 fewer to 142 fewer)</td><td>RR 0.37 (0.26 to 0.53)</td></tr>
<tr><td>Contrast Induced Nephropathy</td><td>17 per 1000</td><td>10 per 1000 (3 to 33)</td><td>8 fewer per 1000 (from 15 fewer to 15 more)</td><td>RR 0.55 (0.16 to 1.89)</td></tr>
</table>
</td>
<td>high value on reduction in mortality.

No data available on harms. Panel noted that there are 3 potential harms of multi-vessel PPCI: (i) using more contrast, (ii) every PCI carries risk (iii) time of procedure is extended.</td>
</tr>
<tr>
<td></td>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are the undesirable anticipated effects small?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes</td>
<td></td>
<td></td>
</tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
		○ Yes ○ Varies		
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		
Resource use	**Are the resources required small?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered costs and resource use when comparing multi vessel vs. culprit only PCI.	
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing multi vessel vs. culprit only PCI) are small relative to benefits. One cost-consequence analysis was identified in the NICE systematic review, based on the HELP-AMI RCT (Di Mario 2004) conducted in Italy. The analysis found that based on the small sample size of 69 patients culprit-only PPCI was more costly over 12 months than immediate multi-vessel PCI; incremental cost of £1412 more per patient (p=0.323). The trial found no significant differences in clinical outcomes between culprit-only and multi-vessel PCI in pa-	Given the probably large anticipated desirable effects but additional cost of the procedure, and no data specific to the KSA setting, the panel judged the cost-effectiveness as 'probably yes' to 'yes'.

	Criteria	Judgements	Research evidence	Additional considerations
			tients who had multi-vessel disease.	
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending multi vessel vs. culprit only PCI.	With multi-vessel PCI there is more use of stents; not everyone may afford it. By doing the longer procedure more resources are used and more stents are used in the primary PCI setting.
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find the intervention an acceptable option.	Some providers may question the reason for the procedure, and why not perform CABG for the patients. Payers would also possibly not find the option acceptable, as well as hospital administrators given resource use requirements.
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. multi vessel PCI vs. culprit only PCI).	

Recommendation **Should multi-vessel PPCI vs. culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests multi-vessel PPCI over culprit-only PCI for patients with multi-vessel coronary artery disease undergoing PPCI. (conditional recommendation; low quality evidence) Remarks: - This recommendation is based on evidence with data predominantly from patients undergoing multi-vessel PCI during the index procedure, but the procedure may also be considered during the index hospitalization. - This recommendation does not apply to patients with cardiogenic shock.
Justification	
Subgroup considerations	Procedure performed either during index PCI or index hospitalization.
Implementation considerations	- There needs to be a policy in terms of how to deal with interaction between surgeons and interventional cardiologists in hospitals as part of the care pathway (e.g. availability of CABG) - Set expiry date for recommendation with publication of COMPLETE trial in 2018.
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Multi-vessel PPCI compared to culprit only PPCI in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2015-03-09
Bibliography: Di Mario 2004, Politi 2010, Wald 2013, Gershlick 2015 (CvLPRIT)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	multi-vessel PPCI	culprit only PPCI	Relative (95% CI)	Absolute (95% CI)		
Mortality - long term												
4	randomised trials	serious [1]	not serious	not serious	serious [2]	none	21/501 (4.2%)	35/478 (7.3%)	**RR 0.63** (0.37 to 1.05)	27 fewer per 1000 (from 4 more to 46 fewer)	⊕⊕◯◯ LOW	CRITICAL
Reinfarction												
4	randomised trials	serious [1]	not serious	not serious	serious [3]	none	12/501 (2.4%)	32/478 (6.7%)	**RR 0.37** (0.19 to 0.71)	42 fewer per 1000 (from 19 fewer to 54 fewer)	⊕⊕◯◯ LOW	CRITICAL
Revascularization												
4	randomised trials	serious [1]	not serious	not serious	not serious	none	38/501 (7.6%)	92/478 (19.2%)	**RR 0.37** (0.26 to 0.53)	121 fewer per 1000 (from 90 fewer to 142 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Contrast Induced Nephropathy												
3	randomised trials	serious [1]	not serious	not serious	serious [2]	none	4/449 (0.9%)	8/461 (1.7%)	**RR 0.55** (0.16 to 1.89)	8 fewer per 1000 (from 15 fewer to 15 more)	⊕⊕◯◯ LOW	IMPORTANT

1. Open label studies. Unclear randomization and allocation concealment in 3 of the 4 trials.
2. Wide confidence interval including from 81% to 29% potential risk reduction.
3. Confidence interval includes appreciable benefit and no benefit, crossing 1 default minimum important difference (0.75) and line of no effect

Guideline Question 5: Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?

Problem: STEMI – patients with cardiogenic shock
Option: early revascularization
Comparison: medical stabilization
Setting: in hospital
Perspective: KSA MoH

Background and Objective: In patients with STEMI, early revascularization is the cornerstone of treatment to improve perfusion and limit myocardial damage. However, patients in cariogenic shock may be too unstable and may benefit from early medical stabilization. This question addresses whether early revascularization versus medical stabilization should be used in patients with cardiogenic shock due to STEMI.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
● Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality at 30 days</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Mortality at 1 year</td><td>CRITICAL</td><td>⊕⊕⊕◯</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted</td></tr>
</table>

	Is there important uncertainty about how much people value the main outcomes?	○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty of variability ● No important uncertainty of variability ○ No known undesirable				that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.
	Are the desirable anticipated effects large?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies				
	Are the undesirable anticipated effects small?	○ No ○ Probably no ○ Uncertain				

		MODERATE
Stroke at 30 days	CRITICAL	⊕⊕⊕◯ MODERATE
Re-infarction at 30 days	CRITICAL	⊕⊕⊕◯ MODERATE
Unplanned revascularization at 30 days	CRITICAL	⊕⊕⊕◯ MODERATE
Class III or IV Heart Failure at 2 weeks	CRITICAL	⊕⊕⊕◯ MODERATE

Summary of findings: Early revascularization compared to medical stabilization in patients with cardiogenic shock due to STEMI

Outcome	**Without early revascularization**	**With early revascularization**	**Difference (95% CI)**	**Relative effect (RR) (95% CI)**
Mortality at 30 days	590 per 1000	**495 per 1000 (413 to 601)**	94 fewer per 1000 (from 12 more to 177 fewer)	**RR 0.84** (0.70 to 1.02)
Mortality at 1 year	671 per 1000	**537 per 1000 (450 to 651)**	134 fewer per 1000 (from 20 fewer to 221 fewer)	**RR 0.80** (0.67 to 0.97)
Stroke at 30	87 per 1000	**13 per 1000**	74 fewer per 1000 (from	**RR 0.15** (0.01 to

<table>
<tr>
<td></td>
<td></td>
<td>● Probably yes
○ Yes
○ Varies</td>
<td rowspan="2">
<table>
<tr><td>days</td><td></td><td>(1 to 251)</td><td>86 fewer to 164 more)</td><td>2.89)</td></tr>
<tr><td>Re-infarction at 30 days</td><td>43 per 1000</td><td>31 per 1000 (2 to 474)</td><td>12 fewer per 1000 (from 41 fewer to 431 more)</td><td>RR 0.72 (0.05 to 10.91)</td></tr>
<tr><td>Unplanned re-vascularization at 30 days</td><td>43 per 1000</td><td>63 per 1000 (6 to 649)</td><td>19 more per 1000 (from 37 fewer to 605 more)</td><td>RR 1.44 (0.14 to 14.92)</td></tr>
<tr><td>Class III or IV Heart Failure at 2 weeks</td><td>375 per 1000</td><td>240 per 1000 (135 to 431)</td><td>135 fewer per 1000 (from 56 more to 240 fewer)</td><td>RR 0.64 (0.36 to 1.15)</td></tr>
</table>
</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are the desirable effects large relative to undesirable effects?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
<td></td>
</tr>
<tr>
<td rowspan="2">Resource use</td>
<td>Are the resources required small?</td>
<td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td>
<td>No evidence identified specific to KSA and no economic evaluations identified comparing early revascularization with medical stabilization in patients with cardiogenic shock due to STEMI.

Panel members considered costs and resource use when comparing early revascularization vs. medical stabilization in patients.</td>
<td>Panel judged resources required as probably not small considering all costs, including downstream costs (e.g. with medical stabilization, cost of extended stay in ICU and risk of heart failure in the future was considered)</td>
</tr>
<tr>
<td>Is the incremental cost small relative to the net benefits?</td>
<td>○ No
○ Probably no</td>
<td>No evidence identified specific to KSA – Panel members considered whether the incremental costs (early revascularization vs. medical stabilization) are small relative to benefits.</td>
<td>Although the resources required are not small, there is a net benefit.</td>
</tr>
</table>

		○ Uncertain ● Probably yes ○ Yes ○ Varies		
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending early revascularization vs. medical stabilization.	The issues with availability of catheterization labs for early revascularization would probably increase inequities.
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether stakeholders in the KSA (e.g. clinicians, policymakers) would find early revascularization an acceptable option over medical stabilization.	

Feasibility	**Is the option feasible to implement?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. early revascularization).	Given that patients would require to be transferred if the hospital does not offer the procedure, and issue with difficulty of universal access to PCI, option is probably not feasible in KSA setting.

Recommendation **Should early revascularization vs. medical stabilization be used in patients with cardiogenic shock due to STEMI?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	○	●

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	○	●

Recommendation	The panel recommends early revascularization for patients with cardiogenic shock due to STEMI (strong recommendation; moderate quality evidence)
Justification	A high weight was placed on the benefits of the intervention. Panel considered that patients with cardiogenic shock are already at high risk.
Subgroup considerations	When a significant delay for early revascularization is expected, full conventional therapy (including fibrinolytics) may be considered.
Implementation considerations	- The feasibility issues of access to PCI should be solved. - Catheterization labs and training of personnel is desirable in peripheral hospitals.
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Early revascularization compared to medical stabilization in patients with cardiogenic shock due to STEMI

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliogrpahy: Hochman 1999, Urban 1999, Hochman 2001, Sleeper 2005

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consid-erations	early revascular-ization	medical stabilization	Relative (95% CI)	Absolute (95% CI)		
Mortality at 30 days												
2	randomised trials	not seri-ous	not serious	not serious	serious [1]	none	93/184 (50.5%)	102/173 (59.0%)	**RR 0.84** (0.70 to 1.02)	94 fewer per 1000 (from 12 more to 177 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Mortality at 1 year												
1	randomised trials	not seri-ous	not serious	not serious	serious [2]	none	82/152 (53.9%)	100/149 (67.1%)	**RR 0.80** (0.67 to 0.97)	134 fewer per 1000 (from 20 fewer to 221 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Stroke at 30 days												
1	randomised trials	not seri-ous	not serious	not serious	serious [3]	none	0/32 (0.0%)	2/23 (8.7%)	**RR 0.15** (0.01 to 2.89)	74 fewer per 1000 (from 86 fewer to 164 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Re-infarction at 30 days												
1	randomised trials	not seri-ous	not serious	not serious	serious [3]	none	1/32 (3.1%)	1/23 (4.3%)	**RR 0.72** (0.05 to 10.91)	12 fewer per 1000 (from 41 fewer to 431 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Unplanned revascularization at 30 days												
1	randomised trials	not seri-ous	not serious	not serious	serious [3]	none	2/32 (6.3%)	1/23 (4.3%)	**RR 1.44** (0.14 to 14.92)	19 more per 1000 (from 37 fewer to 605 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Class III or IV Heart Failure at 2 weeks												
1	randomised trials	not seri-ous	not serious	not serious	serious [1]	none	14/58 (24.1%)	18/48 (37.5%)	**RR 0.64** (0.36 to 1.15)	135 fewer per 1000 (from 56 more to 240 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

1. Wide confidence interval that includes appreciable benefit and no benefit, crossing 1 default minimum important difference (0.75) and line of no effect.

2. Wide confidence interval that includes both large reduction in risk and small reduction in risk.
3. Very wide confidence interval that includes appreciable benefit and appreciable harm. Small sample size and number of events.

Guideline Question 6: Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?

Problem: STEMI – cardiac arrest patients with ROSC who remain unconscious
Option: immediate angiography with PPCI where indicated
Comparison: usual care
Setting: in hospital
Perspective: KSA MoH

Background and Objective: A considerable proportion of patients with STEMI present as out-of-hospital cardiac arrest. Of the patients who are admitted to a hospital with return of spontaneous circulation (ROSC), most are unconscious in the immediate period following the resuscitation. During this time, a variety of treatments may be indicated and providers may need to prioritize treatment options based on the condition of the patient. It is not clear if immediate PPCI is beneficial compared to stabilization in the intensive care unit prior to PPCI. This question addresses whether immediate angiography followed by PPCI where indicated should be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td>The panel noted that with poorly developed EMS services in the KSA, the case of patients who suffer an out of hospital cardiac arrest and achieve return of spontaneous circulation (ROSC) is very infrequent.</td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
● Very low
○ Low</td><td>The relative importance or values of the main outcomes of interest:<table><tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr><tr><td>Mortality at 30 days</td><td>CRITICAL</td><td>⨁◯◯◯</td></tr></table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td></td>
<td>○ Moderate
○ High</td>
<td rowspan="3">
<table>
<tr><td></td><td></td><td>VERY LOW</td></tr>
<tr><td>Stroke at 30 days</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
<tr><td>Good performance on CPC</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
</table>

Summary of findings: Immediate angiography followed by PPCI where indicated compared to usual care in in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest
<table>
<tr><th>Outcome</th><th>Without immediate angiography followed by PPCI where indicated</th><th>With immediate angiography followed by PPCI where indicated</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality at 30 days</td><td>776 per 1000</td><td>396 per 1000 (295 to 535)</td><td>380 fewer per 1000 (from 241 fewer to 481 fewer)</td><td>RR 0.51 (0.38 to 0.69)</td></tr>
<tr><td>Stroke at 30 days</td><td>531 per 1000</td><td>266 per 1000 (149 to 468)</td><td>266 fewer per 1000 (from 64 fewer to 383 fewer)</td><td>RR 0.50 (0.28 to 0.88)</td></tr>
<tr><td>Good performance on CPC</td><td>0 per 1000</td><td>0 per 1000 (0 to 0)</td><td>0 fewer per 1000 (from 0 fewer to 0 fewer)</td><td>RR 3.07 (0.27 to 34.37)</td></tr>
</table>
</td>
<td rowspan="3">patient representative noted that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.

Panel noted that most patients and their families will request resuscitation and intervening to prolong life.

No data available on potential harms of early revascularization based on available studies.</td>
</tr>
<tr>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td>
</tr>
<tr>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
</tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
	Are the undesirable anticipated effects small?	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies		
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		
Resource use	**Are the resources required small?**	● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered costs and resource use when comparing immediate angiography vs. stabilization	
	Is the incremental cost small	○ No	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing immediate angiography vs. stabilization) are small rela-	Panel considered that the incremental cost is probably

	Criteria	Judgements	Research evidence	Additional considerations
	relative to the net benefits?	○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	tive to benefits.	small relative to the net benefit, although the benefit is likely low for patients who survive and recover after the cardiac arrest.
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending immediate angiography vs. stabilization.	
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find immediate angiography an acceptable option over stabilization.	The panel noted that at arrival to hospital many providers may not want to provide the option of immediate angiography and that these patients would get rejected.

	Criteria	Judgements	Research evidence	Additional considerations
Feasibility	**Is the option feasible to implement?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. immediate angiograph).	The panel noted the following reasons why immediate angiography is probably not feasible: - It is difficult to get patients with out of hospital cardiac arrest to the hospital due to poorly developed EMS services in the KSA. - Overall there is a lack of access to PCI services for the population. There are 48 cardiac centres with catheterization labs in the KSA, but due to the geographic distribution, there are 3-4 million patients without access. - Patients with out of hospital cardiac arrest with poor prognosis would be competing for limited spaces for PCI.

Recommendation **Should immediate angiography followed by PPCI where indicated vs. usual care be used in in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests immediate angiography followed by PCI where indicated over usual care in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest. (conditional recommendation; very low quality evidence) Remarks: - For patients with unwitnessed out of hospital arrest, without documented time of arrest, the clinician may re-evaluate the patient for PCI with detailed assessment of the patient's neurological status before proceeding with a potentially futile intervention.
Justification	
Subgroup considerations	Consideration for in-hospital versus out of hospital cardiac arrest, and in the latter for witnessed versus unwitnessed. Panel noted it may be difficult to establish STEMI in patients with out of hospital arrest who remain unconscious. Panel noted that for patients with unwitnessed out of hospital cardiac arrest, without documented time of arrest, the patient should be assessed and re-evaluated by a clinician.
Implementation considerations	None
Monitoring and evaluation	None
Research possibilities	Panel recommends registry study and auditing to determine how many patients in the KSA there are with cardiac arrest who make it to the catheterization lab and what their outcomes are.

Evidence Profile: Immediate angiography followed by PPCI where indicated compared to usual care in in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-28
Bibliography: Bulut 2000, Hong-wei 2012, Pleskot 2008, Liu 2012

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	immediate angiography followed by PPCI where indicated	usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality at 30 days												
3	observational studies	very serious [1]	serious [2]	serious [3]	not serious	none	30/78 (38.5%)	45/58 (77.6%)	**RR 0.51** (0.38 to 0.69)	380 fewer per 1000 (from 241 fewer to 481 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Stroke at 30 days												
1	observational studies	very serious [1]	not serious	serious [4]	serious [5]	none	13/49 (26.5%)	17/32 (53.1%)	**RR 0.50** (0.28 to 0.88)	266 fewer per 1000 (from 64 fewer to 383 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Good performance on CPC [6]												
1	observational studies	very serious [1]	not serious	serious [4]	serious [5]	none	11/14 (78.6%)	0/1 (0.0%)	**RR 3.07** (0.27 to 34.37)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

1. Observational studies (retrospective cohorts) with high risk of bias including selection bias, detection bias, variable treatment in different centers and confounding
2. Heterogeneity between studies; one study effect size and confidence interval very different from 2 other studies
3. Mixed population of conscious and unconscious patients in PPCI group in 2 studies
4. Mixed population of conscious and unconscious patients in PPCI group
5. Wide confidence interval based on few patients and few events

6. Neurological outcome assessed using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC) at discharge from acute hospital. At 1 year follow-up, 13/14 patients in intervention group were rated as having good performance, the 1 patient in the control group remained at moderate cerebral disability.

Guideline Question 7: Should high volume centres versus low volume centres be used for PPCI services?

Problem: STEMI
Option: high volume centres
Comparison: low volume centres
Setting: healthcare system (hospitals/catheterization labs with PPCI services)
Perspective: KSA MoH

Background and Objective: Success of percutaneous coronary intervention depends on individual expertise of the operator and the quality of supporting staff and infrastructure. These include appropriate facilities, trained staff and an ongoing volume of procedures to attain and sustain excellent procedural outcomes. Several studies have identified an inverse relationship between hospital volumes and adverse outcomes for PPCI. This question addresses the extent to which procedural volumes influence patient outcomes.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011). The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
● Very low
○ Low
○ Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>In Hospital Mortality</td><td>CRITICAL</td><td>⨁◯◯◯
VERY LOW</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no important variability or uncertainty in patients' values and preferences in</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td></td><td>Is there important uncertainty about how much people value the main outcomes?</td><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td><td rowspan="3">Summary of findings: High volume centres compared to low volume centres for PPCI services
<table><tr><th>Outcome</th><th>Impact</th></tr><tr><td>In Hospital Mortality</td><td>Five registry studies comparing in-hospital mortality in low- or medium-volume versus high volume centres, defined according to various categories of PPCI procedures per year.

Lower vs. higher volume:
Kontos 2013:
<36 vs. >60: OR=1.17 (1.07, 1.28)
36-60 vs. >60: OR=0.99 (0.93, 1.05)

Kumbhani 2009:
<36 vs. 36-70: OR=1.22 (0.78–1.91)
36-70 vs. >70: OR=1.14 (0.78-1.66)

Canto 2000:
5-11 vs. 12-20: OR=1.15 (0.94, 1.41)
5-11 vs. 21-33: OR=1.20 (1.00, 1.46)
5-11 vs. >33: OR=1.39 (1.15, 1.67)

Higher vs. lower volume:
Srinivas 2009:
>25 vs. =<25: OR=0.61 (0.34, 1.10)
>50 vs. =<50: OR=0.58 (0.38, 0.88)
>75 vs. =<70: OR=0.82 (0.57, 1.17)

Frequencies only:

Magid 2000:
=<16: Mortality 6.2% (n=1423)
17-48: Mortality 4.5% (n=8817)
>=49: Mortality 3.4 % (n=1733)</td></tr></table></td><td rowspan="3">the KSA setting and that patients would place a high value on reduction in mortality.</td></tr>
<tr><td>Are the desirable anticipated effects large?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Are the undesirable anticipated effects small?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
		○ Yes ○ Varies		
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		
Resource use	**Are the resources required small?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered costs and resource use when comparing high- vs. low-volume centres for PPCI service provision.	
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing high- vs. low-volume centres) are small relative to benefits.	

	Criteria	Judgements	Research evidence	Additional considerations
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ○ Uncertain ● Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending high-volume vs. low-volume centres.	Prioritizing high-volume centres for PPCI services would improve patients' outcomes and in general increasing volume at existing low-volume centres would improve access.
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find the option of PPCI service provision in high-volume vs. low-volume centres acceptable.	Patients' access to PPCI would be reduced if PPCI services are restricted to high volume centers
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of high- vs. low-volume centres.	It requires debate from policy makers

Recommendation **Should high volume centres vs. low volume centres be used for PPCI services?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○
Recommendation	The panel suggests prioritizing the management of patients with STEMI to high volume centres. (conditional recommendation; very low quality evidence) Remark: The implementation of this recommendation should not restrict care for patients who require PPCI in settings where only low-volume centres are available.			
Justification	The panel did not set any restriction on centre size, which would further reduce access. The recommendation is to prioritize expansion of existing PCI services to increase volume.			
Subgroup considerations	None			
Implementation considerations	Priority should be made to increase the capacity of existing low-volume centres.			
Monitoring and evaluation	None			
Research possibilities	Assess outcomes for patients receiving PPCI at low-volume centres vs. thrombolytics.			

Evidence Profile: High volume centres compared to low volume centres for PPCI services

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15

Quality assessment							№ of patients		Impact	Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	high volume centres	low volume centres			
In Hospital Mortality											
5	observational studies	very serious [1,2,3]	not serious	not serious	serious [4]	none			Five registry studies comparing in-hospital mortality in low- or medium-volume versus high volume centres, defined according to various categories of PPCI procedures per year. **Lower vs. higher volume:** Kontos 2013: <36 vs. >60: OR=1.17 (1.07, 1.28) 36-60 vs. >60: OR=0.99 (0.93, 1.05) Kumbhani 2009: <36 vs. 36-70: OR=1.22 (0.78–1.91) 36-70 vs. >70: OR=1.14 (0.78-1.66) Canto 2000: 5-11 vs. 12-20: OR=1.15 (0.94, 1.41) 5-11 vs. 21-33: OR=1.20 (1.00, 1.46) 5-11 vs. >33: OR=1.39 (1.15, 1.67) **Higher vs. lower volume:** Srinivas 2009: >25 vs. =<25: OR=0.61 (0.34, 1.10) >50 vs. =<50: OR=0.58 (0.38, 0.88) >75 vs. =<70: OR=0.82 (0.57, 1.17) **Frequencies only**:	⊕◯◯◯ VERY LOW	CRITICAL

									Magid 2000: =<16: Mortality 6.2% (n=1423) 17-48: Mortality 4.5% (n=8817) >=49: Mortality 3.4 % (n=1733)		

OR – odds ratio

1. Data not adjusted for possible confounders
2. Registry with voluntary participation; possible selection bias which was considered important
3. Retrospective cohort data; possible selection bias
4. Wide confidence intervals across effect estimates in the studies, including both benefit and harm

Guideline Question 8: Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?

Problem: STEMI
Option: rescue PCI
Comparison: conservative therapy
Setting: in hospital
Perspective: KSA MoH

Background and Objective: Fibrinolytic therapy restores flow in the coronary artery by lysing the thrombus leading to preserved myocardial function and decreased mortality. Complete reperfusion with normal flow in the infarct related artery is found only in approximately 50% of the patients who receive fibrinolytic therapy. Options for further revascularization include repeat fibrinolysis and immediate referral for coronary angiography and PCI (rescue PCI). A third alternative is conservative therapy with continued medical therapy without repeat fibrinolysis or rescue PCI.

Comparison 1: Rescue PCI versus conservative therapy

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
● Low
○ Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td>
<td>
<table>
<tr><td>Reinfarction at 6 months to 1 year</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Heart Failure at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Stroke at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Unplanned revascularization at 6 to 12 months</td><td>IMPORTANT</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Major bleeding at 30 days</td><td>IMPORTANT</td><td>⊕⊕◯◯
LOW</td></tr>
</table>
</td>
<td rowspan="3">high value on reduction in mortality.</td>
</tr>
<tr>
<td></td>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
<td>
Summary of findings: Rescue PCI compared to conservative management in patients with STEMI who fail to reperfuse after fibrinolytic therapy
<table>
<tr><th>Outcome</th><th>Without rescue PCI</th><th>With rescue PCI</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality at 6 months</td><td>123 per 1000</td><td>87 per 1000 (54 to 139)</td><td>36 fewer per 1000 (from 16 more to 69 fewer)</td><td>RR 0.71 (0.44 to 1.13)</td></tr>
<tr><td>Reinfarction at 6</td><td>108 per</td><td>51 per</td><td>57 fewer per</td><td>RR 0.47</td></tr>
</table>
</td>
</tr>
<tr>
<td></td>
<td>Are the undesirable anticipated effects small?</td>
<td>○ No
○ Probably no</td>
</tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th colspan="5">Research evidence</th><th>Additional considerations</th></tr>
<tr><td rowspan="2"></td><td></td><td>○ Uncertain
● Probably yes
○ Yes
○ Varies</td><td colspan="5" rowspan="2"><table>
<tr><td>months to 1 year</td><td>1000</td><td>1000 (28 to 91)</td><td>1000 (from 17 fewer to 80 fewer)</td><td>(0.26 to 0.84)</td></tr>
<tr><td>Heart Failure at 6 months</td><td>200 per 1000</td><td>156 per 1000 (112 to 218)</td><td>44 fewer per 1000 (from 18 more to 88 fewer)</td><td>RR 0.78 (0.56 to 1.09)</td></tr>
<tr><td>Stroke at 6 months</td><td>10 per 1000</td><td>34 per 1000 (9 to 122)</td><td>24 more per 1000 (from 1 fewer to 111 more)</td><td>RR 3.33 (0.93 to 11.95)</td></tr>
<tr><td>Unplanned revascularization at 6 to 12 months</td><td>245 per 1000</td><td>135 per 1000 (96 to 191)</td><td>110 fewer per 1000 (from 54 fewer to 150 fewer)</td><td>RR 0.55 (0.39 to 0.78)</td></tr>
<tr><td>Major bleeding at 30 days</td><td>35 per 1000</td><td>28 per 1000 (7 to 101)</td><td>8 fewer per 1000 (from 28 fewer to 66 more)</td><td>RR 0.78 (0.21 to 2.86)</td></tr>
</table></td><td></td></tr>
<tr><td>Are the desirable effects large relative to undesirable effects?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>● No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes</td><td colspan="5">No evidence identified specific to KSA – Panel members considered costs and resource use when comparing rescue PCI vs. conservative management (e.g. considered resource use implications such as costs of procedure and drugs, future costs of management, etc.)</td><td>Rescue PCI may require significant resources, which may depend on the city and whether PPCI services are available. It is an expensive procedure compared to conservative management.</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
		○ Varies		
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing rescue PCI vs. conservative management) are small relative to benefits.	There is a net benefit but resources required are not small. If you perform the rescue PCI you are less likely to have events in the future and a reduction in overall cost.
Equity	**What would be the impact on health inequities?**	● Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending rescue PCI vs. conservative management.	Inequities would be increased in the KSA, because not everyone has access to the PCI procedure. In the main cities there is access to PCI, but not in the periphery areas. People are going to be treated differently depending on their geographical location. It is also hard for patients to be referred to a MoH hospital. There is already inequity. A recommendation for rescue PCI would push to refer patients for rescue PCI, but some patients would still be denied the procedure. Therefore inequity would be increased.

	Criteria	Judgements	Research evidence	Additional considerations
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find the option of rescue PCI vs. conservative management acceptable.	
Feasibility	**Is the option feasible to implement?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of rescue PCI as an option.	Given the current situation and levels of access, rescue PCI may be difficult to implement universally. There are geographical locations where rescue PCI is already routinely performed.

Recommendation **Should rescue PCI vs. conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests rescue PCI over conservative management in patients with STEMI who fail to reperfuse after fibrinolytic therapy (conditional recommendation; low quality evidence)
Justification	There is a net benefit for most patient important outcomes based on low quality evidence. However, there are issues regarding the impact on health inequity and feasibility of implementation in the KSA healthcare setting given current lack of universal access to PCI services.
Subgroup considerations	None
Implementation considerations	In order to implement the recommendation the feasibility issues regarding lack of universal access to PCI services in specific geographical regions of the KSA need to be addressed.
Monitoring and evaluation	None
Research possibilities	The panel suggests future research that would inform implementation issues including a registry study to provide information regarding the number of patients eligible for rescue PCI that did not receive rescue PCI. Keeping track of patients who don't have access and don't get treatment will provide support for policymakers to improve access.

Evidence Profile: Rescue PCI compared to conservative management in patients with STEMI who fail to reperfuse after fibrinolytic therapy

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliography: Kunadian 2007 (MERLIN), Gershlick 2005 (REACT), Ellis 2000 (RESCUE II)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rescue PCI	conservative management	Relative (95% CI)	Absolute (95% CI)		
Mortality at 6 months												
3	randomised trials	serious [1]	not serious	not serious	serious [2]	none	27/311 (8.7%)	38/310 (12.3%)	**RR 0.71** (0.44 to 1.13)	36 fewer per 1000 (from 16 more to 69 fewer)	⊕⊕◯◯ LOW	CRITICAL
Reinfarction at 6 months to 1 year												
2	randomised trials	serious [1,3]	not serious	not serious	not serious	none	15/297 (5.1%)	32/295 (10.8%)	**RR 0.47** (0.26 to 0.84)	57 fewer per 1000 (from 17 fewer to 80 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Heart Failure at 6 months												
2	randomised trials	serious [1,3]	not serious	not serious	serious [2]	none	46/297 (15.5%)	59/295 (20.0%)	**RR 0.78** (0.56 to 1.09)	44 fewer per 1000 (from 18 more to 88 fewer)	⊕⊕◯◯ LOW	CRITICAL
Stroke at 6 months												
2	randomised trials	serious [1,3]	not serious	not serious	serious [4]	none	10/297 (3.4%)	3/295 (1.0%)	**RR 3.33** (0.93 to 11.95)	24 more per 1000 (from 1 fewer to 111 more)	⊕⊕◯◯ LOW	CRITICAL
Unplanned revascularization at 6 to 12 months												
3	randomised trials	serious [1,3]	not serious	not serious	not serious	none	42/311 (13.5%)	76/310 (24.5%)	**RR 0.55** (0.39 to 0.78)	110 fewer per 1000 (from 54 fewer to 150 fewer)	⊕⊕⊕◯ MODERATE	IMPORTANT

Major bleeding at 30 days												
1	randomised trials	serious [1,3]	not serious	not serious	very seri-ous [5]	none	4/144 (2.8%)	5/141 (3.5%)	**RR 0.78** (0.21 to 2.86)	8 fewer per 1000 (from 28 fewer to 66 more)	⊕⊕◯◯ LOW	IMPORTANT

1. Recruitment stopped early due to inability to fund/recruit in 2 of the 3 studies
2. Wide confidence interval including appreciable benefit and including line of no effect (i.e. no benefit)
3. Unclear allocation concealment
4. Very wide confidence interval including appreciable harm and crossing line of no effect (i.e. no harm)
5. Very wide confidence interval including appreciable benefit and harm

Problem: STEMI
Option: repeat fibrinolysis
Comparison: conservative therapy
Setting: in hospital
Perspective: KSA MoH

Background and Objective: Fibrinolytic therapy restores flow in the coronary artery by lysing the thrombus leading to preserved myocardial function and decreased mortality. Complete reperfusion with normal flow in the infarct related artery is found only in approximately 50% of the patients who receive fibrinolytic therapy. Options for further revascularization include repeat fibrinolysis and immediate referral for coronary angiography and PCI (rescue PCI). A third alternative is conservative therapy with continued medical therapy without repeat fibrinolysis or rescue PCI.

Comparison 2: Repeat fibrinolysis versus conservative therapy

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
● Low
○ Moderate</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality before 6 weeks</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no im-</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td></td>
<td>○ High</td>
<td rowspan="3">
<table>
<tr><td>Reinfarction at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Heart Failure at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Stroke at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Unplanned revascularization before discharge</td><td>IMPORTANT</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Major bleeding before hospital discharge</td><td>IMPORTANT</td><td>⊕⊕◯◯
LOW</td></tr>
</table>
Summary of findings: Repeated fibrinolysis compared to conservative management in patients with STEMI who fail to reperfuse after fibrinolytic therapy
<table>
<tr><th>Outcome</th><th>Without repeated fibrinolysis</th><th>With repeated fibrinolysis</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality before 6 weeks</td><td>222 per 1000</td><td>62 per 1000 (22 to 180)</td><td>160 fewer per 1000 (from 42 fewer to 200 fewer)</td><td>RR 0.28 (0.10 to 0.81)</td></tr>
<tr><td>Reinfarction at 6 months</td><td>85 per 1000</td><td>106 per 1000 (51 to 218)</td><td>20 more per 1000 (from 34 fewer to 133 more)</td><td>RR 1.24 (0.60 to 2.56)</td></tr>
<tr><td>Heart Failure at 6 months</td><td>78 per 1000</td><td>70 per 1000 (31 to 161)</td><td>8 fewer per 1000 (from 47 fewer to 83 more)</td><td>RR 0.90 (0.40 to 2.06)</td></tr>
</table>
</td>
<td rowspan="3">portant variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.

With respect to harms, the panel noted that the risk of bleeding would be much higher if using streptokinase versus for example tPA or TNKase.</td>
</tr>
<tr>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty or variability
● No important uncertainty or variability
○ No known undesirable</td>
</tr>
<tr>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td>
</tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considera-tions</th></tr>
<tr><td rowspan="2"></td><td>Are the undesir-able anticipated effects small?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td rowspan="2"><table>
<tr><td>Stroke at 6 months</td><td>7 per 1000</td><td>7 per 1000 (0 to 111)</td><td>0 fewer per 1000 (from 7 fewer to 104 more)</td><td>RR 0.99 (0.06 to 15.72)</td></tr>
<tr><td>Unplanned revascu-larization before discharge</td><td>22 per 1000</td><td>311 per 1000 (43 to 1000)</td><td>289 more per 1000 (from 20 more to 1000 more)</td><td>RR 14.00 (1.92 to 102.03)</td></tr>
<tr><td>Major bleeding be-fore hospital dis-charge</td><td>32 per 1000</td><td>43 per 1000 (15 to 121)</td><td>11 more per 1000 (from 17 fewer to 88 more)</td><td>RR 1.33 (0.47 to 3.74)</td></tr>
</table></td><td rowspan="2"></td></tr>
<tr><td>Are the desirable effects large rel-ative to undesir-able effects?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>○ No
● Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td>No evidence identified specific to KSA – Panel members considered costs and resource use when comparing repeat fibrinolysis vs. conservative management (e.g. considered resource use implications such as costs of drugs, future costs of management, etc.)</td><td>While cost of streptokinase is low (estimated at 350 SAR) the cost of tPA and TNKase is much higher (e.g. cost of TNKase esti-mated at 5000 SAR).</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
	Is the incremental cost small relative to the net benefits?	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing repeat fibrinolysis vs. conservative management) are small relative to benefits.	Increased resource use for repeat fibrinolysis and probably no anticipated benefit for patients.
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	No evidence identified specific to KSA – Panel to considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending repeat fibrinolysis vs. conservative management.	Both treatment options are equally available in the KSA setting, but given cost of tPA and TNKase health inequity would probably be increased. This does not apply to streptokinase, which should not be repeated due to risk of bleeding.

	Criteria	Judgements	Research evidence	Additional considera-tions
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Would key stakeholders in the KSA (e.g. clinicians, policymakers) find the option of repeat fibrinolysis vs. conservative management acceptable?	Most cardiologists would not provide repeated fibrinolysis.
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel to consider feasibility of repeat fibrinolysis as an option. What are the issues specific to KSA related to the feasibility of the option?	The option of repeat fibrinolysis is feasible, given availability of tPA and TNKase.

Recommendation **Should repeated fibrinolysis vs. conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	●	○	○	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	●	○	○

Recommendation	The panel suggests not offering repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy (conditional recommendation; low quality evidence) Remark: - When there is no available immediate urgent access for the patient at a catheterization lab for the rescue PCI procedure, treating clinicians should determine with a lab if access to rescue PCI can become available for such patients. - There should not be a repeated administration of streptokinase. The risk of adverse events with repeat administration of streptokinase is higher than the benefit.
Justification	
Subgroup considerations	The panel advises additional caution for patients with higher risk of bleeding (e.g. elderly) when considering repeat administration of fibrinolysis, but not with streptokinase, under the conditions where rescue PCI procedure is not available.
Implementation considerations	None
Monitoring and evaluation	None
Research possibilities	As in previous comparison of rescue PCI versus conservative management, registry study is required to determine access to treatment.

Evidence Profile: Repeated fibrinolysis compared to conservative management in patients with STEMI who fail to reperfuse after fibrinolytic therapy

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliography: Gershlick 2005 (REACT), Mounsey 1995, Srullo 2000, Ellis 1994 (RESCUE I)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	repeated fibrinolysis	conservative management	Relative (95% CI)	Absolute (95% CI)		
Mortality before 6 weeks												
2	randomised trials	serious [1,2]	not serious	not serious	not serious	none	4/64 (6.3%)	14/63 (22.2%)	**RR 0.28** (0.10 to 0.81) [3]	160 fewer per 1000 (from 42 fewer to 200 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Reinfarction at 6 months												
1	randomised trials	serious [1]	not serious	not serious	serious [4]	none	15/142 (10.6%)	12/141 (8.5%)	**RR 1.24** (0.60 to 2.56)	20 more per 1000 (from 34 fewer to 133 more)	⊕⊕◯◯ LOW	CRITICAL
Heart Failure at 6 months												
1	randomised trials	serious [1]	not serious	not serious	serious [4]	none	10/142 (7.0%)	11/141 (7.8%)	**RR 0.90** (0.40 to 2.06)	8 fewer per 1000 (from 47 fewer to 83 more)	⊕⊕◯◯ LOW	CRITICAL
Stroke at 6 months												
1	randomised trials	serious [1]	not serious	not serious	serious [4]	none	1/142 (0.7%)	1/141 (0.7%)	**RR 0.99** (0.06 to 15.72)	0 fewer per 1000 (from 7 fewer to 104 more)	⊕⊕◯◯ LOW	CRITICAL
Unplanned revascularization before discharge												
1	randomised trials	serious [1,5]	not serious	not serious	serious [6]	none	14/45 (31.1%)	1/45 (2.2%)	**RR 14.00** (1.92 to 102.03)	289 more per 1000 (from 20 more to 1000 more)	⊕⊕◯◯ LOW	IMPORTANT

Major bleeding before hospital discharge												
2	randomised trials	serious [1]	not serious	not serious	serious [4]	none	8/187 (4.3%)	6/186 (3.2%)	**RR 1.33** (0.47 to 3.74)	11 more per 1000 (from 17 fewer to 88 more)	⊕⊕◯◯ LOW	IMPORTANT

1. Unclear allocation concealment, randomization by sequentially numbered boxes.
2. Unexpectedly and unexplained high mortality (29%) in the conservative management group in one trial.
3. The meta-analysis for this outcome includes 2 studies with a total of 127 patients (64 in the repeat fibrinolysis arm and 63 in the conservative arm). One of these studies had an unexpectedly high (29%) mortality in the conservative arm which seems to be driving the statistically significant result. Another RCT, included in the reference list is the REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Fibrinolysis) Trial which recruited 142 patients to repeat fibrinolysis and 141 to conservative therapy. Two publications are included with results from this trial, one short term outcome published in the NEJM (reference #2) and a longer term outcome in the Journal of the American College of Cardiology (reference #1). This study reported outcomes as time to event, and was not included in the meta-analysis. There was no difference in outcomes between the 2 groups including in the longer term follow-up of patients, based on time to event analysis at a median of 4.4 years of follow up. Mortality at 6 months was 12.7% in repeat fibrinolysis group and 12.8% in the conservative group and mortality at 4.4 years was 22.3% in the repeat fibrinolysis group and 22.4% in the conservative group.
4. Wide confidence intervals including appreciable benefit and appreciable harm, crossing the line of no effect.
5. One small trial with high mortality in the conservative management group and rather high urgent PTCA/CABG in the intervention group
6. Wide confidence interval and small sample size with small number of events.

Problem: STEMI
Option: rescue PCI
Comparison: repeat fibrinolysis
Setting: in hospital
Perspective: KSA MoH

Background and Objective: Fibrinolytic therapy restores flow in the coronary artery by lysing the thrombus leading to preserved myocardial function and decreased mortality. Complete reperfusion with normal flow in the infarct related artery is found only in approximately 50% of the patients who receive fibrinolytic therapy. Options for further revascularization include repeat fibrinolysis and immediate referral for coronary angiography and PCI (rescue PCI). A third alternative is conservative therapy with continued medical therapy without repeat fibrinolysis or rescue PCI.

Comparison 3: Rescue PCI versus repeat fibrinolysis

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td rowspan="2">Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
● Low
○ Moderate
○ High</td><td rowspan="2">The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Heart Failure at 6 months</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Stroke at 6 months</td><td>CRITICAL</td><td>⨁⨁◯◯
LOW</td></tr>
<tr><td>Major bleeding before hospital discharge</td><td>IMPORTANT</td><td>⨁⨁◯◯
LOW</td></tr>
</table></td><td rowspan="2">No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative noted that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.</td></tr>
<tr><td>Is there important uncertainty about how much people value the main</td><td>○ Important uncertainty or variability</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td></td><td>outcomes?</td><td>○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td><td rowspan="3">Summary of findings: Rescue PCI compared to repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy
<table><tr><th>Outcome</th><th>Without rescue PCI</th><th>With rescue PCI</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr><tr><td>Heart Failure at 6 months</td><td>70 per 1000</td><td>49 per 1000 (19 to 124)</td><td>22 fewer per 1000 (from 51 fewer to 54 more)</td><td>RR 0.69 (0.27 to 1.76)</td></tr><tr><td>Stroke at 6 months</td><td>7 per 1000</td><td>21 per 1000 (2 to 198)</td><td>14 more per 1000 (from 5 fewer to 191 more)</td><td>RR 2.96 (0.31 to 28.10)</td></tr><tr><td>Major bleeding before hospital discharge</td><td>49 per 1000</td><td>28 per 1000 (8 to 93)</td><td>22 fewer per 1000 (from 41 fewer to 43 more)</td><td>RR 0.56 (0.17 to 1.88)</td></tr></table></td><td rowspan="3"></td></tr>
<tr><td>Are the desirable anticipated effects large?</td><td>○ No
○ Probably no
● Uncertain
○ Probably yes
○ Yes
○ Varies</td></tr>
<tr><td>Are the undesirable anticipated effects small?</td><td>○ No
○ Probably no
● Uncertain
○ Probably yes
○ Yes
○ Varies</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies		
Resource use	**Are the resources required small?**	● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered costs and resource use when comparing rescue PCI vs. repeat fibrinolysis (e.g. considered resource use implications such as costs of procedure and drugs, future costs of management, etc.)	Resources required for rescue PCI would not be small.
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs (when comparing rescue PCI vs. repeat fibrinolysis) are small relative to benefits.	Uncertainty about the incremental cost relative to the net benefits as the net benefits are uncertain based on available evidence.
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending rescue PCI vs. repeat fibrinolysis.	There is already inequity due to lack of access to PCI in certain geographical areas in the KSA. A recommendation for rescue PCI would push to refer patients for

	Criteria	Judgements	Research evidence	Additional considerations
		○ Uncertain ○ Probably reduced ○ Reduced ○ Varies		rescue PCI, but some patients would still be denied the procedure. Therefore inequity would be increased.
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether stakeholders in the KSA (e.g. clinicians, policymakers) would find the option of rescue PCI vs. repeat fibrinolysis acceptable.	
Feasibility	**Is the option feasible to implement?**	○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of rescue PCI as an option.	Given the current situation and levels of access, rescue PCI may be difficult to implement universally. There are geographical locations where rescue PCI is already routinely performed.

Recommendation **Should rescue PCI vs. repeated fibrinolysis be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests rescue PCI over repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy (conditional recommendation; low quality evidence) Remark: - There should not be a repeated administration of streptokinase. The risk of adverse events with repeat administration of streptokinase is higher than the benefit.
Justification	Low quality evidence based on one trial is inconclusive, with uncertainty around the estimates of effects.
Subgroup considerations	None
Implementation considerations	None
Monitoring and evaluation	None
Research possibilities	As in previous comparison of rescue PCI versus conservative management, registry study is required to determine access to treatment.

Evidence Profile: Rescue PCI compared to repeated fibrinolysis in patients with STEMI who fail to reperfuse after fibrinolytic therapy

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliography: Gershlick 2005 (REACT)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**rescue PCI**	**repeated fibrinolysis**	**Relative (95% CI)**	**Absolute (95% CI)**		
Heart Failure at 6 months												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	7/144 (4.9%)	10/142 (7.0%)	**RR 0.69** (0.27 to 1.76)	22 fewer per 1000 (from 51 fewer to 54 more)	⊕⊕◯◯ LOW	CRITICAL
Stroke at 6 months												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	3/144 (2.1%)	1/142 (0.7%)	**RR 2.96** (0.31 to 28.10)	14 more per 1000 (from 5 fewer to 191 more)	⊕⊕◯◯ LOW	CRITICAL
Major bleeding before hospital discharge												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	4/144 (2.8%)	7/142 (4.9%)	**RR 0.56** (0.17 to 1.88)	22 fewer per 1000 (from 41 fewer to 43 more)	⊕⊕◯◯ LOW	IMPORTANT

1. Unclear allocation concealment
2. Wide confidence intervals cross default minimum important difference lines and line of no effect (i.e. the intervention may cause appreciable benefit and appreciable harm)

Guideline Question 9: Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?

Problem: STEMI successfully treated by fibrinolysis
Option: routine early angiography
Comparison: routine deferred or selective angiography
Setting: in hospital
Perspective: KSA MoH

Background and Objective: To evaluate the coronary anatomy and prescribe the most appropriate mode of treatment for patients with STEMI who are treated with fibrinolysis, coronary angiography may be recommended. The role and optimal timing of angiography has been studied in clinical trials. This question addresses whether routine early versus routine deferred or selective angiography should be used for management of patients with STEMI successfully treated by fibrinolysis.

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>The Saudi population has been reported to show a high burden of cardiovascular risk factors and early manifestation in a younger cohort in comparison, for example, to European populations – e.g. mean age 58 years (SD +/- 12.9) in SPACE registry study (Khan 2014, AlHabib et al 2011).

The SPACE registry study of 5055 acute coronary syndrome patients admitted to 17 hospitals in Saudi Arabia between December 2005 and December 2007 reported that 41.5% had STEMI (AlHabib et al 2011). Additionally, the GULF RACE-2 registry study conducted in 65 hospitals from 6 Arabian Gulf countries (including Saudi Arabia) between October 2008 and June 2009 reported that of 7930 patient enrolled 45.6% had STEMI, and 1-year mortality in STEMI patients was 11.5% (AlHabib et al 2012).</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
● Moderate</td><td>The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Mortality at 6 to 12 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
</table></td><td>No evidence specific to KSA identified in literature search for patients' values and preferences.

Panel members, including patient representative not-</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considera-tions</th></tr>
<tr><td rowspan="3"></td><td></td><td>○ High</td><td rowspan="3"><table>
<tr><td>Reinfarction - 6 to 12 months</td><td>CRITICAL</td><td>⊕⊕⊕◯
MODERATE</td></tr>
<tr><td>Heart Failure at 6 to 12 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Stroke at 6 to 12 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Major bleeding at 30 days</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Recurrent Ischaemia at 6 to 12 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Unplanned revascularization at 6 months</td><td>CRITICAL</td><td>⊕⊕◯◯
LOW</td></tr>
<tr><td>Length of hospital stay</td><td>IMPORTANT</td><td>⊕⊕⊕◯
MODERATE</td></tr>
</table>
Summary of findings: Routine early angiography compared to routine deferred or selective angiography for STEMI successfully treated by fibrinolysis
<table>
<tr><th>Outcome</th><th>Without routine early angiography</th><th>With routine early angiography</th><th>Difference (95% CI)</th><th>Relative effect (RR) (95% CI)</th></tr>
<tr><td>Mortality at 6 to 12 months</td><td>50 per 1000</td><td>44 per 1000 (30 to 63)</td><td>6 fewer per 1000 (from 13 more to 19 fewer)</td><td>RR 0.88 (0.61 to 1.27)</td></tr>
</table></td><td rowspan="3">ed that there is no important variability or uncertainty in patients' values and preferences in the KSA setting and that patients would place a high value on reduction in mortality.</td></tr>
<tr><td>Is there important uncertainty about how much people value the main outcomes?</td><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty of variability
● No important uncertainty of variability
○ No known undesirable</td></tr>
<tr><td>Are the desirable anticipated effects large?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td></tr>
</table>

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considera-tions</th></tr>
<tr><td></td><td>Are the undesir-able anticipated effects small?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td rowspan="2"><table>
<tr><td>Reinfarction - 6 to 12 months</td><td>67 per 1000</td><td>39 per 1000 (27 to 55)</td><td>28 fewer per 1000 (from 11 fewer to 39 fewer)</td><td>RR 0.58 (0.41 to 0.83)</td></tr>
<tr><td>Heart Failure at 6 to 12 months</td><td>143 per 1000</td><td>140 per 1000 (67 to 293)</td><td>3 fewer per 1000 (from 76 fewer to 150 more)</td><td>RR 0.98 (0.47 to 2.05)</td></tr>
<tr><td>Stroke at 6 to 12 months</td><td>37 per 1000</td><td>18 per 1000 (6 to 60)</td><td>19 fewer per 1000 (from 23 more to 31 fewer)</td><td>RR 0.49 (0.15 to 1.61)</td></tr>
<tr><td>Major bleeding at 30 days</td><td>53 per 1000</td><td>50 per 1000 (36 to 69)</td><td>3 fewer per 1000 (from 16 fewer to 16 more)</td><td>RR 0.95 (0.69 to 1.31)</td></tr>
<tr><td>Recurrent Is-chaemia at 6 to 12 months</td><td>242 per 1000</td><td>126 per 1000 (99 to 160)</td><td>116 fewer per 1000 (from 82 fewer to 143 fewer)</td><td>RR 0.52 (0.41 to 0.66)</td></tr>
<tr><td>Unplanned revas-cularization at 6 months</td><td>365 per 1000</td><td>121 per 1000 (91 to 161)</td><td>245 fewer per 1000 (from 205 fewer to 274 fewer)</td><td>RR 0.33 (0.25 to 0.44)</td></tr>
<tr><td>Length of hospital stay</td><td>-</td><td>The mean length of hospital stay in the intervention group was 3.4 lower (4.39 lower to 2.41 lower)</td><td>MD 3.4 lower (4.39 lower to 2.41 lower)</td><td>-</td></tr>
</table></td><td rowspan="2"></td></tr>
<tr><td>Are the desirable effects large rel-ative to undesir-able effects?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td></tr>
<tr><td>Resource use</td><td>Are the re-sources required small?</td><td>○ No</td><td colspan="2">No evidence identified specific to the KSA setting – Panel members considered costs and resource of routine early vs. deferred angiography (e.g. considered transportation costs for transfer, initial costs and follow-up costs, catheterization laboratory capacity and</td><td>Panel considered cost of transfer to catheterization lab and cost of angiography</td></tr>
</table>

	Criteria	Judgements	Research evidence	Additional considerations
		○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	costs) A pilot trial by Abdul-Rahman et al (2012) comparing routine early coronary angiography versus a conservative strategy with risk stratification based on stress myocardial perfusion imaging performed a cost-analysis including total hospital costs, costs of therapy, subsequent hospitalization, subsequent noninvasive tests (e.g. MPI), or repeat revascularization. The analysis showed overall higher cost for invasive strategy vs conservative strategy ($4953.5 ± 3108.5 vs. $2764.6 ± 2636.7, respectively). The systematic review from NICE included one published cost-utility analysis based on the NORDISTEMI trial (Bohmer 2010) showing that routine early angiography was not cost effective compared to routine deferred angiography (angiography where clinically indicated or otherwise within 2 weeks of hospital discharge) following STEMI successfully treated by fibrinolysis (ICER - £62,648 per QALY gained). Important to note are potential limitations and applicability of the analysis – the cost difference may be overestimated as half of the costs in the early angiography group were attributed to helicopter ambulance costs, and the mortality rate in the study population was lower than in the general STEMI population suggesting that it was a lower risk population potentially underestimating the benefits of early angiography (i.e. reducing the cost-effectiveness).	for routine early angiography.
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel members considered whether the incremental costs of routine early angiography are small relative to benefits. See note about cost-utility analysis above.	Incremental cost was considered probably small relative to the net benefits, given probably large benefit, and resources required for routine early angiography. Compared to the evidence reviewed it was considered that the cost per QALY in the KSA would be lower.
Equity	**What would be the impact on health inequities?**	○ Increased ● Probably increased	No evidence identified specific to KSA – Panel members considered the impact on health inequity in the KSA (reduced, increased, uncertain) if recommending routine early angiography.	Due to lack of access to catheterization labs in certain regions of the KSA, many patients may not receive routine early angiography, probably increas-

	Criteria	Judgements	Research evidence	Additional considera-tions
		○ Uncertain ○ Probably reduced ○ Reduced ○ Varies		ing health inequity.
Acceptability	**Is the option acceptable to key stakehold-ers?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No evidence identified specific to KSA – Panel considered whether key stakeholders in the KSA (e.g. clinicians, policymakers) would find routine early angiography an acceptable option.	
Feasibility	**Is the option feasible to im-plement?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	No evidence identified specific to KSA – Panel considered feasibility of intervention option (i.e. routine early angiography).	For patients with access to catheterization labs the option was considered fea-sible, but the panel noted that across the KSA approx-imately 25% of patients do not have good access to catheterization labs.

Recommendation **Should routine early angiography vs. routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?**					
Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	The panel suggests routine early angiography over routine deferred or selective angiography in patients with STEMI successfully treated by fibrinolysis. (conditional recommendation; moderate quality evidence)
Justification	Panel placed high weight on benefit of early angiography and in consideration of feasibility issues in the KSA setting the strength of recommendation is conditional.
Subgroup considerations	None
Implementation considerations	None
Monitoring and evaluation	None
Research possibilities	None

Evidence Profile: Routine early angiography compared to routine deferred or selective angiography for STEMI successfully treated by fibrinolysis

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15
Bibliography: Le May 2005 (CAPITAL AMI), Geng 2013, Fernandez-Aviles 2004 (GRACIA-1), Bohmer 2010 (NORDISTEMI), SIAM III 2003, TRANSFER-AMI 2009, Agati 2007, Armstrong 2006 (WEST)

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	routine early angiography	routine deferred or selective angi-ography	Relative (95% CI)	Absolute (95% CI)		
Mortality at 6 to 12 months												
6	randomised trials	serious [1]	not serious	not serious	serious [2]	none	52/1190 (4.4%)	58/1171 (5.0%)	**RR 0.88** (0.61 to 1.27)	6 fewer per 1000 (from 13 more to 19 fewer)	⊕⊕◯◯ LOW	CRITICAL
Reinfarction - 6 to 12 months												
6	randomised trials	serious [1]	not serious	not serious	not serious	none	46/1190 (3.9%)	78/1171 (6.7%)	**RR 0.58** (0.41 to 0.83)	28 fewer per 1000 (from 11 fewer to 39 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Heart Failure at 6 to 12 months												
1	randomised trials	serious [3]	not serious	not serious	serious [2]	none	12/86 (14.0%)	12/84 (14.3%)	**RR 0.98** (0.47 to 2.05)	3 fewer per 1000 (from 76 fewer to 150 more)	⊕⊕◯◯ LOW	CRITICAL
Stroke at 6 to 12 months												
2	randomised trials	serious [1]	not serious	not serious	serious [2]	none	4/220 (1.8%)	8/216 (3.7%)	**RR 0.49** (0.15 to 1.61)	19 fewer per 1000 (from 23 more to 31 fewer)	⊕⊕◯◯ LOW	CRITICAL
Major bleeding at 30 days												
8	randomised	serious [1]	not serious	not serious	serious [2]	none	67/1332 (5.0%)	69/1312 (5.3%)	**RR 0.95**	3 fewer per 1000 (from 16	⊕⊕◯◯	CRITICAL

	trials								(0.69 to 1.31)	fewer to 16 more)	LOW	
Recurrent Ischaemia at 6 to 12 months												
5	randomised trials	serious [1]	serious [4]	not serious	not serious	none	83/662 (12.5%)	160/660 (24.2%)	**RR 0.52** (0.41 to 0.66)	116 fewer per 1000 (from 82 fewer to 143 fewer)	⨁⨁◯◯ LOW	CRITICAL
Unplanned revascularization at 6 months												
3	randomised trials	serious [1]	serious [5]	not serious	not serious	none	51/416 (12.3%)	152/416 (36.5%)	**RR 0.33** (0.25 to 0.44)	245 fewer per 1000 (from 205 fewer to 274 fewer)	⨁⨁◯◯ LOW	CRITICAL
Length of hospital stay												
1	randomised trials	serious [3]	not serious	not serious	not serious	none	248	251	-	MD **3.4 lower** (4.39 lower to 2.41 lower)	⨁⨁⨁◯ MODERATE	IMPORTANT

MD – mean difference, RR – relative risk

1. In many studies, unclear randomization and allocation concealment
2. Wide confidence intervals including both appreciable benefit and no benefit, crossing line of no effect, or harm
3. Unclear randomization and allocation concealment
4. Unexplained heterogeneity I squared is 69%
5. Unexplained heterogeneity I squared is 90%

Appendix 2: Search Strategies and Results

Benefits & Harms Searches:

Q1. Should fibrinolysis vs. delayed percutaneous coronary intervention (PPCI) be used for treatment of STEMI in patients who present within 12 hours of symptom onset?

Q1A: PCI terms AND fibrinolysis terms AND timing terms, with Excluded Study Designs filter

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 28/10/2014**

1. exp *myocardial infarction/ [112227]
2. myocardial infarct*.ti,ab. [152612]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35449]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25063]
5. acute coronary syndrome/[8199]
6. acute coronary syndrome*.ti,ab,kw. [19740]
7. or/1-6 [226505]

8. exp *stents/ [38725]
9. exp *angioplasty, balloon, coronary/ [24153]
10. *coronary angiography/ [14590]
11. exp *catheterization, peripheral/ [5629]
12. *myocardial reperfusion/ [3419]
13. percutaneous coronary intervention*.ti,ab. [18958]
14. (peripheral adj3 catheter*).ti,ab. [1255]
15. (coronary adj3 angiograph*).ti,ab. [30225]
16. ((heart or myocardi*) adj3 reperfusion).ti,ab. [9272]
17. ((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [25772]
18. coronary artery dilat*.ti,ab. [262]
19. stent*.ti,ab. [67689]
20. angioplasty/ [5812]
21. or/8-20 [155146]

22. exp *thrombolytic therapy/ [12784]
23. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [10785]
24. (thrombolysis or fibrinolysis).ti,ab. [33279]
25. fibrinolytic agents/ [24436]
26. or/22-25[59618]
27. time factors/ [1041375]
28. (delay* or timing or time).ti,ab. [2448903]
29. 27 or 28 [3187562]

30. 21 and 26 and 29 [3579]
31. 7 and 30 [2812]

32. letter/ [878154]

33. editorial/ [374361] 34. news/ [173899] 35. exp historical article/ [331782] 36. Anecdotes as Topic/ [4658] 37. comment/ [622104] 38. case report/ [1728347] 39. (letter or comment*).ti. [101839] 40. or/32-39[3474406] 41. randomized controlled trial/ or random*.ti,ab. [867136] 42. 40 not 41 [3455983] 43. animals/ not humans/ [3988180] 44. exp Animals, Laboratory/ [760032] 45. exp Animal Experimentation/ [6677] 46. exp Models, Animal/ [443546] 47. exp Rodentia/ [2788527] 48. (rat or rats or mouse or mice).ti. [1152122] 49. or/42-48[8083027] 50. 31 not 49 [2571] 51. limit 50 to ed=20121129-20141028 [239] 52. limit 51 to english language [229]	
Records Retrieved	PCI terms AND fibrinolysis terms AND timing terms: 229

Q1B: PCI terms AND fibrinolysis terms, with Excluded study designs, SRs, and RCTs filters

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 28/10/2014**
1. exp *myocardial infarction/ [112227] 2. myocardial infarct*.ti,ab. [152612] 3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35449] 4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25063] 5. acute coronary syndrome/[8199] 6. acute coronary syndrome*.ti,ab,kw. [19740] 7. or/1-6 [226505] 8. exp *stents/ [38725] 9. exp *angioplasty, balloon, coronary/ [24153] 10. *coronary angiography/ [14590] 11. exp *catheterization, peripheral/ [5629] 12. *myocardial reperfusion/ [3419] 13. percutaneous coronary intervention*.ti,ab. [18958] 14. (peripheral adj3 catheter*).ti,ab. [1255] 15. (coronary adj3 angiograph*).ti,ab. [30225] 16. ((heart or myocardi*) adj3 reperfusion).ti,ab. [9272] 17. ((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [25772] 18. coronary artery dilat*.ti,ab. [262] 19. stent*.ti,ab. [67689]	

20. angioplasty/ [5812]
21. or/8-20 [155146]

22. exp *thrombolytic therapy/ [12784]
23. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [10785]
24. (thrombolysis or fibrinolysis).ti,ab. [33279]
25. fibrinolytic agents/ [24436]
26. or/22-25[59618]

27. time factors/ [1041375]
28. (delay* or timing or time).ti,ab. [2448903]
29. 27 or 28 [3187562]

30. 21 and 26 [9295]
31. 7 and 30[6679]

32. letter/ [878154]
33. editorial/ [374361]
34. news/ [173899]
35. exp historical article/ [331782]
36. Anecdotes as Topic/ [4658]
37. comment/ [622104]
38. case report/ [1728347]
39. (letter or comment*).ti. [101839]
40. or/32-39[3474406]
41. randomized controlled trial/ or random*.ti,ab. [867136]
42. 40 not 41 [3455983]
43. animals/ not humans/ [3988180]
44. exp Animals, Laboratory/ [760032]
45. exp Animal Experimentation/ [6677]
46. exp Models, Animal/ [443546]
47. exp Rodentia/ [2788527]
48. (rat or rats or mouse or mice).ti. [1152122]
49. or/42-48[8083027]

50. 31 not 49 [5825]

51. randomized controlled trial.pt. [398206]
52. controlled clinical trial.pt. [90540]
53. randomi#ed.ab. [380120]
54. placebo.ab. [163163]
55. randomly.ab. [227680]
56. Clinical Trials as topic.sh. [175990]
57. trial.ti. [138109]
58. or/51-57[980709]

59. meta-analysis/ [54029]
60. meta-analysis as topic/ [14524]
61. (meta analy* or metanaly* or metaanaly*).ti,ab. [72743]
62. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28047]
63. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [84362]

64. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30394] 65. (search* adj4 literature).ab. [30568] 66. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103109] 67. cochrane.jw. [11775] 68. or/59-67[225024] 69. 58 or 68 [1143492] 70. 50 and 69 [1968] 71. limit 70 to ed=20121129-20141028 [169] 72. limit 71 to english language [163]	
Records Retrieved	PCI terms AND fibrinolysis terms: 163

Q1A: PCI terms AND fibrinolysis terms AND timing terms, with Excluded study designs filter

Database: **EMBASE 1974 to 2014 October 27**	
Search strategy: search terms [number of results]	**Date of search: 28/10/2014**
1. myocardial infarct*.ti,ab. [195971] 2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50412] 3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [37732] 4. acute coronary syndrome/[28955] 5. acute coronary syndrome*.ti,ab,kw. [31196] 6. exp *heart infarction/ [140475] 7. exp st segment elevation myocardial infarction/ [15853] 8. or/1-7 [303584] 9. percutaneous coronary intervention*.ti,ab. [29511] 10. ((heart or myocardi$) adj3 reperfusion).ti,ab. [11354] 11. ((Primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [31790] 12. Coronary artery dilat$.ti,ab. [320] 13. Stent$.ti,ab. [100370] 14. exp *stent/ [44413] 15. exp *transluminal coronary angioplasty/ [10881] 16. exp *percutaneous transluminal angioplasty/ [9021] 17. angioplasty/ [18281] 18. catheterization/ [36491] 19. heart muscle reperfusion/ [11566] 20. or/9-19 [207455] 21. fibrinolytic agent/ [21956] 22. exp *fibrinolytic therapy/ [6038] 23. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [13472] 24. (thrombolysis or fibrinolysis).ti,ab. [43057] 25. or/21-24[66814] 26. (delay$ or timing or time).ti,ab. [2969285]	

27. time/ [371211] 28. 26 or 27 [3224036] 29. 20 and 25 and 28 [3426] 30. 8 and 29 [2539] 31. letter.pt. or letter/ [861374] 32. note.pt. [572650] 33. editorial.pt. [458077] 34. case report/ or case study/ [1968339] 35. (letter or comment*).ti. [151330] 36. or/31-35[3708573] 37. randomized controlled trial/ or random*.ti,ab. [1003373] 38. 36 not 37 [3679911] 39. animal/ not human/ [1201273] 40. nonhuman/ [4392754] 41. exp Animal Experiment/ [1810110] 42. exp Experimental Animal/ [419463] 43. animal model/ [778781] 44. exp Rodent/ [2923658] 45. (rat or rats or mouse or mice).ti. [1283086] 46. or/38-45[9979807] 47. 30 not 46 [2382] 48. limit 47 to em=201247-201444 [366] 49. limit 48 to english language [345]	
Records Retrieved	PCI terms AND fibrinolysis terms AND timing terms: 345

Q1B: PCI terms AND fibrinolysis terms, with Excluded study designs, SRs, and RCTs filters

Database: **EMBASE 1974 to 2014 October 27**	
Search strategy: search terms [number of results]	**Date of search: 28/10/2014**
1. myocardial infarct*.ti,ab. [195971] 2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50412] 3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [37732] 4. acute coronary syndrome/[28955] 5. acute coronary syndrome*.ti,ab,kw. [31196] 6. exp *heart infarction/ [140475] 7. exp st segment elevation myocardial infarction/ [15853] 8. or/1-7 [303584] 9. percutaneous coronary intervention*.ti,ab. [29511] 10. ((heart or myocardi$) adj3 reperfusion).ti,ab. [11354] 11. ((Primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [31790] 12. Coronary artery dilat$.ti,ab. [320] 13. Stent$.ti,ab. [100370] 14. exp *stent/ [44413] 15. exp *transluminal coronary angioplasty/ [10881]	

16. exp *percutaneous transluminal angioplasty/ [9021]
17. angioplasty/ [18281]
18. catheterization/ [36491]
19. heart muscle reperfusion/ [11566]
20. or/9-19 [207455]

21. fibrinolytic agent/ [21956]
22. exp *fibrinolytic therapy/ [6038]
23. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [13472]
24. (thrombolysis or fibrinolysis).ti,ab. [43057]
25. or/21-24[66814]

26. (delay$ or timing or time).ti,ab. [2969285]
27. time/ [371211]
28. 26 or 27 [3224036]

29. 20 and 25 [11131]
30. 29 and 8[7463]

31. letter.pt. or letter/ [861374]
32. note.pt. [572650]
33. editorial.pt. [458077]
34. case report/ or case study/ [1968339]
35. (letter or comment*).ti. [151330]
36. or/31-35[3708573]
37. randomized controlled trial/ or random*.ti,ab. [1003373]
38. 36 not 37 [3679911]
39. animal/ not human/ [1201273]
40. nonhuman/ [4392754]
41. exp Animal Experiment/ [1810110]
42. exp Experimental Animal/ [419463]
43. animal model/ [778781]
44. exp Rodent/ [2923658]
45. (rat or rats or mouse or mice).ti. [1283086]
46. or/38-45[9979807]

47. 30 not 46 [6526]

48. random*.ti,ab. [920084]
49. factorial*.ti,ab. [24057]
50. (crossover* or cross over*).ti,ab. [72607]
51. ((doubl* or singl*) adj blind*).ti,ab. [164019]
52. (assign* or allocat* or volunteer* or placebo*).ti,ab. [679350]
53. crossover procedure/ [40434]
54. single blind procedure/ [18935]
55. randomized controlled trial/ [354208]
56. double blind procedure/ [118305]
57. or/48-56[1474665]

58. systematic review/ [80780]
59. meta-analysis/ [83763]

60. (meta analy* or metanaly* or metaanaly*).ti,ab. [87796] 61. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [92775] 62. systematic review/ [80780] 63. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31095] 64. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31554] 65. (search* adj4 literature).ab. [36416] 66. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [113061] 67. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41428] 68. cochrane.jw. [11566] 69. or/58-67[307964] 70. 57 or 69 [1691784] 71. 47 and 70 [1857] 72. limit 71 to em=201247-201444 [225] 73. limit 72 to english language [209]	
Records Retrieved	PCI terms AND fibrinolysis terms: 209

Q1A: PCI terms AND fibrinolysis terms AND timing terms
and
Q1B: PCI terms AND fibrinolysis terms

Database: **Cochrane Library**	
Search strategy:	**Date of search: 28/10/2014**
#1 MeSH descriptor: [Myocardial Infarction] explode all trees #2 (myocardial next infarct*):ti,ab #3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab #4 (st-elevat* or st-segment* or stemi):ti,ab,kw #5 st next elevat*:ti,ab,kw #6 st next segment:ti,ab,kw #7 (("acute coronary") next syndrome*):ti,ab,kw #8 MeSH descriptor: [Acute Coronary Syndrome] this term only #9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) #10 MeSH descriptor: [Stents] explode all trees #11 MeSH descriptor: [Angioplasty, Balloon, Coronary] explode all trees #12 MeSH descriptor: [Coronary Angiography] explode all trees #13 MeSH descriptor: [Catheterization, Peripheral] explode all trees #14 MeSH descriptor: [Myocardial Reperfusion] explode all trees #15 (percutaneous next coronary next intervention*):ti,ab #16 (peripheral near/3 catheter*):ti,ab #17 ((heart or myocardi*) near/3 reperfusion):ti,ab #18 ((coronary or transluminal or balloon) near/3 angioplasty):ti,ab #19 (Coronary next artery next dilat*):ti,ab #20 Stent*:ti,ab	

#21	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20
#22	MeSH descriptor: [Thrombolytic Therapy] explode all trees
#23	MeSH descriptor: [Fibrinolytic Agents] this term only
#24	((thrombolytic or fibrinolytic) next therap*):ti,ab
#25	(thrombolysis or fibrinolysis):ti,ab
#26	#22 or #23 or #24 or #25
#27	MeSH descriptor: [Time Factors] explode all trees
#28	(delay* or timing or time):ti,ab
#29	#27 or #28
#30	#21 and #26
#31	#21 and #26 and #29
#32	#9 and #31 Publication Year from 2012 * PCI terms AND fibrinolysis terms AND timing terms
#33	#9 and #30 Publication Year from 2012 * PCI terms AND fibrinolysis terms
Records Retrieved	PCI terms AND fibrinolysis terms AND timing terms: 64 PCI terms AND fibrinolysis terms: 151

Summary of Searches Q1A and Q1B Combined

Total No. Retrieved:	**1161**
Medline: Embase: Cochrane Library:	392 554 215
Duplicates:	368
No. Total without duplicates**:**	**793**
Screening (Title and Abstract Review)	
No. Excluded:	**775**
Included for Full Text review:	**18**
Selection (Full Text Review)	
No. Excluded:	**18**
Publications included from update:	**0**
Total Publications included:	**6**

Q2. Should facilitated percutaneous coronary intervention (fPPCI) versus percutaneous coronary intervention (PPCI) be used in patients with STEMI?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 28/10/2014**

1. exp *myocardial infarction/ [112227]
2. myocardial infarct*.ti,ab. [152612]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35449]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25063]
5. acute coronary syndrome/[8199]
6. acute coronary syndrome*.ti,ab,kw. [19740]
7. or/1-6 [226505]

8. exp *stents/ [38725]
9. angioplasty/ [5812]
10. exp *Angioplasty, Balloon, Coronary/ [24153]
11. *Coronary Angiography/ [14590]
12. exp *Catheterization, Peripheral/ [5629]
13. *Myocardial Reperfusion/ [3419]
14. percutaneous coronary intervention*.ti,ab. [18958]
15. (peripheral adj3 catheter$).ti,ab. [1255]
16. (coronary adj3 angiograph$).ti,ab. [30225]
17. ((heart or myocardi$) adj3 reperfusion).ti,ab. [9272]
18. ((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [25772]
19. Coronary artery dilat$.ti,ab. [262]
20. Stent$.ti,ab. [67689]
21. or/8-20 [155146]

22. (Alteplase or Actilyse or Activase or Altepase or Activacin).ti,ab. [1652]
23. (Reteplase or Rapilysin or Retavase or ecokinase).ti,ab. [319]
24. (Tenecteplase or Metalyse or TNKase).ti,ab. [362]
25. (Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or plasminokinase or stretodecase or zykinase).ti,ab. [6744]
26. (abciximab or ReoPro or abcixi or centorx).ti,ab. [1994]
27. (Eptifibatide or Integrilin or integrelin or intrifiban).ti,ab. [883]
28. (Tirofiban or Aggrastat or aggrastet).ti,ab. [989]
29. Tissue plasminogen activator/ [15867]
30. Fibrinolytic agents/ [24436]
31. Streptokinase/ [7794]
32. Platelet Glycoprotein GPIIb-IIIa Complex/ [5840]
33. (Glycoprotein* adj2 IIb*).ti,ab. [5496]
34. or/22-33[52044]

35. heparin/ or heparin, low-molecular-weight/ or dalteparin/ or enoxaparin/ or nadroparin/ or heparinoids/ [57959]
36. (Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Par-

naparin or Reviparin or Tedelparin).mp. [5964]
37. or/35-36[58967]

38. 34 or 37 [104277]
39. 21 and 38 [8405]
40. 7 and 39 [5346]

41. letter/ [878154]
42. editorial/ [374361]
43. news/ [173899]
44. exp historical article/ [331782]
45. Anecdotes as Topic/ [4658]
46. comment/ [622104]
47. case report/ [1728347]
48. (letter or comment*).ti. [101839]
49. or/41-48[3474406]
50. randomized controlled trial/ or random*.ti,ab. [867136]
51. 49 not 50 [3455983]
52. animals/ not humans/ [3988180]
53. exp Animals, Laboratory/ [760032]
54. exp Animal Experimentation/ [6677]
55. exp Models, Animal/ [443546]
56. exp Rodentia/ [2788527]
57. (rat or rats or mouse or mice).ti. [1152122]
58. or/51-57[8083027]

59. 40 not 58 [4630]

60. randomized controlled trial.pt. [398206]
61. controlled clinical trial.pt. [90540]
62. randomi#ed.ab. [380120]
63. placebo.ab. [163163]
64. randomly.ab. [227680]
65. Clinical Trials as topic.sh. [175990]
66. trial.ti. [138109]
67. or/60-66[980709]

68. meta-analysis/ [54029]
69. meta-analysis as topic/ [14524]
70. (meta analy* or metanaly* or metaanaly*).ti,ab. [72743]
71. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28047]
72. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [84362]
73. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30394]
74. (search* adj4 literature).ab. [30568]
75. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103109]
76. cochrane.jw. [11775]
77. or/68-76[225024]

78. 67 or 77 [1143492]

79. 59 and 78 [2161]
80. limit 79 to ed=20121129-20141028 [168]
81. limit 80 to english language [156]

Records Retrieved	156

Database: **EMBASE 1974 to 2014 October 27**

Search strategy: search terms [number of results] | **Date of search: 28/10/2014**

1. myocardial infarct*.ti,ab. [195971]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50412]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [37732]
4. acute coronary syndrome/[28955]
5. acute coronary syndrome*.ti,ab,kw. [31196]
6. exp *heart infarction/ [140475]
7. exp st segment elevation myocardial infarction/ [15853]
8. or/1-7 [303584]

9. exp *stent/ [44413]
10. Stent$.ti,ab. [100370]
11. *angioplasty/ [6326]
12. exp *percutaneous transluminal angioplasty/ [9021]
13. exp transluminal coronary angioplasty/ [24588]
14. ((Primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [31790]
15. Coronary artery dilat$.ti,ab. [320]
16. *percutaneous coronary intervention/ [13681]
17. percutaneous coronary intervention*.ti,ab. [29511]
18. catheterization/ [36491]
19. heart muscle reperfusion/ [11566]
20. ((heart or myocardi$) adj3 reperfusion).ti,ab. [11354]
21. or/9-20 [209120]

22. (Alteplase or Actilyse or Activase or Altepase or Activacin).ti,ab. [2196]
23. (Reteplase or Rapilysin or Retavase or ecokinase).ti,ab. [423]
24. (Tenecteplase or Metalyse or TNKase).ti,ab. [487]
25. (Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or plasminokinase or stretodecase or zykinase).ti,ab. [7893]
26. (abciximab or ReoPro or abcixi or centorx).ti,ab. [2623]
27. (Eptifibatide or Integrilin or integrelin or intrifiban).ti,ab. [1170]
28. (Tirofiban or Aggrastat or aggrastet).ti,ab. [1366]
29. (Glycoprotein* adj2 IIb*).ti,ab. [6553]
30. Alteplase/ [13424]
31. Plasminogen activator/ [9711]
32. reteplase/ [1811]
33. tenecteplase/ [1903]
34. streptokinase/ [18025]
35. Abciximab/ [9104]
36. Eptifibatide/ [4614]
37. Tirofiban/ [4979]

38. fibrinogen receptor antagonist/ [9077]
39. or/22-38[57385]

40. heparin/ or low molecular weight heparin/ or dalteparin/ or enoxaparin/ or nadroparin/ or heparinoid/ [142768]
41. (Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Parnaparin or Reviparin or Tedelparin).mp. [23383]
42. or/40-41[143563]

43. 39 or 42 [182692]
44. 21 and 43 [20441]
45. 8 and 44 [11420]

46. letter.pt. or letter/ [861374]
47. note.pt. [572650]
48. editorial.pt. [458077]
49. case report/ or case study/ [1968339]
50. (letter or comment*).ti. [151330]
51. or/46-50[3708573]
52. randomized controlled trial/ or random*.ti,ab. [1003373]
53. 51 not 52 [3679911]
54. animal/ not human/ [1201273]
55. nonhuman/ [4392754]
56. exp Animal Experiment/ [1810110]
57. exp Experimental Animal/ [419463]
58. animal model/ [778781]
59. exp Rodent/ [2923658]
60. (rat or rats or mouse or mice).ti. [1283086]
61. or/53-60[9979807]

62. 45 not 61 [9364]

63. random*.ti,ab. [920084]
64. factorial*.ti,ab. [24057]
65. (crossover* or cross over*).ti,ab. [72607]
66. ((doubl* or singl*) adj blind*).ti,ab. [164019]
67. (assign* or allocat* or volunteer* or placebo*).ti,ab. [679350]
68. crossover procedure/ [40434]
69. single blind procedure/ [18935]
70. randomized controlled trial/ [354208]
71. double blind procedure/ [118305]
72. or/63-71[1474665]

73. systematic review/ [80780]
74. meta-analysis/ [83763]
75. (meta analy* or metanaly* or metaanaly*).ti,ab. [87796]
76. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [92775]
77. systematic review/ [80780]
78. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31095]

79. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31554]
80. (search* adj4 literature).ab. [36416]
81. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [113061]
82. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41428]
83. cochrane.jw. [11566]
84. or/73-82[307964]

85. 72 or 84 [1691784]
86. 62 and 85 [3363
87. limit 86 to em=201247-201444 [424]
88. limit 87 to english language [407]

Records Retrieved	407

Database: **Cochrane Library**

Search strategy:	**Date of search: 28/10/2014**

#1 MeSH descriptor: [Myocardial Infarction] explode all trees
#2 (myocardial next infarct*):ti,ab
#3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab
#4 (st-elevat* or st-segment* or stemi):ti,ab,kw
#5 st next elevat*:ti,ab,kw
#6 st next segment:ti,ab,kw
#7 (("acute coronary") next syndrome*):ti,ab,kw
#8 MeSH descriptor: [Acute Coronary Syndrome] this term only
#9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)
#10 MeSH descriptor: [Stents] explode all trees
#11 MeSH descriptor: [Angioplasty, Balloon, Coronary] explode all trees
#12 MeSH descriptor: [Coronary Angiography] explode all trees
#13 MeSH descriptor: [Catheterization, Peripheral] explode all trees
#14 MeSH descriptor: [Myocardial Reperfusion] explode all trees
#15 (percutaneous next coronary next intervention*):ti,ab
#16 (peripheral near/3 catheter*):ti,ab
#17 ((heart or myocardi*) near/3 reperfusion):ti,ab
#18 ((coronary or transluminal or balloon) near/3 angioplasty):ti,ab
#19 (Coronary next artery next dilat*):ti,ab
#20 Stent*:ti,ab
#21 #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #19 or #20
#22 (Alteplase or Actilyse or Activase or Altepase or Activacin):ti,ab
#23 (Reteplase or Rapilysin or Retavase or ecokinase):ti,ab
#24 (Tenecteplase or Metalyse or TNKase):ti,ab
#25 (Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or plasminokinase or stretodecase or zykinase):ti,ab
#26 (abciximab or ReoPro or abcixi or centorx):ti,ab
#27 (Eptifibatide or Integrilin or integrelin or intrifiban):ti,ab
#28 (Tirofiban or Aggrastat or aggrastet):ti,ab
#29 (Glycoprotein* near/2 IIb*):ti,ab
#30 MeSH descriptor: [Tissue Plasminogen Activator] this term only

#31	MeSH descriptor: [Fibrinolytic Agents] this term only
#32	MeSH descriptor: [Streptokinase] explode all trees
#33	#22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32
#34	MeSH descriptor: [Heparin] explode all trees
#35	MeSH descriptor: [Dalteparin] this term only
#36	MeSH descriptor: [Enoxaparin] this term only
#37	MeSH descriptor: [Nadroparin] this term only
#38	(Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Parnaparin or Reviparin or Tedelparin):ti,ab
#39	#34 or #35 or #36 or #37 or #38
#40	#33 or #39
#41	#21 and #40
#42	#9 and #41 Publication Year from 2012
Records Retrieved	151

Summary of Searches

Total No. Retrieved:	**714**
Medline:	156
Embase:	407
Cochrane Library:	151
Duplicates:	71
No. Total without duplicates**:**	**643**
Screening (Title and Abstract Review)	
No. Excluded:	**606**
Included for Full Text review:	**37**
Selection (Full Text Review)	
No. Excluded:	**35**
Publications included from update:	**2**
Total Publications included:	**26**

Q3. Should thrombus extraction devices during percutaneous coronary intervention (PPCI) versus percutaneous coronary intervention (PPCI) alone be used for treatment of STEMI?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 29/04/2015**

November 2, 2014 Search:

1. exp *myocardial infarction/ [112283]
2. myocardial infarct*.ti,ab. [152431]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35423]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [24978]
5. acute coronary syndrome/[8215]
6. acute coronary syndrome*.ti,ab,kw. [19656]
7. or/1-6 [226277]

8. exp heart catheterization/ [64772]
9. exp stents/ [55486]
10. myocardial reperfusion/ [6942]
11. exp angioplasty/ [56452]
12. exp myocardial revascularization/ [82521]
13. percutaneous coronary intervention*.ti,ab. [18913]
14. ((heart or cardiac) adj3 catheter*).ti,ab. [21288]
15. ((heart or myocardi*) adj3 reperfusion).ti,ab. [9271]
16. ((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [26474]
17. (ppci or pci or ptca).ti,ab. [21149]
18. coronary artery dilat*.ti,ab. [262]
19. stent*.ti,ab. [67570]
20. revasc*.ti,ab. [43667]
21. or/8-20 [270232]
22. exp thrombectomy/ [3647]
23. mechanical thrombolysis/ [279]
24. suction/ [10636]
25. embolectomy/ [1037]
26. (thrombectomy or thrombectomies or embolectomy or embolectomies).ti,ab. [7238]
27. (emboli* adj2 protect*).ti,ab. [765]
28. thromboaspiration.ti,ab. [112]
29. ((thrombus or clot* or embol*) adj2 (remov* or extract* or aspirat*)).ti,ab. [2080]
30. ((mechanical or manual) adj2 (clot disrupt* or thrombolysis or aspirat*)).ti,ab. [851]
31. ((catheter* or thrombo*) adj2 aspirat*).ti,ab. [580]
32. (quickcat or thromcat or angiojet or x-sizer).ti,ab. [230]
33. or/22-32[22246]
34. 21 and 33 [4052]

35. 34 and 7[1169]

36. letter/ [878101]
37. editorial/ [374385]
38. news/ [174040]
39. exp historical article/ [331876]

40. Anecdotes as Topic/ [4660]
41. comment/ [622729]
42. case report/ [1729127]
43. (letter or comment*).ti. [101908]
44. or/36-43[3475545]
45. randomized controlled trial/ or random*.ti,ab. [867886]
46. 44 not 45 [3457111]
47. animals/ not humans/ [3990083]
48. exp Animals, Laboratory/ [760413]
49. exp Animal Experimentation/ [6682]
50. exp Models, Animal/ [443932]
51. exp Rodentia/ [2790025]
52. (rat or rats or mouse or mice).ti. [1152472]
53. or/46-52[8086375]
54. 35 not 53 [820]
55. randomized controlled trial.pt. [398577]
56. controlled clinical trial.pt. [90551]
57. randomi#ed.ab. [380413]
58. placebo.ab. [163253]
59. randomly.ab. [227899]
60. Clinical Trials as topic.sh. [176047]
61. trial.ti. [138227]
62. or/55-61[981395]
63. meta-analysis/ [54171]
64. meta-analysis as topic/ [14537]
65. (meta analy* or metanaly* or metaanaly*).ti,ab. [72885]
66. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28085]
67. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [84512]
68. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30418]
69. (search* adj4 literature).ab. [30618]
70. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103219]
71. cochrane.jw. [11775]
72. or/63-71[225278]
73. 62 or 72 [1144355]
74. 54 and 73 [298]
75. limit 74 to ed=20121129-20141102 [68]
76. limit 75 to english language [67]

April 29, 2015 Update:

75. limit 74 to ed=20141101-20141231 [3]
76. limit 74 to yr="2015-Current" [9]
77. 75 or 76 [12]
78. limit 77 to english language [11]

Records Retrieved	78 (67 + 11)

Database: **EMBASE 1974 to 2015 April 28**	
Search strategy: search terms [number of results]	**Date of search: 29/04/2015**

November 2, 2014 Search:

1. myocardial infarct*.ti,ab. [197374]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50861]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38309]
4. acute coronary syndrome/[29384]
5. acute coronary syndrome*.ti,ab,kw. [31630]
6. exp *heart infarction/ [141058]
7. exp st segment elevation myocardial infarction/ [16312]
8. or/1-7 [305641]

9. percutaneous coronary intervention*.ti,ab. [30043]
10. ((heart or myocardi*) adj3 reperfusion).ti,ab. [11407]
11. ((coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [29629]
12. coronary artery dilat*.ti,ab. [320]
13. stent*.ti,ab. [101313]
14. exp *stent/ [44719]
15. exp *transluminal coronary angioplasty/ [10889]
16. exp *percutaneous transluminal angioplasty/ [9033]
17. catheterization/ [36658]
18. heart muscle reperfusion/ [11578]
19. or/9-18 [199779]
20. artificial embolism/ [41475]
21. exp thrombectomy/ [10960]
22. coronary artery thrombosis/ [6092]
23. exp percutaneous thrombectomy/ [3927]
24. embolectomy/ [3437]
25. (thrombus adj2 (aspirat* or extracti*)).ti,ab. [997]
26. thrombectomy.ti,ab. [7083]
27. thromboaspiration.ti,ab. [204]
28. (emboli* adj2 protect*).ti,ab. [1130]
29. embolectomy.ti,ab. [3004]
30. emboli#ation.ti,ab. [45814]
31. (export or pronto or diver or angiojet or (x adj sizer) or rescue).ti,ab. [69042]
32. or/20-31[148767]
33. 19 and 32 [13754]

34. 8 and 33 [4073]

35. letter.pt. or letter/ [861695]
36. note.pt. [573194]
37. editorial.pt. [458372]
38. case report/ or case study/ [1970328]
39. (letter or comment*).ti. [151392]
40. or/35-39[3711637]
41. randomized controlled trial/ or random*.ti,ab. [1006443]
42. 40 not 41 [3682922]

43. animal/ not human/ [1201843]
44. nonhuman/ [4394608]
45. exp Animal Experiment/ [1810952]
46. exp Experimental Animal/ [420934]
47. animal model/ [779559]
48. exp Rodent/ [2926969]
49. (rat or rats or mouse or mice).ti. [1284197]
50. or/42-49[9987741]

51. 34 not 50 [3111]

52. random*.ti,ab. [923100]
53. factorial*.ti,ab. [24094]
54. (crossover* or cross over*).ti,ab. [72730]
55. ((doubl* or singl*) adj blind*).ti,ab. [164444]
56. (assign* or allocat* or volunteer* or placebo*).ti,ab. [681112]
57. crossover procedure/ [40505]
58. single blind procedure/ [18963]
59. randomized controlled trial/ [354750]
60. double blind procedure/ [118418]
61. or/52-60[1478721]

62. systematic review/ [81126]
63. meta-analysis/ [84200]
64. (meta analy* or metanaly* or metaanaly*).ti,ab. [88276]
65. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93188]
66. systematic review/ [81126]
67. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31186]
68. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31629]
69. (search* adj4 literature).ab. [36541]
70. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [113543]
71. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41563]
72. cochrane.jw. [11566]
73. or/62-71[308977]

74. 61 or 73 [1696431]
75. 51 and 74 [896]
76. limit 75 to em=201247-201445 [206]
77. limit 76 to english language [199]

April 29, 2015 Update:

76. limit 75 to em=201445-201452 [36]
77. limit 75 to yr="2015 -Current" [19]
78. 76 or 77 [55]
79. limit 78 to english language [55]

Records Retrieved	254 (199 + 55)

Database: **Cochrane Library**	
Search strategy:	**Date of search: 29/04/2015**

November 2, 2014 Search:

#1 MeSH descriptor: [Myocardial Infarction] explode all trees
#2 (myocardial next infarct*):ti,ab
#3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab
#4 (st-elevat* or st-segment* or stemi):ti,ab,kw
#5 st next elevat*:ti,ab,kw
#6 st next segment:ti,ab,kw
#7 (("acute coronary") next syndrome*):ti,ab,kw
#8 MeSH descriptor: [Acute Coronary Syndrome] this term only
#9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)
#10 MeSH descriptor: [Cardiac Catheterization] explode all trees
#11 MeSH descriptor: [Stents] explode all trees
#12 MeSH descriptor: [Myocardial Reperfusion] this term only
#13 MeSH descriptor: [Angioplasty] explode all trees
#14 MeSH descriptor: [Myocardial Revascularization] explode all trees
#15 "percutaneous coronary intervention*":ti,ab
#16 ((heart or cardiac) near/3 catheter*):ti,ab
#17 ((heart or myocardi*) near/3 reperfusion):ti,ab
#18 ((percutaneous or primary or coronary or transluminal or balloon) near/3 angioplasty):ti,ab
#19 (PPCI or PCI or PTCA):ti,ab
#20 (revasc* or stent*):ti,ab
#21 (coronary next artery next dilat*):ti,ab
#22 (#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21)
#23 MeSH descriptor: [Thrombectomy] explode all trees
#24 MeSH descriptor: [Suction] this term only
#25 MeSH descriptor: [Embolectomy] this term only
#26 MeSH descriptor: [Mechanical Thrombolysis] this term only
#27 (thrombectomy or thrombectomies or embolectomy or embolectomies or thromboaspiration or quickcat or thromcat or angiojet or x-sizer):ti,ab
#28 (emboli* near/2 protect*):ti,ab
#29 ((thrombus or clot* or emboli*) near/2 (remov* or extract* or aspirat*)):ti,ab
#30 ((mechanical or manual) near/2 ("clot disrupt*" or thrombolysis or aspirat*)):ti,ab
#31 ((catheter* or thrombo*) next aspirat*):ti,ab
#32 (#23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31)
#33 (#22 and #32)
#34 #33 and #9 Publication Year from 2012

April 29, 2015 Update:
#34 #33 and #9 Publication Year from 2015 [1]

Records Retrieved	66 (65+1)

Summary of Searches

Total No. Retrieved:	**398**
Medline:	78
Embase:	254
Cochrane Library:	66
Duplicates:	117
No. Total without duplicates**:**	**281**
Screening (Title and Abstract Review)	
No. Excluded:	**258**
Included for Full Text review:	**23**
Selection (Full Text Review)	
No. Excluded:	**18**
Publications included from update:	**5**
Total Publications included:	**25**

Q4. Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 22/03/2015**

November 6, 2014 Search:

1. exp *myocardial infarction/ [112402]
2. myocardial infarct*.ti,ab. [152571]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35491]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25000]
5. acute coronary syndrome/[8253]
6. acute coronary syndrome*.ti,ab,kw. [19681]
7. or/1-6 [226541]

8. exp *stents/ [38801]
9. percutaneous coronary intervention*.ti,ab. [18932]
10. ((primary or coronary or percutaneous or transluminal or balloon) adj3 angioplasty).ti,ab. [26484]
11. coronary artery dilat*.ti,ab. [262]
12. stent*.ti,ab. [67699]
13. (PPCI or PCI or PTCA).ti,ab. [21167]
14. exp angioplasty/ [56482]
15. or/8-14 [123197]
16. (culprit or non-culprit or nonculprit).ti,ab. [4345]
17. ((infarct-related or infarct related or non-infarct-related) adj2 (artery or arteries)).ti,ab. [2359]
18. (complete adj2 revasc*).ti,ab. [1310]
19. ((multivessel or multi-vessel or single-vessel or single vessel) adj3 (percutaneous coronary intervention* or PCI or stent* or revasc* or recanali* or angioplast*)).ti,ab. [962]
20. or/16-19[8623]
21. 15 and 20 [3414]

22. 7 and 21 [2674]

23. letter/ [884590]
24. editorial/ [375499]
25. news/ [174176]
26. exp historical article/ [332852]
27. Anecdotes as Topic/ [4668]
28. comment/ [626358]
29. case report/ [1736150]
30. (letter or comment*).ti. [102128]
31. or/23-30[3490648]
32. randomized controlled trial/ or random*.ti,ab. [870244]
33. 31 not 32 [3472118]
34. animals/ not humans/ [3997516]
35. exp Animals, Laboratory/ [762478]
36. exp Animal Experimentation/ [6709]
37. exp Models, Animal/ [445841]
38. exp Rodentia/ [2796241]

39. (rat or rats or mouse or mice).ti. [1154555]
40. or/33-39[8110518]

41. 22 not 40 [2477]

42. meta-analysis/ [54494]
43. meta-analysis as topic/ [14579]
44. (meta analy* or metanaly* or metaanaly*).ti,ab. [73233]
45. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28189]
46. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [84902]
47. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30518]
48. (search* adj4 literature).ab. [30743]
49. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103676]
50. cochrane.jw. [11917]
51. or/42-50[226168]

52. randomized controlled trial.pt. [399847]
53. controlled clinical trial.pt. [90656]
54. randomi#ed.ab. [381587]
55. placebo.ab. [163635]
56. randomly.ab. [228453]
57. Clinical Trials as topic.sh. [176288]
58. trial.ti. [138673]
59. or/52-58[983830]

60. 51 or 59 [1147370]

61. epidemiologic studies/ [6265]
62. exp case control studies/ [709767]
63. exp cohort studies/ [1437567]
64. cross-sectional studies/ [192612]
65. case control.ti,ab. [85030]
66. (cohort adj (study or studies or analys*)).ti,ab. [102881]
67. ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab. [158955]
68. ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab. [851972]
69. or/61-68[2114382]

70. 60 or 69 [2993049]

71. 41 and 70 [1601]
72. limit 71 to ed=20121129-20141106 [215]
73. limit 72 to english language [206]

March 22, 2015 Update:

79. limit 71 to ed=20141101-20141231 [16]
80. limit 71 to yr="2015 -Current" [15]
81. 72 or 73 [31]

82. limit 74 to english language [31]	
Records Retrieved	237 (206 + 31)

Database: **EMBASE 1974 to 2015 March 20**	
Search strategy: search terms [number of results]	**Date of search: 22/03/2015**

November 6, 2014 Search:

1. myocardial infarct*.ti,ab. [197455]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50883]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38334]
4. acute coronary syndrome/[29412]
5. acute coronary syndrome*.ti,ab,kw. [31647]
6. exp *heart infarction/ [141093]
7. exp st segment elevation myocardial infarction/ [16333]
8. or/1-7 [305771]

9. percutaneous coronary intervention*.ti,ab. [30071]
10. coronary artery dilat*.ti,ab. [320]
11. stent*.ti,ab. [101387]
12. exp *stent/ [44743]
13. *percutaneous transluminal angioplasty/ or *angioplasty/ or *laser angioplasty/ [15748]
14. exp *percutaneous coronary intervention/ [24697]
15. (PPCI or PCI or PTCA).ti,ab. [38541]
16. ((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [32950]
17. or/9-16 [163112]
18. (culprit or non-culprit or nonculprit).ti,ab. [7435]
19. ((infarct-related or infarct related or non-infarct-related) adj2 (artery or arteries)).ti,ab. [3215]
20. (complete adj2 revasc*).ti,ab. [1840]
21. ((multivessel or multi-vessel or single vessel or single-vessel) adj3 (percutaneous coronary intervention* or PCI or stent* or revasc* or recanali* or angioplast*)).ti,ab. [1479]
22. or/18-21[13267]
23. 17 and 22 [5612]

24. 8 and 23 [4514]

25. letter.pt. or letter/ [862257]
26. note.pt. [573856]
27. editorial.pt. [458680]
28. case report/ or case study/ [1971211]
29. (letter or comment*).ti. [151453]
30. or/25-29[3713893]
31. randomized controlled trial/ or random*.ti,ab. [1007306]
32. 30 not 31 [3685159]
33. animal/ not human/ [1202277]
34. nonhuman/ [4397524]
35. exp Animal Experiment/ [1812000]
36. exp Experimental Animal/ [421161]
37. animal model/ [780228]
38. exp Rodent/ [2928225]

39. (rat or rats or mouse or mice).ti. [1284613]
40. or/32-39[9993197]

41. 24 not 40 [4241]

42. systematic review/ [81324]
43. meta-analysis/ [84307]
44. (meta analy* or metanaly* or metaanaly*).ti,ab. [88429]
45. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93403]
46. systematic review/ [81324]
47. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31222]
48. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31671]
49. (search* adj4 literature).ab. [36590]
50. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [113720]
51. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41601]
52. cochrane.jw. [11566]
53. or/42-51[309390]

54. random*.ti,ab. [923927]
55. factorial*.ti,ab. [24105]
56. (crossover* or cross over*).ti,ab. [72778]
57. ((doubl* or singl*) adj blind*).ti,ab. [164529]
58. (assign* or allocat* or volunteer* or placebo*).ti,ab. [681564]
59. crossover procedure/ [40537]
60. single blind procedure/ [18992]
61. randomized controlled trial/ [355063]
62. double blind procedure/ [118502]
63. or/54-62[1479829]

64. 53 or 63 [1697829]

65. clinical study/ [105660]
66. exp case control study/ [89766]
67. family study/ [10557]
68. longitudinal study/ [70353]
69. retrospective study/ [364686]
70. prospective study/ [265234]
71. cross-sectional study/ [124950]
72. cohort analysis/ [181041]
73. follow-up/ [847746]
74. cohort*.ti,ab. [427147]
75. 73 and 74 [88593]
76. case control.ti,ab. [95934]
77. (cohort adj (study or studies or analys*)).ti,ab. [125698]
78. ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab. [196828]
79. ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab. [1098752]

80. or/65-72,75-79 [1831840] 81. 64 or 80 [3240732] 82. 41 and 81 [1691] 83. limit 82 to em=201247-201445 [487] 84. limit 83 to english language [475] March 22, 2015 Update: 80. limit 82 to em=201445-201452 [81] 81. limit 82 to yr="2015 -Current" [18] 82. 83 or 84 [99] 83. limit 74 to english language [99]	
Records Retrieved	574 (475 + 99)

Database: **Cochrane Library**	
Search strategy:	**Date of search: 22/03/2015**
November 6, 2014 Search: #1 MeSH descriptor: [Myocardial Infarction] explode all trees #2 (myocardial next infarct*):ti,ab #3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab #4 (st-elevat* or st-segment* or stemi):ti,ab,kw #5 st next elevat*:ti,ab,kw #6 st next segment:ti,ab,kw #7 (("acute coronary") next syndrome*):ti,ab,kw #8 MeSH descriptor: [Acute Coronary Syndrome] this term only #9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) #10 MeSH descriptor: [Stents] explode all trees #11 MeSH descriptor: [Angioplasty] explode all trees #12 stent*:ti,ab #13 (PCI or PCTA or PPCI):ti,ab #14 "percutaneous coronary intervention":ti,ab #15 (("coronary artery") next dilat*):ti,ab #16 ((primary or coronary or percutaneous or transluminal or balloon) near/3 angioplasty):ti,ab #17 #10 or #11 or #12 or #13 or #14 or #15 or #16 #18 (culprit or nonculprit or non-culprit):ti,ab #19 ((infarct-related or "infarct related" or non-infarct-related) next (artery or arteries)):ti,ab #20 (complete next revasc*):ti,ab #21 ((multivessel or multi-vessel or "single vessel" or single-vessel) near/3 (angioplas* or pci or stent* or "percutaneous coronary intervention" or recanali* or revasc*)):ti,ab #22 #18 or #19 or #20 or #21 #23 #17 and #22 #24 #9 and #23 Publication Year from 2012 March 22, 2015 Update: #24 #9 and #23 Publication Year from 2015 [0]	
Records Retrieved	91

Summary of Searches

Total No. Retrieved:	**902**
Medline: Embase: Cochrane Library:	237 574 91
Duplicates:	129
No. Total without duplicates**:**	**773**
Screening (Title and Abstract Review)	
No. Excluded:	**743**
Included for Full Text review:	**27**
Selection (Full Text Review)	
No. Excluded:	**25**
Publications included from update:	**2**
Total Publications included:	**4**

Q5. Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. exp *myocardial infarction/ [112417]
2. myocardial infarct*.ti,ab. [152623]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35509]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25014]
5. acute coronary syndrome/[8255]
6. acute coronary syndrome*.ti,ab,kw. [19694]
7. or/1-6 [226623]
8. shock.ti,ab. [137023]
9. 7 and 8 [9199]

10. exp shock, cardiogenic/ [6555]
11. (cardio* adj3 shock).ti,ab. [8396]
12. 9 or 10 or 11 [14359]

13. exp *stents/ [38828]
14. *myocardial reperfusion/ [3422]
15. percutaneous coronary intervention*.ti,ab. [18944]
16. ((heart or myocardi*) adj3 reperfusion).ti,ab. [9282]
17. coronary artery dilat*.ti,ab. [262]
18. stent*.ti,ab. [67758]
19. ((primary or coronary or percutaneous or transluminal or balloon) adj3 angioplasty).ti,ab. [26488]
20. (PPCI or PCI or PTCA).ti,ab. [21175]
21. exp myocardial revascularization/ [82641]
22. exp angioplasty/ [56491]
23. revasc*.ti,ab. [43899]
24. CABG.ti,ab. [13460]
25. ((heart or coronary or aortocoronary or cardio*) adj2 bypass).ti,ab. [61997]
26. (bypass adj2 (surg* or graft*)).ti,ab. [50693]
27. exp *heart catheterization/ [33712]
28. ((heart or coronary) adj3 catheter*).ti,ab. [8163]
29. or/13-28[266184]

30. 12 and 29 [3996]

31. letter/ [885046]
32. editorial/ [375726]
33. news/ [174256]
34. exp historical article/ [332881]
35. Anecdotes as Topic/ [4669]
36. comment/ [626992]
37. case report/ [1736501]
38. (letter or comment*).ti. [102207]

39. or/31-38[3491894]
40. randomized controlled trial/ or random*.ti,ab. [870858]
41. 39 not 40 [3473351]
42. animals/ not humans/ [3998174]
43. exp Animals, Laboratory/ [762616]
44. exp Animal Experimentation/ [6710]
45. exp Models, Animal/ [446006]
46. exp Rodentia/ [2796752]
47. (rat or rats or mouse or mice).ti. [1154912]
48. or/41-47[8112710]
49. 30 not 48 [3027]
50. meta-analysis/ [54536]
51. meta-analysis as topic/ [14587]
52. (meta analy* or metanaly* or metaanaly*).ti,ab. [73355]
53. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28226]
54. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [85037]
55. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30549]
56. (search* adj4 literature).ab. [30790]
57. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103773]
58. cochrane.jw. [11918]
59. or/50-58[226418]
60. randomized controlled trial.pt. [399988]
61. controlled clinical trial.pt. [90669]
62. randomi#ed.ab. [381894]
63. placebo.ab. [163741]
64. randomly.ab. [228612]
65. Clinical Trials as topic.sh. [176325]
66. trial.ti. [138778]
67. or/60-66[984414]
68. 59 or 67 [1148151]
69. 49 and 68 [526]
70. limit 69 to ed=20121129-20141109 [51]
71. limit 70 to english language [50]

Records Retrieved	50

Database: **EMBASE 1974 to 2014 November 07**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. myocardial infarct*.ti,ab. [197891]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50992]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38432]
4. acute coronary syndrome/[29530]
5. acute coronary syndrome*.ti,ab,kw. [31768]

6. exp *heart infarction/ [141261]
7. exp st segment elevation myocardial infarction/ [16413]
8. or/1-7 [306391]

9. shock.ti,ab. [163802]
10. 8 and 9 [11627]
11. exp cardiogenic shock/ [15208]
12. (cardio* adj3 shock).ti,ab. [12380]
13. 10 or 11 or 12 [23014]

14. percutaneous coronary intervention*.ti,ab. [30202]
15. coronary artery dilat*.ti,ab. [321]
16. stent*.ti,ab. [101635]
17. exp *stent/ [44828]
18. (PPCI or PCI or PTCA).ti,ab. [38723]
19. ((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [32976]
20. heart muscle revascularization/ [22664]
21. *heart muscle reperfusion/ [3731]
22. exp coronary artery surgery/ [90608]
23. *heart catheterization/ [12075]
24. ((heart or coronary) adj3 catheter*).ti,ab. [11592]
25. exp percutaneous coronary intervention/ [62262]
26. angioplasty/ or percutaneous transluminal angioplasty/ [39867]
27. revasc*.ti,ab. [60379]
28. CABG.ti,ab. [21348]
29. ((heart or coronary or aortocoronary or cardio*) adj2 bypass).ti,ab. [75615]
30. (bypass adj2 (surg* or graft*)).ti,ab. [62015]
31. or/14-30[336645]

32. 13 and 31 [7296]

33. letter.pt. or letter/ [862676]
34. note.pt. [574449]
35. editorial.pt. [458901]
36. case report/ or case study/ [1972290]
37. (letter or comment*).ti. [151583]
38. or/33-37[3716060]
39. randomized controlled trial/ or random*.ti,ab. [1009084]
40. 38 not 39 [3687285]
41. animal/ not human/ [1202650]
42. nonhuman/ [4399394]
43. exp Animal Experiment/ [1812695]
44. exp Experimental Animal/ [421900]
45. animal model/ [780759]
46. exp Rodent/ [2930043]
47. (rat or rats or mouse or mice).ti. [1285271]
48. or/40-47[9998511]

49. 32 not 48 [5654]

50. systematic review/ [81649]
51. meta-analysis/ [84646]
52. (meta analy* or metanaly* or metaanaly*).ti,ab. [88808]
53. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93843]
54. systematic review/ [81649]
55. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31277]
56. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31763]
57. (search* adj4 literature).ab. [36753]
58. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [114149]
59. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41703]
60. cochrane.jw. [11566]
61. or/50-59[310331]
62. random*.ti,ab. [925671]
63. factorial*.ti,ab. [24147]
64. (crossover* or cross over*).ti,ab. [72840]
65. ((doubl* or singl*) adj blind*).ti,ab. [164682]
66. (assign* or allocat* or volunteer* or placebo*).ti,ab. [682538]
67. crossover procedure/ [40579]
68. single blind procedure/ [19009]
69. randomized controlled trial/ [355452]
70. double blind procedure/ [118572]
71. or/62-70[1482223]
72. 61 or 71 [1700866]

73. 49 and 72 [907]
74. limit 73 to em=201247-201445 [217]
75. limit 74 to english language [211]

Records Retrieved	211

Database: **Cochrane Library**

Search strategy:	**Date of search: 09/11/2014**

#1 MeSH descriptor: [Myocardial Infarction] explode all trees
#2 myocardial infarct*:ti,ab
#3 st next segment:ti,ab
#4 st next elevat*:ti,ab
#5 (cardiac near/3 (infarct* or attack* or arrest* or event*)):ti,ab
#6 stemi:ti,ab
#7 MeSH descriptor: [Acute Coronary Syndrome] explode all trees
#8 (#1 or #2 or #3 or #4 or #5 or #6 or #7)
#9 shock:ti,ab,kw
#10 (#8 and #9)
#11 MeSH descriptor: [Shock, Cardiogenic] explode all trees
#12 (cardio* next shock):ti,ab
#13 (#10 or #11 or #12)
#14 MeSH descriptor: [Stents] explode all trees

#15	MeSH descriptor: [Myocardial Reperfusion] explode all trees
#16	MeSH descriptor: [Myocardial Revascularization] explode all trees
#17	MeSH descriptor: [Angioplasty] explode all trees
#18	("percutaneous coronary intervention"):ti,ab
#19	((heart or myocardial or coronary) near/3 reperfusion):ti,ab
#20	(("coronary artery" or "coronary arteries") next dilat*):ti,ab
#21	stent*:ti,ab
#22	((primary or coronary or percutaneous or transluminal or balloon) near/3 angioplast*):ti,ab
#23	(PCI or PPCI or PTCA or CABG or revasc*):ti,ab
#24	(bypass near/2 (surg* or graft*)):ti,ab
#25	((heart or cardiac or coronary or aortocoronary or cardio*) next bypass):ti,ab
#26	MeSH descriptor: [Myocardial Infarction] explode all trees
#27	MeSH descriptor: [Cardiac Catheterization] explode all trees
#28	((heart or coronary) near/3 catheter*):ti,ab
#29	(#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28)
#30	#13 and #29 Publication Year from 2012
Records Retrieved	79

Summary of Searches

Total No. Retrieved:	**340**
Medline:	50
Embase:	211
Cochrane Library:	79
Duplicates:	45
No. Total without duplicates**:**	**295**
Screening (Title and Abstract Review)	
No. Excluded:	**284**
Included for Full Text review:	**11**
Selection (Full Text Review)	
No. Excluded:	**11**
Publications included from update:	**0**
Total Publications included:	**9**

Q6. Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. exp *myocardial infarction/ [112417]
2. myocardial infarct*.ti,ab. [152623]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35509]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25014]
5. acute coronary syndrome/[8255]
6. acute coronary syndrome*.ti,ab,kw. [19694]
7. or/1-6 [226623]

8. heart arrest/ [23487]
9. ((heart or cardiac) adj2 arrest*).ti,ab. [23250]
10. ((surviv* or resuscit* or postresuscit* or unconscious*) adj6 arrest*).ti,ab. [7317]
11. or/8-10 [36215]

12. 7 and 11 [22894]

13. percutaneous coronary intervention*.ti,ab. [18944]
14. ((heart or myocardi*) adj3 reperfusion).ti,ab. [9282]
15. ((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [26488]
16. coronary artery dilat*.ti,ab. [262]
17. stent*.ti,ab. [67758]
18. exp stents/ [55629]
19. exp angioplasty/ [56491]
20. myocardial reperfusion/ [6945]
21. exp myocardial revascularization/ [82641]
22. revasc*.ti,ab. [43899]
23. (PPCI or PCI or PTCA).ti,ab. [21175]
24. ((heart or cardiac) adj3 catheter*).ti,ab. [21315]
25. exp heart catheterization/ [64875]
26. coronary angiography/ [50677]
27. (coronary adj3 angiograph*).ti,ab. [30192]
28. or/13-27[305084]

29. 12 and 28 [1919]

30. letter/ [885046]
31. editorial/ [375726]
32. news/ [174256]
33. exp historical article/ [332881]
34. Anecdotes as Topic/ [4669]
35. comment/ [626992]
36. case report/ [1736501]
37. (letter or comment*).ti. [102207]

38. or/30-37[3491894]
39. randomized controlled trial/ or random*.ti,ab. [870858]
40. 38 not 39 [3473351]
41. animals/ not humans/ [3998174]
42. exp Animals, Laboratory/ [762616]
43. exp Animal Experimentation/ [6710]
44. exp Models, Animal/ [446006]
45. exp Rodentia/ [2796752]
46. (rat or rats or mouse or mice).ti. [1154912]
47. or/40-46[8112710]
48. 29 not 47 [1224]
49. meta-analysis/ [54536]
50. meta-analysis as topic/ [14587]
51. (meta analy* or metanaly* or metaanaly*).ti,ab. [73355]
52. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28226]
53. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [85037]
54. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30549]
55. (search* adj4 literature).ab. [30790]
56. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103773]
57. cochrane.jw. [11918]
58. or/49-57[226418]
59. randomized controlled trial.pt. [399988]
60. controlled clinical trial.pt. [90669]
61. randomi#ed.ab. [381894]
62. placebo.ab. [163741]
63. randomly.ab. [228612]
64. Clinical Trials as topic.sh. [176325]
65. trial.ti. [138778]
66. or/59-65[984414]
67. 58 or 66 [1148151]
68. 48 and 67 [184]
69. limit 68 to ed=20121129-20141109 [27]
70. limit 69 to english language [23]

Records Retrieved	23

Database: **EMBASE 1974 to 2014 November 07**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. myocardial infarct*.ti,ab. [197891]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50992]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38432]
4. acute coronary syndrome/[29530]
5. acute coronary syndrome*.ti,ab,kw. [31768]

6. exp *heart infarction/ [141261]
7. exp st segment elevation myocardial infarction/ [16413]
8. or/1-7 [306391]

9. *heart arrest/ or "out of hospital cardiac arrest"/ [22735]
10. ((heart or cardiac) adj2 arrest).ti,ab. [30657]
11. ((surviv* or resuscit* or postresuscit* or unconscious*) adj6 arrest*).ti,ab. [9963]
12. or/9-11 [40493]

13. 8 and 12 [30762]

14. percutaneous coronary intervention*.ti,ab. [30202]
15. ((heart or myocardi*) adj3 reperfusion).ti,ab. [11443]
16. ((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab. [32976]
17. coronary artery dilat*.ti,ab. [321]
18. stent*.ti,ab. [101635]
19. exp *stent/ [44828]
20. exp *percutaneous coronary intervention/ [24764]
21. *percutaneous transluminal angioplasty/ [9040]
22. *angioplasty/ [6384]
23. *heart muscle reperfusion/ [3731]
24. heart muscle revascularization/ [22664]
25. revasc*.ti,ab. [60379]
26. (PPCI or PCI or PTCA).ti,ab. [38723]
27. ((heart or cardiac) adj3 catheter*).ti,ab. [28443]
28. *heart catheterization/ [12075]
29. angiocardiography/ [80505]
30. (coronary adj3 angiograph*).ti,ab. [43111]
31. or/14-30[312919]

32. 13 and 31 [2517]

33. letter.pt. or letter/ [862676]
34. note.pt. [574449]
35. editorial.pt. [458901]
36. case report/ or case study/ [1972290]
37. (letter or comment*).ti. [151583]
38. or/33-37[3716060]
39. randomized controlled trial/ or random*.ti,ab. [1009084]
40. 38 not 39 [3687285]
41. animal/ not human/ [1202650]
42. nonhuman/ [4399394]
43. exp Animal Experiment/ [1812695]
44. exp Experimental Animal/ [421900]
45. animal model/ [780759]
46. exp Rodent/ [2930043]
47. (rat or rats or mouse or mice).ti. [1285271]
48. or/40-47[9998511]

49. 32 not 48 [1745]

50. systematic review/ [81649]
51. meta-analysis/ [84646]
52. (meta analy* or metanaly* or metaanaly*).ti,ab. [88808]
53. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93843]
54. systematic review/ [81649]
55. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31277]
56. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31763]
57. (search* adj4 literature).ab. [36753]
58. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [114149]
59. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41703]
60. cochrane.jw. [11566]
61. or/50-59[310331]
62. random*.ti,ab. [925671]
63. factorial*.ti,ab. [24147]
64. (crossover* or cross over*).ti,ab. [72840]
65. ((doubl* or singl*) adj blind*).ti,ab. [164682]
66. (assign* or allocat* or volunteer* or placebo*).ti,ab. [682538]
67. crossover procedure/ [40579]
68. single blind procedure/ [19009]
69. randomized controlled trial/ [355452]
70. double blind procedure/ [118572]
71. or/62-70[1482223]
72. 61 or 71 [1700866]

73. 49 and 72 [214]
74. limit 73 to em=201247-201445 [57]
75. limit 74 to english language [51]

Records Retrieved	51

Database: **Cochrane Library**

Search strategy:	**Date of search: 09/11/2014**

#1 MeSH descriptor: [Heart Arrest] this term only
#2 MeSH descriptor: [Out-of-Hospital Cardiac Arrest] this term only
#3 ((heart or cardiac) next arrest*):ti,ab
#4 ((unconscious or resuscit* or postresuscit* or surviv*) near/6 arrest):ti,ab
#5 (#1 or #2 or #3 or #4)
#6 MeSH descriptor: [Cardiac Catheterization] explode all trees
#7 MeSH descriptor: [Stents] explode all trees
#8 MeSH descriptor: [Myocardial Reperfusion] this term only
#9 MeSH descriptor: [Angioplasty] explode all trees
#10 MeSH descriptor: [Myocardial Revascularization] explode all trees
#11 (percutaneous next coronary next intervention*):ti,ab
#12 ((heart or cardiac) near/3 catheter*):ti,ab
#13 ((heart or myocardi*) near/3 reperfusion):ti,ab

#14	((percutaneous or primary or coronary or transluminal or balloon) near/3 angioplasty):ti,ab
#15	(PPCI or PCI or PTCA):ti,ab
#16	(revasc* or stent*):ti,ab
#17	(coronary next artery next dilat*):ti,ab
#18	(coronary next angiograph*):ti,ab
#19	MeSH descriptor: [Coronary Angiography] this term only
#20	(#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19)
#21	#5 and #20 Publication Year from 2012
Records Retrieved	20

Summary of Searches

Total No. Retrieved:	**94**
Medline:	23
Embase:	51
Cochrane Library:	20
Duplicates:	25
No. Total without duplicates**:**	**69**
Screening (Title and Abstract Review)	
No. Excluded:	**64**
Included for Full Text review:	**5**
Selection (Full Text Review)	
No. Excluded:	**5**
Publications included from update:	**0**
Total Publications included:	**3**

Q7. Should high volume centres versus low volume centres be used for PPCI services?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**
1. workload/ [16234] 2. ((surg* or physician* or operat* or procedure* or hospital* or cardiol*) adj4 (volume* or workload* or caseload*)).ti,ab. [14449] 3. 1 or 2 [29796] 4. exp Angioplasty/ [56491] 5. percutaneous coronary intervention*.ti,ab. [18944] 6. ((primary or coronary or transluminal or balloon) adj3 angioplast*).ti,ab. [25972] 7. or/4-6 [71328] 8. 3 and 7 [402] 9. letter/ [885046] 10. editorial/ [375726] 11. news/ [174256] 12. exp historical article/ [332881] 13. Anecdotes as Topic/ [4669] 14. comment/ [626992] 15. case report/ [1736501] 16. (letter or comment*).ti. [102207] 17. or/9-16 [3491894] 18. randomized controlled trial/ or random*.ti,ab. [870858] 19. 17 not 18 [3473351] 20. animals/ not humans/ [3998174] 21. exp Animals, Laboratory/ [762616] 22. exp Animal Experimentation/ [6710] 23. exp Models, Animal/ [446006] 24. exp Rodentia/ [2796752] 25. (rat or rats or mouse or mice).ti. [1154912] 26. or/19-25[8112710] 27. 8 not 26 [355] 28. limit 27 to ed=20121129-20141109 [44] 29. limit 28 to english language [43]	
Records Retrieved	43

Database: **EMBASE 1974 to 2014 November 07**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**
1. workload/ [28961] 2. ((surg* or physician* or operat* or procedure* or hospital* or cardiol*) adj4 (volume* or workload* or caseload*)).ti,ab. [19572]	

3. 1 or 2 [47286] 4. exp Angioplasty/ [67096] 5. percutaneous coronary intervention*.ti,ab. [30202] 6. ((primary or coronary or transluminal or balloon) adj3 angioplast*).ti,ab. [32278] 7. or/4-6 [97443] 8. 3 and 7 [609] 9. letter.pt. or letter/ [862676] 10. note.pt. [574449] 11. editorial.pt. [458901] 12. case report/ or case study/ [1972290] 13. (letter or comment*).ti. [151583] 14. or/9-13 [3716060] 15. randomized controlled trial/ or random*.ti,ab. [1009084] 16. 14 not 15 [3687285] 17. animal/ not human/ [1202650] 18. nonhuman/ [4399394] 19. exp Animal Experiment/ [1812695] 20. exp Experimental Animal/ [421900] 21. animal model/ [780759] 22. exp Rodent/ [2930043] 23. (rat or rats or mouse or mice).ti. [1285271] 24. or/16-23[9998511] 25. 8 not 24 [571] 26. limit 25 to em=201247-201445 [158] 27. limit 26 to english language [155]

Records Retrieved	155

Database: **Cochrane Library**	
Search strategy:	**Date of search: 09/11/2014**
#1 MeSH descriptor: [Workload] this term only #2 (surg* or physician* or operat* or procedure* or hospital* or cardiol*) near/4 (volume* or workload* or caseload*):ti,ab #3 (#1 or #2) #4 MeSH descriptor: [Angioplasty] explode all trees #5 ("percutaneous coronary intervention" or "percutaneous coronary interventions"):ti,ab #6 ((primary or coronary or transluminal or balloon) near/3 angioplast*):ti,ab #7 (#4 or #5 or #6) #8 (#3 and #7) Publication Year from 2012	
Records Retrieved	14

Summary of Searches

Total No. Retrieved:	**212**
Medline:	43
Embase:	155
Cochrane Library:	14
Duplicates: 25	
No. Total without duplicates**:**	**187**
Screening (Title and Abstract Review)	
No. Excluded:	**179**
Included for Full Text review:	**8**
Selection (Full Text Review)	
No. Excluded:	**7**
Publications included from update:	**1**
Total Publications included:	**6**

Q8. Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. exp *myocardial infarction/ [112417]
2. myocardial infarct*.ti,ab. [152623]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35509]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25014]
5. acute coronary syndrome/[8255]
6. acute coronary syndrome*.ti,ab,kw. [19694]
7. or/1-6 [226623]

8. exp *stents/ [38828]
9. exp *angioplasty, balloon, coronary/ [24161]
10. percutaneous coronary intervention*.ti,ab. [18944]
11. ((rescue or emergency or unplanned) adj4 (percutaneous or angioplast*)).ti,ab. [1049]
12. (rescue adj1 (PPCI or PCI)).ti,ab. [188]
13. exp *thrombolytic therapy/ [12814]
14. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [10800]
15. (thrombolysis or fibrinolysis).ti,ab. [33311]
16. exp *tissue plasminogen activator/ [9720]
17. exp *urokinase-type plasminogen activator/ [6350]
18. exp *streptokinase/ [5897]
19. (alteplase or actilyse or reteplase or rapilysin or tenecteplase or metalyse or urokinase or syner-?kinase or streptokinase or streptase).ti,ab. [20888]
20. or/8-19 [125300]
21. recurrence/ [165812]
22. retreatment/ [5754]
23. treatment failure/ [28142]
24. ((fail* or after or repeat* or rescue) adj2 (reperfus* or treat* or therap* or thromb* or fibrino*)).ti,ab. [376994]
25. or/21-24[554428]
26. 20 and 25 [17702]

27. 7 and 26 [6738]

28. letter/ [885046]
29. editorial/ [375726]
30. news/ [174256]
31. exp historical article/ [332881]
32. Anecdotes as Topic/ [4669]
33. comment/ [626992]
34. case report/ [1736501]
35. (letter or comment*).ti. [102207]
36. or/28-35[3491894]
37. randomized controlled trial/ or random*.ti,ab. [870858]
38. 36 not 37 [3473351]

39. animals/ not humans/ [3998174]
40. exp Animals, Laboratory/ [762616]
41. exp Animal Experimentation/ [6710]
42. exp Models, Animal/ [446006]
43. exp Rodentia/ [2796752]
44. (rat or rats or mouse or mice).ti. [1154912]
45. or/38-44[8112710]

46. 27 not 45 [5850]

47. meta-analysis/ [54536]
48. meta-analysis as topic/ [14587]
49. (meta analy* or metanaly* or metaanaly*).ti,ab. [73355]
50. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28226]
51. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [85037]
52. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30549]
53. (search* adj4 literature).ab. [30790]
54. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103773]
55. cochrane.jw. [11918]
56. or/47-55[226418]
57. randomized controlled trial.pt. [399988]
58. controlled clinical trial.pt. [90669]
59. randomi#ed.ab. [381894]
60. placebo.ab. [163741]
61. randomly.ab. [228612]
62. Clinical Trials as topic.sh. [176325]
63. trial.ti. [138778]
64. or/57-63[984414]
65. 56 or 64 [1148151]

66. 46 and 65 [2092]
67. limit 66 to ed=20121129-20141109 [167]
68. limit 67 to english language [161]

Records Retrieved	161

Database: **EMBASE 1974 to 2014 November 07**

Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. myocardial infarct*.ti,ab. [197891]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50992]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38432]
4. acute coronary syndrome/[29530]
5. acute coronary syndrome*.ti,ab,kw. [31768]
6. exp *heart infarction/ [141261]
7. exp st segment elevation myocardial infarction/ [16413]
8. or/1-7 [306391]

9. exp *stent/ [44828]
10. exp *transluminal coronary angioplasty/ [10894]
11. exp *percutaneous transluminal angioplasty/ [9040]
12. percutaneous coronary intervention*.ti,ab. [30202]
13. ((rescue or emergency or unplanned) adj4 (percutaneous or angioplast*)).ti,ab. [1339]
14. (rescue adj1 (PPCI or PCI)).ti,ab. [334]
15. exp *fibrinolytic therapy/ [6086]
16. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [13604]
17. (thrombolysis or fibrinolysis).ti,ab. [43822]
18. exp *tissue plasminogen activator/ [9070]
19. exp *urokinase/ [8807]
20. exp *streptokinase/ [10372]
21. (alteplase or actilyse or reteplase or rapilysin or tenecteplase or metalyse or urokinase or syner-?kinase or streptokinase or streptase).ti,ab. [24635]
22. or/9-21 [160788]
23. exp recurrent disease/ [129645]
24. exp treatment failure/ [86626]
25. exp retreatment/ [6106]
26. ((fail* or after or repeat* or rescue*) adj2 (reperfus* or treat* or therap* or thromb* or fi-brino*)).ti,ab. [484687]
27. or/23-26[670804]
28. 22 and 27 [19097]

29. 8 and 28[7238]

30. letter.pt. or letter/ [862676]
31. note.pt. [574449]
32. editorial.pt. [458901]
33. case report/ or case study/ [1972290]
34. (letter or comment*).ti. [151583]
35. or/30-34[3716060]
36. randomized controlled trial/ or random*.ti,ab. [1009084]
37. 35 not 36 [3687285]
38. animal/ not human/ [1202650]
39. nonhuman/ [4399394]
40. exp Animal Experiment/ [1812695]
41. exp Experimental Animal/ [421900]
42. animal model/ [780759]
43. exp Rodent/ [2930043]
44. (rat or rats or mouse or mice).ti. [1285271]
45. or/37-44[9998511]

46. 29 not 45 [6203]

47. systematic review/ [81649]
48. meta-analysis/ [84646]
49. (meta analy* or metanaly* or metaanaly*).ti,ab. [88808]
50. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93843]
51. systematic review/ [81649]
52. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

[31277]
53. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31763]
54. (search* adj4 literature).ab. [36753]
55. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [114149]
56. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41703]
57. cochrane.jw. [11566]
58. or/47-56[310331]
59. random*.ti,ab. [925671]
60. factorial*.ti,ab. [24147]
61. (crossover* or cross over*).ti,ab. [72840]
62. ((doubl* or singl*) adj blind*).ti,ab. [164682]
63. (assign* or allocat* or volunteer* or placebo*).ti,ab. [682538]
64. crossover procedure/ [40579]
65. single blind procedure/ [19009]
66. randomized controlled trial/ [355452]
67. double blind procedure/ [118572]
68. or/59-67[1482223]
69. 58 or 68 [1700866]

70. 46 and 69 [1782]
71. limit 70 to em=201247-201445 [283]
72. limit 71 to english language [266]

Records Retrieved	266

Database: **Cochrane Library**

Search strategy:	**Date of search: 09/11/2014**

#1 MeSH descriptor: [Myocardial Infarction] explode all trees
#2 (myocardial next infarct*):ti,ab
#3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab
#4 (st-elevat* or st-segment* or stemi):ti,ab,kw
#5 st next elevat*:ti,ab,kw
#6 st next segment:ti,ab,kw
#7 (("acute coronary") next syndrome*):ti,ab,kw
#8 MeSH descriptor: [Acute Coronary Syndrome] this term only
#9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)
#10 MeSH descriptor: [Stents] explode all trees
#11 MeSH descriptor: [Angioplasty, Balloon, Coronary] explode all trees
#12 percutaneous next coronary next intervention*:ti,ab
#13 ((rescue or emergency or unplanned) near/4 (percutaneous or angioplast*)):ti,ab
#14 (rescue next (PPCI or PCI)):ti,ab
#15 MeSH descriptor: [Thrombolytic Therapy] explode all trees
#16 ((thrombolytic or fibrinolytic) next therap*):ti,ab
#17 (thrombolysis or fibrinolysis):ti,ab
#18 MeSH descriptor: [Tissue Plasminogen Activator] explode all trees
#19 MeSH descriptor: [Urokinase-Type Plasminogen Activator] explode all trees
#20 MeSH descriptor: [Streptokinase] explode all trees

#21 (alteplase or actilyse or reteplase or rapilysin or Tenecteplase or metalyse or urokinase or syner-kinase or Streptokinase or streptase):ti,ab	
#22 #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21	
#23 MeSH descriptor: [Recurrence] explode all trees	
#24 MeSH descriptor: [Retreatment] explode all trees	
#25 MeSH descriptor: [Treatment Failure] explode all trees	
#26 ((fail* or after or repeat* or rescue*) near/2 (reperfus* or treat* or therap* or thromb* or fibrino*)):ti,ab	
#27 #23 or #24 or #25 or #26	
#28 #22 and #27	
#29 #9 and #28 Publication Year from 2012	
Records Retrieved	172

Summary of Searches

Total No. Retrieved:	**599**
Medline:	161
Embase:	266
Cochrane Library:	172
Duplicates:	109
No. Total without duplicates**:**	**490**
Screening (Title and Abstract Review)	
No. Excluded:	**485**
Included for Full Text review:	**5**
Selection (Full Text Review)	
No. Excluded:	**5**
Publications included from update:	**0**
Total Publications included:	**10**

Q9. Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. exp *myocardial infarction/ [112417]
2. myocardial infarct*.ti,ab. [152623]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [35509]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25014]
5. acute coronary syndrome/[8255]
6. acute coronary syndrome*.ti,ab,kw. [19694]
7. or/1-6 [226623]

8. exp *thrombolytic therapy/ [12814]
9. exp *fibrinolytic agents/ [90206]
10. (antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis).ti,ab. [66975]
11. or/8-10 [138505]

12. *coronary angiography/ [14627]
13. (angiogram or angiograph* or angioplasty or stent*).ti,ab. [222783]
14. exp *angioplasty/ [40657]
15. exp *stents/ [38828]
16. or/12-15[239785]

17. 11 and 16 [14485]
18. 7 and 17 [8005]

19. letter/ [885046]
20. editorial/ [375726]
21. news/ [174256]
22. exp historical article/ [332881]
23. Anecdotes as Topic/ [4669]
24. comment/ [626992]
25. case report/ [1736501]
26. (letter or comment*).ti. [102207]
27. or/19-26[3491894]
28. randomized controlled trial/ or random*.ti,ab. [870858]
29. 27 not 28 [3473351]
30. animals/ not humans/ [3998174]
31. exp Animals, Laboratory/ [762616]
32. exp Animal Experimentation/ [6710]
33. exp Models, Animal/ [446006]
34. exp Rodentia/ [2796752]
35. (rat or rats or mouse or mice).ti. [1154912]
36. or/29-35[8112710]

37. 18 not 36 [6964]

38. meta-analysis/ [54536]
39. meta-analysis as topic/ [14587]
40. (meta analy* or metanaly* or metaanaly*).ti,ab. [73355]
41. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [28226]
42. ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. [85037]
43. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [30549]
44. (search* adj4 literature).ab. [30790]
45. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [103773]
46. cochrane.jw. [11918]
47. or/38-46[226418]
48. randomized controlled trial.pt. [399988]
49. controlled clinical trial.pt. [90669]
50. randomi#ed.ab. [381894]
51. placebo.ab. [163741]
52. randomly.ab. [228612]
53. Clinical Trials as topic.sh. [176325]
54. trial.ti. [138778]
55. or/48-54[984414]
56. 47 or 55 [1148151]

57. 37 and 56 [2505]
58. limit 57 to ed=20121129-20141109 [207]
59. limit 58 to english language [200]

Records Retrieved	200

Database: **EMBASE 1974 to 2014 November 07**

Search strategy: search terms [number of results]	**Date of search: 09/11/2014**

1. myocardial infarct*.ti,ab. [197891]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [50992]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [38432]
4. acute coronary syndrome/[29530]
5. acute coronary syndrome*.ti,ab,kw. [31768]
6. exp *heart infarction/ [141261]
7. exp st segment elevation myocardial infarction/ [16413]
8. or/1-7 [306391]

9. exp *fibrinolytic therapy/ [6086]
10. exp *fibrinolytic agent/ [53155]
11. (antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis).ti,ab. [86769]
12. or/9-11 [117047]

13. exp *angiocardiography/ [19741]
14. exp *angioplasty/ [28538]

15. exp *stent/ [44828]
16. (angiogram or angiograph* or angioplasty or stent*).ti,ab. [298924]
17. or/13-16[313978]

18. 12 and 17 [15060]
19. 8 and 18[7988]

20. letter.pt. or letter/ [862676]
21. note.pt. [574449]
22. editorial.pt. [458901]
23. case report/ or case study/ [1972290]
24. (letter or comment*).ti. [151583]
25. or/20-24[3716060]
26. randomized controlled trial/ or random*.ti,ab. [1009084]
27. 25 not 26 [3687285]
28. animal/ not human/ [1202650]
29. nonhuman/ [4399394]
30. exp Animal Experiment/ [1812695]
31. exp Experimental Animal/ [421900]
32. animal model/ [780759]
33. exp Rodent/ [2930043]
34. (rat or rats or mouse or mice).ti. [1285271]
35. or/27-34[9998511]

36. 19 not 35 [7008]

37. systematic review/ [81649]
38. meta-analysis/ [84646]
39. (meta analy* or metanaly* or metaanaly*).ti,ab. [88808]
40. ((systematic or evidence) adj2 (review* or overview*)).ti,ab. [93843]
41. systematic review/ [81649]
42. (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. [31277]
43. (search strategy or search criteria or systematic search or study selection or data extraction).ab. [31763]
44. (search* adj4 literature).ab. [36753]
45. (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. [114149]
46. ((pool* or combined) adj2 (data or trials or studies or results)).ab. [41703]
47. cochrane.jw. [11566]
48. or/37-46[310331]
49. random*.ti,ab. [925671]
50. factorial*.ti,ab. [24147]
51. (crossover* or cross over*).ti,ab. [72840]
52. ((doubl* or singl*) adj blind*).ti,ab. [164682]
53. (assign* or allocat* or volunteer* or placebo*).ti,ab. [682538]
54. crossover procedure/ [40579]
55. single blind procedure/ [19009]
56. randomized controlled trial/ [355452]
57. double blind procedure/ [118572]
58. or/49-57[1482223]

59. 48 or 58 [1700866] 60. 36 and 59 [1960] 61. limit 60 to em=201247-201445 [211] 62. limit 61 to english language [200]	
Records Retrieved	200

Database: **Cochrane Library**	
Search strategy:	**Date of search: 09/11/2014**
#1 MeSH descriptor: [Myocardial Infarction] explode all trees #2 (myocardial next infarct*):ti,ab #3 (cardiac next (infarct* or attack* or arrest* or event*)):ti,ab #4 (st-elevat* or st-segment* or stemi):ti,ab,kw #5 st next elevat*:ti,ab,kw #6 st next segment:ti,ab,kw #7 (("acute coronary") next syndrome*):ti,ab,kw #8 MeSH descriptor: [Acute Coronary Syndrome] this term only #9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) #10 MeSH descriptor: [Thrombolytic Therapy] explode all trees #11 MeSH descriptor: [Fibrinolytic Agents] explode all trees #12 (antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis):ti,ab,kw #13 (#10 or #11 or #12) #14 MeSH descriptor: [Coronary Angiography] explode all trees #15 MeSH descriptor: [Angioplasty] explode all trees #16 MeSH descriptor: [Stents] explode all trees #17 (angiogram or angiograph* or angioplasty or stent*):ti,ab,kw #18 (#14 or #15 or #16 or #17) #19 (#13 and #18) #20 #9 and #19 Publication Year from 2012	
Records Retrieved	153

Summary of Searches

Total No. Retrieved:	**553**
Medline:	200
Embase:	200
Cochrane Library:	153
Duplicates:	93
No. Total without duplicates**:**	**460**
Screening (Title and Abstract Review)	
No. Excluded:	**450**
Included for Full Text	**10**

review:	
Selection (Full Text Review)	
No. Excluded:	**9**
Publications included from update:	**1**
Total Publications included:	**9**

Cost-Effectiveness Search:

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 08/12/2014**

1. exp *myocardial infarction/ [113231]
2. myocardial infarct*.ti,ab. [154154]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [36035]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25376]
5. acute coronary syndrome/ [8507]
6. acute coronary syndrome*.ti,ab,kw. [20062]
7. or/1-6 [229025]

8. *angiography/ [18889]
9. angiocardiography/ [9217]
10. *coronary angiography/ [14762]
11. (angiograph* or arteriograph* or angiocardiograph* or angiogram* or cardioangiograph* or angiocardiogram* or angio cardiograph* or coronarograph*).ti,ab. [171760]
12. *myocardial revascularization/ [5752]
13. *myocardial reperfusion/ [3435]
14. ((myocardi* or coronary or heart or cardiac) adj2 (revasculari* or reperfus*)).ti,ab. [21614]
15. pci.ti,ab. [14909]
16. ptca.ti,ab. [6271]
17. exp angioplasty/ [56728]
18. blunt microdissection.ti,ab. [17]
19. angioplast*.ti,ab. [37752]
20. ((percutaneous or balloon or coronary or transluminal or primary) adj3 (dilation or dilatation or intervention*)).ti,ab. [38831]
21. ((coronary or drug-eluting or "bare metal") adj2 stent*).ti,ab. [14274]
22. or/8-21 [285107]

23. 7 or 22 [459649]

24. economics/ or exp economics, hospital/ or exp economics, medical/ or economics, nursing/ or economics, pharmaceutical/ [67468]
25. exp "Costs and Cost Analysis"/ [191966]
26. Value-Based Purchasing/ [230]
27. exp "Fees and Charges"/ [28304]
28. budget$.mp. or Budgets/ [26133]
29. (low adj cost).mp. [28126]
30. (high adj cost).mp. [8852]
31. (health?care adj cost$).mp. [5216]
32. (cost adj estimate$).mp. [1566]
33. (cost adj variable$).mp. [117]

34. (unit adj cost$).mp. [1730]
35. (fiscal or funding or financial or finance).tw. [91780]
36. (economic$ or pharmacoeconomic$ or price$ or pricing).tw. [191926]
37. (price* or pricing*).ti,ab. [26985]
38. or/24-37 [514912]

39. 23 and 38 [7916]

40. letter/ [892488]
41. editorial/ [380556]
42. news/ [175408]
43. exp historical article/ [334605]
44. Anecdotes as Topic/ [4690]
45. comment/ [633825]
46. case report/ [1747171]
47. (letter or comment*).ti. [103389]
48. or/40-47 [3518852]
49. randomized controlled trial/ or random*.ti,ab. [884788]
50. 48 not 49 [3500065]
51. animals/ not humans/ [4024066]
52. exp Animals, Laboratory/ [768963]
53. exp Animal Experimentation/ [6762]
54. exp Models, Animal/ [451270]
55. exp Rodentia/ [2819193]
56. (rat or rats or mouse or mice).ti. [1162351]
57. or/50-56 [8173358]

58. 39 not 57 [7208]

59. Saudi Arab$.mp,in. or Saudi Arabia/ [30054]
60. Riyadh.mp,in. [15818]
61. Jeddah.mp,in. [3367]
62. Kh*bar.mp,in. [753]
63. Dammam.mp,in. [1310]
64. 59 or 60 or 61 or 62 or 63 [30526]
65. Kuwait$.mp,in. or Kuwait/ [6903]
66. United Arab Emirates.mp,in. or United Arab Emirates/ [4401]
67. Qatar$.mp,in. or Qatar/ [2392]
68. Oman$.mp,in. or Oman/ [3888]
69. Yemen$.mp,in. or Yemen/ [1928]
70. Bahr*in$.mp,in. or Bahrain/ [1231]
71. 65 or 66 or 67 or 68 or 69 or 70 [19890]
72. Middle East$.mp,in. or Middle East/ [12221]
73. Jordan$.mp,in. or Jordan/ [10281]
74. Libya$.mp,in. or Libya/ [1857]
75. Egypt$.mp,in. or Egypt/ [37873]

76. Syria$.mp,in. or Syria/ [10954] 77. Iraq$/ or Iraq.mp,in. [8299] 78. Morocc$.mp,in. or Morocco/ [8690] 79. Tunisia$.mp,in. or Tunisia/ [12710] 80. Leban$.mp,in. or Lebanon/ [15011] 81. West Bank.mp,in. [761] 82. Iran$.mp,in. or Iran/ [64951] 83. Turkey/ or (Turkey or Turkish).mp,in. [148622] 84. Algeria$.mp,in. or Algeria/ [4270] 85. Arab$.mp,in. or Arabs/ [125255] 86. 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 [325846] 87. 85 or 86 [442588] 88. 64 or 71 or 87 [454955] 89. 58 and 88 [82]	
Records Retrieved	82

Database: **EMBASE 1974 to 2014 December 07**	
Search strategy: search terms [number of results]	**Date of search: 08/12/2014**

1. myocardial infarct*.ti,ab. [199796]
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [52039]
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [39027]
4. acute coronary syndrome/ [30169]
5. acute coronary syndrome*.ti,ab,kw. [32377]
6. exp *heart infarction/ [142047]
7. exp st segment elevation myocardial infarction/ [16896]
8. or/1-7 [309825]

9. *Angiography/ [24490]
10. Angiocardiography/ [81244]
11. Coronary Angiography/ [81244]
12. Angiograph*.ti,ab. [186980]
13. Arteriograph*.ti,ab. [22071]
14. Angiocardiograph*.ti,ab. [3929]
15. Coronary Arteriogra*.ti,ab. [5762]
16. Angiogram*.ti,ab. [24543]
17. Cardioangiograph*.ti,ab. [210]
18. Angiocardiogram*.ti,ab. [284]
19. Angio Cardiograph*.ti,ab. [26]
20. Coronary Arteriogra*.ti,ab. [5762]
21. Coronarograph*.ti,ab. [1844]
22. *Heart Muscle Revascularization/ [6426]
23. Angioplasty, Transluminal, Percutaneous Coronary/ [24723]
24. (Myocardial adj (revascularisation or revascularization)).ti,ab. [5070]
25. PCI.ti,ab. [30851]

26. Percutaneous coronary intervention.ti,ab. [28038]
27. Percutaneous transluminal coronary angioplasty.ti,ab. [7269]
28. PTCA.ti,ab. [7790]
29. exp Angioplasty/ [67625]
30. Blunt Microdissection.ti,ab. [20]
31. ((laser or patch) adj angioplasty).ti,ab. [1642]
32. Percutaneous Transluminal Angioplasty.ti,ab. [4759]
33. Transluminal Coronary Angioplasty.ti,ab. [7578]
34. (Balloon adj3 coronary).ti,ab. [1903]
35. (Balloon adj3 angioplasty).ti,ab. [10154]
36. (Coronary adj2 stent*).ti,ab. [10316]
37. or/9-36 [349942]

38. 8 or 37 [585004]

39. economic evaluation$.mp. or exp economic evaluation/ [221716]
40. fee$.mp. or exp fee/ [612172]
41. health care cost$.mp. or exp "health care cost"/ [216279]
42. hospital cost$.mp. or exp "hospital cost"/ [29779]
43. pharmacoeconomics.mp. or exp pharmacoeconomics/ [172598]
44. health economics.mp. or health economics/ [36246]
45. budget$.mp. or budget/ [36827]
46. socioeconomics.mp. or socioeconomics/ [111508]
47. 39 or 40 or 41 or 42 or 43 or 44 [1089196]
48. 45 or 47 [1112053]
49. 46 or 48 [1206351]
50. (low adj cost).mp. [31000]
51. (high adj cost).mp. [9939]
52. (health?care adj cost$).mp. [14501]
53. (cost adj estimate$).mp. [2110]
54. (cost adj variable$).mp. [171]
55. (unit adj cost$).mp. [2646]
56. (fiscal or funding or financial or finance).tw. [110413]
57. (economic$ or pharmacoeconomic$ or price$ or pricing).tw. [238073]
58. 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 [383106]
59. 49 or 58 [1446380]

60. 38 and 59 [22649]

61. letter.pt. or letter/ [867208]
62. note.pt. [578045]
63. editorial.pt. [461703]
64. case report/ or case study/ [1985944]
65. (letter or comment*).ti. [152349]
66. or/61-65 [3738319]
67. randomized controlled trial/ or random*.ti,ab. [1017887]

68.	66 not 67 [3709351]
69.	animal/ not human/ [1203738]
70.	nonhuman/ [4421684]
71.	exp Animal Experiment/ [1821006]
72.	exp Experimental Animal/ [425520]
73.	animal model/ [786695]
74.	exp Rodent/ [2943311]
75.	(rat or rats or mouse or mice).ti. [1289580]
76.	or/68-75 [10047179]
77.	60 not 76 [18210]
78.	Saudi Arab$.mp,in. or Saudi Arabia/ [50390]
79.	Riyadh.mp,in. [27230]
80.	Jeddah.mp,in. [7206]
81.	Kh*bar.mp,in. [1290]
82.	Dammam.mp,in. [2061]
83.	78 or 79 or 80 or 81 or 82 [50691]
84.	Kuwait$.mp,in. or Kuwait/ [11227]
85.	United Arab Emirates.mp,in. or United Arab Emirates/ [10173]
86.	Qatar$.mp,in. or Qatar/ [5093]
87.	Oman$.mp,in. or Oman/ [5778]
88.	Yemen$.mp,in. or Yemen/ [2648]
89.	Bahr*in$.mp,in. or Bahrain/ [3140]
90.	84 or 85 or 86 or 87 or 88 or 89 [35913]
91.	Middle East$.mp,in. or Middle East/ [15630]
92.	Jordan$.mp,in. or Jordan/ [31067]
93.	Libya$.mp,in. or Libya/ [3058]
94.	Egypt$.mp,in. or Egypt/ [70823]
95.	Syria$.mp,in. or Syria/ [16292]
96.	Iraq$/ or Iraq.mp,in. [10623]
97.	Morocc$.mp,in. or Morocco/ [19001]
98.	Tunisia$.mp,in. or Tunisia/ [25612]
99.	Leban$.mp,in. or Lebanon/ [27607]
100.	West Bank.mp,in. [1114]
101.	Iran$.mp,in. or Iran/ [115180]
102.	Turkey/ or (Turkey or Turkish).mp,in. [260907]
103.	Algeria$.mp,in. or Algeria/ [8207]
104.	Arab$.mp,in. or Arabs/ [160279]
105.	91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 [586452]
106.	104 or 105 [724555]
107.	83 or 90 or 106 [744262]
108.	77 and 107 [422]

Records Retrieved	422

Summary of Searches

Total No. Retrieved:	**504**
Medline:	82
Embase:	422
Duplicates:	55
No. Total without duplicates**:**	**449**
Screening (Title and Abstract Review)	
No. Excluded:	**443**
Included for Full Text review:	**6**
Selection (Full Text Review)	
No. Excluded:	**5**
Publications included from search:	**1**

Patients' Values and Preferences Search:

Database: **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present**	
Search strategy: search terms [number of results]	**Date of search: 08/12/2014**

1. exp *myocardial infarction/ [113231]
2. myocardial infarct*.ti,ab. [154154]
3. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [36035]
4. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [25376]
5. acute coronary syndrome/ [8507]
6. acute coronary syndrome*.ti,ab,kw. [20062]
7. or/1-6 [229025]

8. *angiography/ [18889]
9. angiocardiography/ [9217]
10. *coronary angiography/ [14762]
11. (angiograph* or arteriograph* or angiocardiograph* or angiogram* or cardioangiograph* or angiocardiogram* or angio cardiograph* or coronarograph*).ti,ab. [171760]
12. *myocardial revascularization/ [5752]
13. *myocardial reperfusion/ [3435]
14. ((myocardi* or coronary or heart or cardiac) adj2 (revasculari* or reperfus*)).ti,ab. [21614]
15. pci.ti,ab. [14909]
16. ptca.ti,ab. [6271]
17. exp angioplasty/ [56728]
18. blunt microdissection.ti,ab. [17]
19. angioplast*.ti,ab. [37752]
20. ((percutaneous or balloon or coronary or transluminal or primary) adj3 (dilation or dilatation or intervention*)).ti,ab. [38831]
21. ((coronary or drug-eluting or "bare metal") adj2 stent*).ti,ab. [14274]
22. exp *thrombolytic therapy/ [12912]
23. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [10879]
24. (thrombolysis or fibrinolysis).ti,ab. [33649]
25. fibrinolytic agents/ [24733]
26. or/8-25 [332242]

27. 7 or 26 [498986]

28. patient$ participation.mp. or exp patient participation/ [20427]
29. patient$ satisfaction.mp. or exp patient satisfaction/ [78131]
30. attitude to health.mp. or exp Attitude to health/ [391311]
31. (patient$ preference$ or patient$ perception$ or patient$ decision$ or patient$ perspective$ or user$ view$ or patient$ view$ or patient$ value$).mp. [26307]
32. (patient$ utilit$ or health utilit$).mp. [1503]
33. health related quality of life.mp. or exp "quality of life"/ [133901]
34. (health stat$ utilit$ or health stat$ indicator$ or (health stat$ adj 2 valu$)).mp. or exp Health Status Indicators/ [213496]
35. 28 or 29 or 30 or 31 or 32 or 33 or 34 [713321]

36. 27 and 35 [19211]	
37. Saudi Arab$.mp,in. or Saudi Arabia/ [30054]	
38. Riyadh.mp,in. [15818]	
39. Jeddah.mp,in. [3367]	
40. Kh*bar.mp,in. [753]	
41. Dammam.mp,in. [1310]	
42. 37 or 38 or 39 or 40 or 41 [30526]	
43. Kuwait$.mp,in. or Kuwait/ [6903]	
44. United Arab Emirates.mp,in. or United Arab Emirates/ [4401]	
45. Qatar$.mp,in. or Qatar/ 2392	
46. Oman$.mp,in. or Oman/ [3888]	
47. Yemen$.mp,in. or Yemen/ [1928]	
48. Bahr*in$.mp,in. or Bahrain/ [1231]	
49. 43 or 44 or 45 or 46 or 47 or 48 [19890]	
50. Middle East$.mp,in. or Middle East/ [12221]	
51. Jordan$.mp,in. or Jordan/ [10281]	
52. Libya$.mp,in. or Libya/ [1857]	
53. Egypt$.mp,in. or Egypt/ [37873]	
54. Syria$.mp,in. or Syria/ [10954]	
55. Iraq$/ or Iraq.mp,in. [8299]	
56. Morocc$.mp,in. or Morocco/ [8690]	
57. Tunisia$.mp,in. or Tunisia/ [12710]	
58. Leban$.mp,in. or Lebanon/ [15011]	
59. West Bank.mp,in. [761]	
60. Iran$.mp,in. or Iran/ [64951]	
61. Turkey/ or (Turkey or Turkish).mp,in. [148622]	
62. Algeria$.mp,in. or Algeria/ [4270]	
63. Arab$.mp,in. or Arabs/ [125255]	
64. 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 [325846]	
65. 63 or 64 [442588]	
66. 42 or 49 or 65 [454955]	
67. 36 and 66 [644]	
Records Retrieved	644

Database: **EMBASE 1974 to 2014 December 07**	
Search strategy: search terms [number of results]	**Date of search: 08/12/2014**
1. myocardial infarct*.ti,ab. [199796]	
2. (cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab. [52039]	
3. (stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab. [39027]	
4. acute coronary syndrome/ [30169]	
5. acute coronary syndrome*.ti,ab,kw. [32377]	
6. exp *heart infarction/ [142047]	
7. exp st segment elevation myocardial infarction/ [16896]	
8. or/1-7 [309825]	
9. *Angiography/ [24490]	
10. Angiocardiography/ [81244]	

11. Coronary Angiography/ [81244]
12. Angiograph*.ti,ab. [186980]
13. Arteriograph*.ti,ab. [22071]
14. Angiocardiograph*.ti,ab. [3929]
15. Coronary Arteriogra*.ti,ab. [5762]
16. Angiogram*.ti,ab. [24543]
17. Cardioangiograph*.ti,ab. [210]
18. Angiocardiogram*.ti,ab. [284]
19. Angio Cardiograph*.ti,ab. [26]
20. Coronary Arteriogra*.ti,ab. [5762]
21. Coronarograph*.ti,ab. [1844]
22. *Heart Muscle Revascularization/ [6426]
23. Angioplasty, Transluminal, Percutaneous Coronary/ [24723]
24. (Myocardial adj (revascularisation or revascularization)).ti,ab. [5070]
25. PCI.ti,ab. [30851]
26. Percutaneous coronary intervention.ti,ab. [28038]
27. Percutaneous transluminal coronary angioplasty.ti,ab. [7269]
28. PTCA.ti,ab. [7790]
29. exp Angioplasty/ [67625]
30. Blunt Microdissection.ti,ab. [20]
31. ((laser or patch) adj angioplasty).ti,ab. [1642]
32. Percutaneous Transluminal Angioplasty.ti,ab. [4759]
33. Transluminal Coronary Angioplasty.ti,ab. [7578]
34. (Balloon adj3 coronary).ti,ab. [1903]
35. (Balloon adj3 angioplasty).ti,ab. [10154]
36. (Coronary adj2 stent*).ti,ab. [10316]
37. fibrinolytic agent/ [22190]
38. exp *fibrinolytic therapy/ [6129]
39. ((thrombolytic or fibrinolytic) adj1 therap*).ti,ab. [13688]
40. (thrombolysis or fibrinolysis).ti,ab. [44104]
41. or/9-40 [402473]

42. 8 or 41 [627080]

43. patient$ participation.mp. or exp patient participation/ [18998]
44. patient$ satisfaction.mp. or exp patient satisfaction/ [96017]
45. attitude to health.mp. or exp Attitude to health/ [81551]
46. (patient$ preference$ or patient$ perception$ or patient$ decision$ or patient$ perspective$ or user$ view$ or patient$ view$ or patient$ value$).mp. [39320]
47. (patient$ utilit$ or health utilit$).mp. [2063]
48. health related quality of life.mp. or exp "quality of life"/ [286160]
49. (health stat$ utilit$ or health stat$ indicator$ or (health stat$ adj 2 valu$)).mp. or exp Health Status Indicators/ [8863]
50. 43 or 44 or 45 or 46 or 47 or 48 or 49 [495342]

51. 42 and 50 [9047]

52. Saudi Arab$.mp,in. or Saudi Arabia/ [50390]
53. Riyadh.mp,in. [27230]
54. Jeddah.mp,in. [7206]

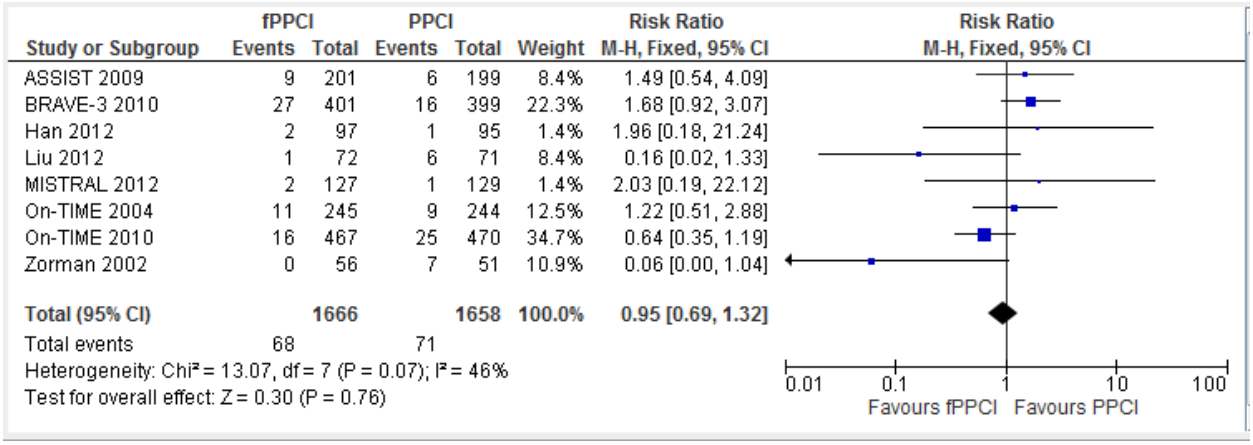
55. Kh*bar.mp,in. [1290] 56. Dammam.mp,in. [2061] 57. 52 or 53 or 54 or 55 or 56 [50691] 58. Kuwait$.mp,in. or Kuwait/ [11227] 59. United Arab Emirates.mp,in. or United Arab Emirates/ [10173] 60. Qatar$.mp,in. or Qatar/ [5093] 61. Oman$.mp,in. or Oman/ [5778] 62. Yemen$.mp,in. or Yemen/ [2648] 63. Bahr*in$.mp,in. or Bahrain/ [3140] 64. 58 or 59 or 60 or 61 or 62 or 63 [35913] 65. Middle East$.mp,in. or Middle East/ [15630] 66. Jordan$.mp,in. or Jordan/ [31067] 67. Libya$.mp,in. or Libya/ [3058] 68. Egypt$.mp,in. or Egypt/ [70823] 69. Syria$.mp,in. or Syria/ [16292] 70. Iraq$/ or Iraq.mp,in. [10623] 71. Morocc$.mp,in. or Morocco/ [19001] 72. Tunisia$.mp,in. or Tunisia/ [25612] 73. Leban$.mp,in. or Lebanon/ 27607 74. West Bank.mp,in. [1114] 75. Iran$.mp,in. or Iran/ [115180] 76. Turkey/ or (Turkey or Turkish).mp,in. [260907] 77. Algeria$.mp,in. or Algeria/ [8207] 78. Arab$.mp,in. or Arabs/ [160279] 79. 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 [586452] 80. 78 or 79 [724555] 81. 57 or 64 or 80 [744262] 82. 51 and 81 [253]	
Records Retrieved	253

Summary of Searches

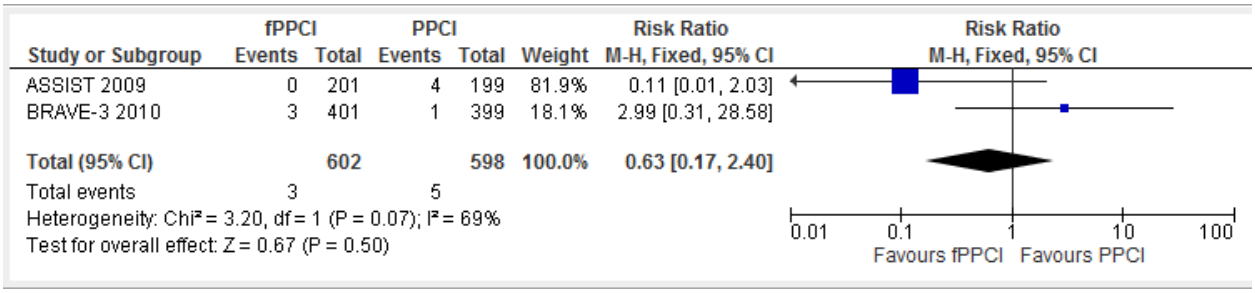
Total No. Retrieved:	**897**
Medline:	644
Embase:	253
Duplicates:	95
No. Total without duplicates**:**	**802**
Screening (Title and Abstract Review)	
No. Excluded:	**767**
Included for Full Text review:	**35**
Selection (Full Text Review)	
No. Excluded:	**31**
Publications included from search:	**4**

Appendix 3: Forest Plots

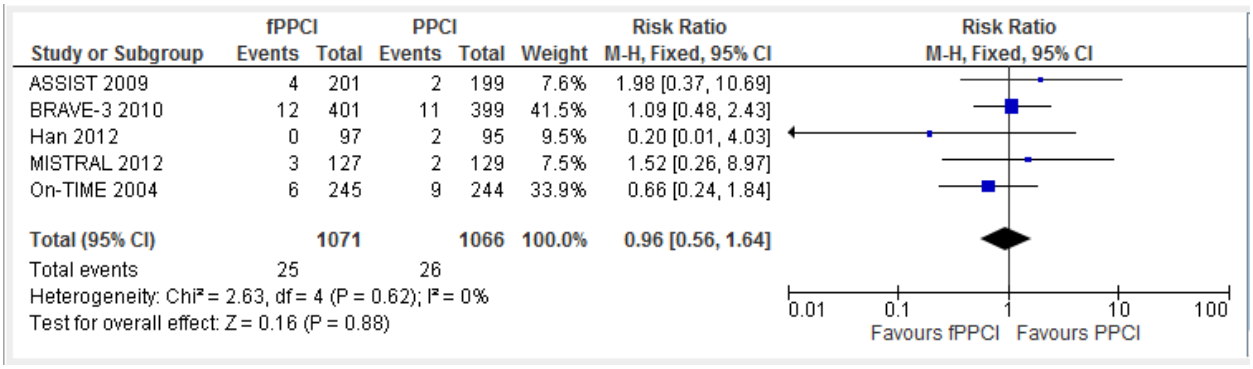
Guideline Question 2 Forest Plots: Should facilitated percutaneous coronary intervention (fPPCI) versus percutaneous coronary intervention (PPCI) be used in patients with STEMI?



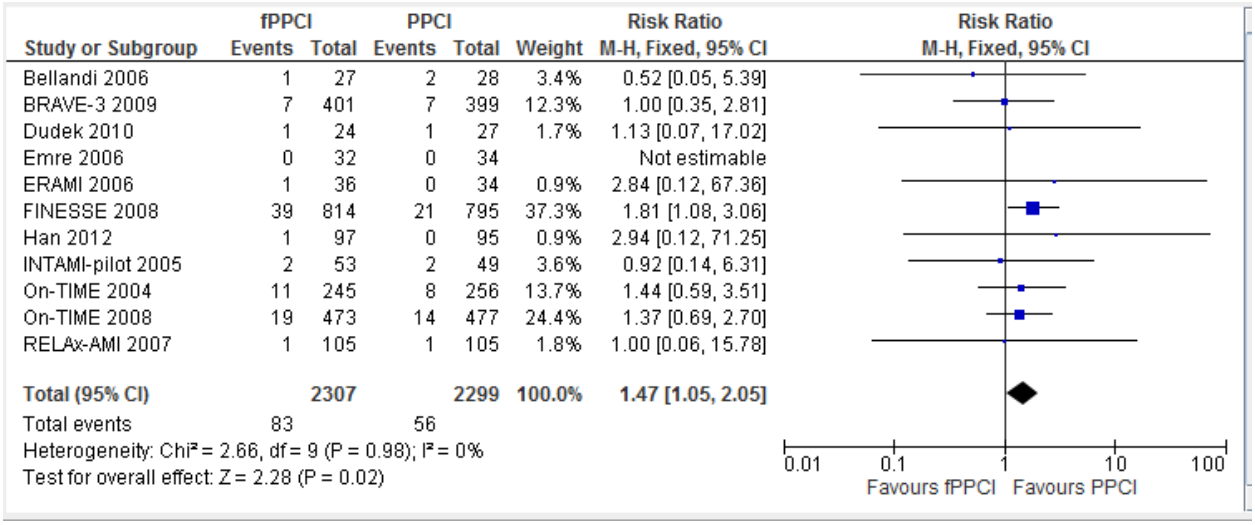
Longer term mortality



Longer term stroke

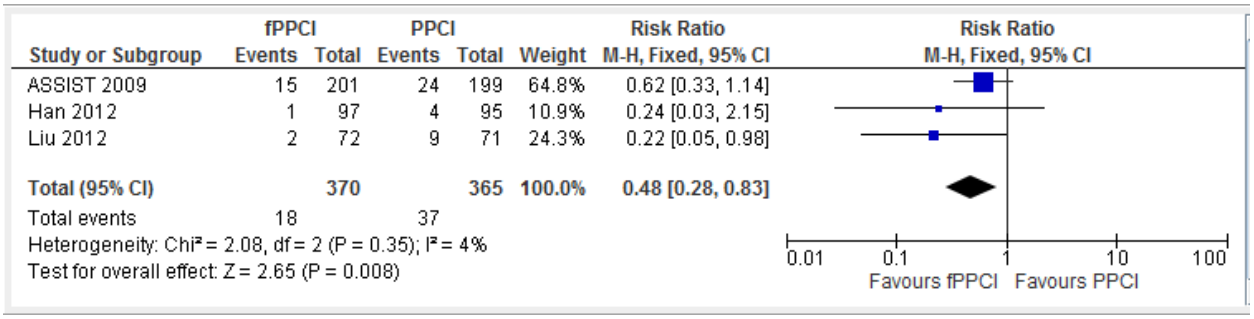


Reinfarction – long term



Major bleeding – short term

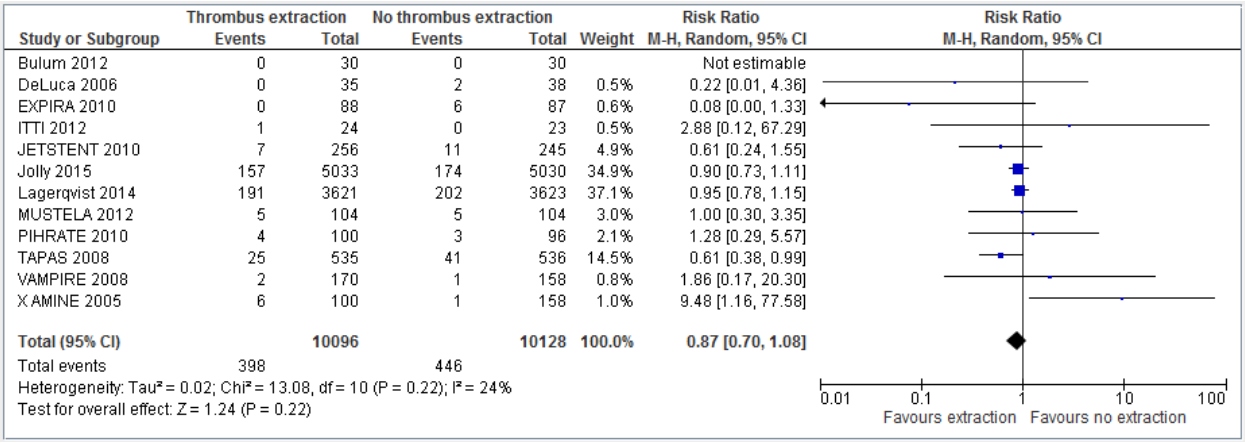
Minor bleeding – In hospital



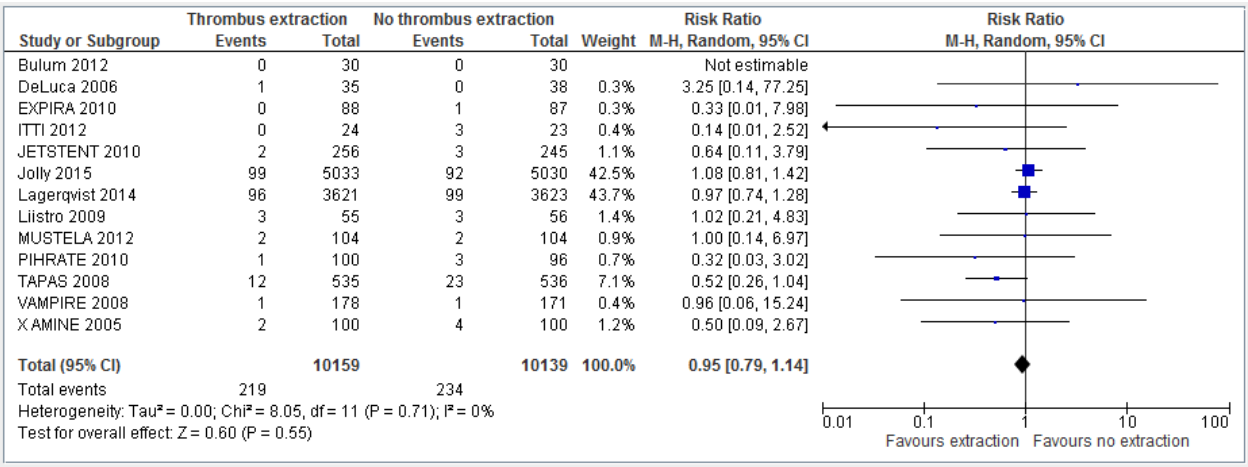
Heart Failure – Longer term

Repeat revascularization – longer term

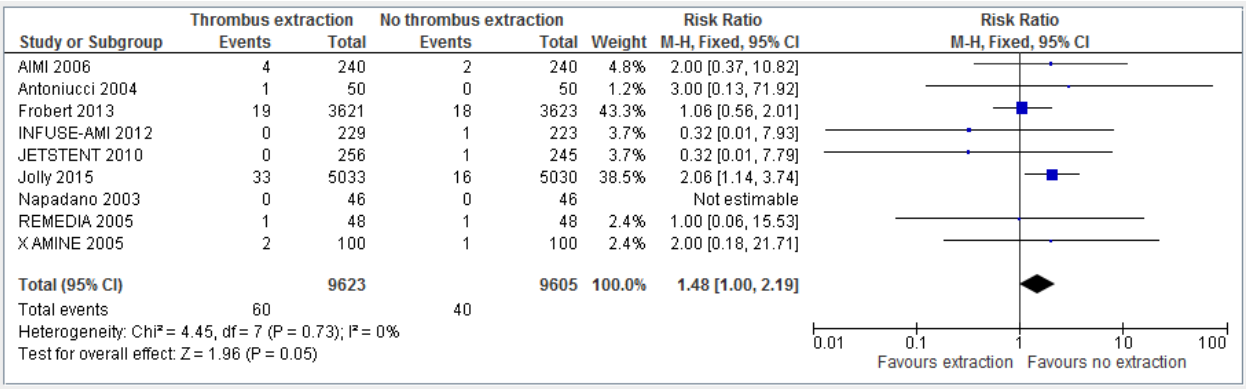
Guideline Question 3 Forest Plots: Should routine thrombus extraction devices during percutaneous coronary intervention (PPCI) versus percutaneous coronary intervention (PPCI) alone be used for treatment of STEMI?



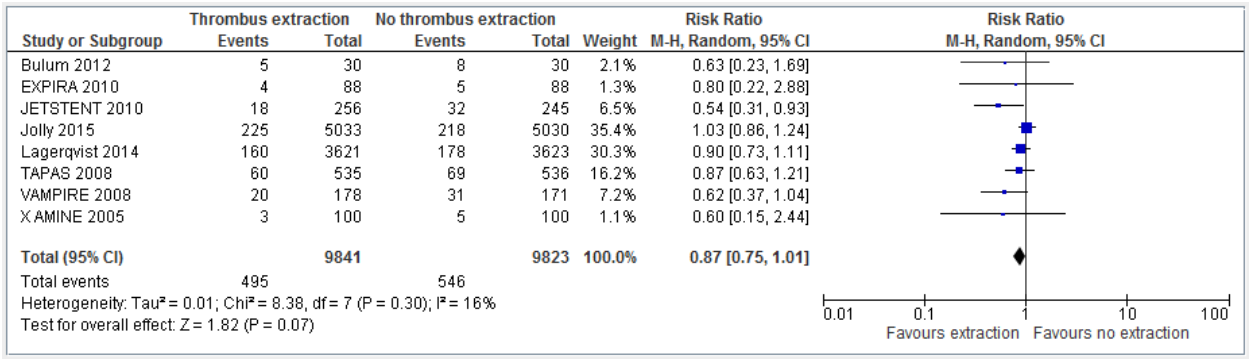
Mortality at 6 to 12 months



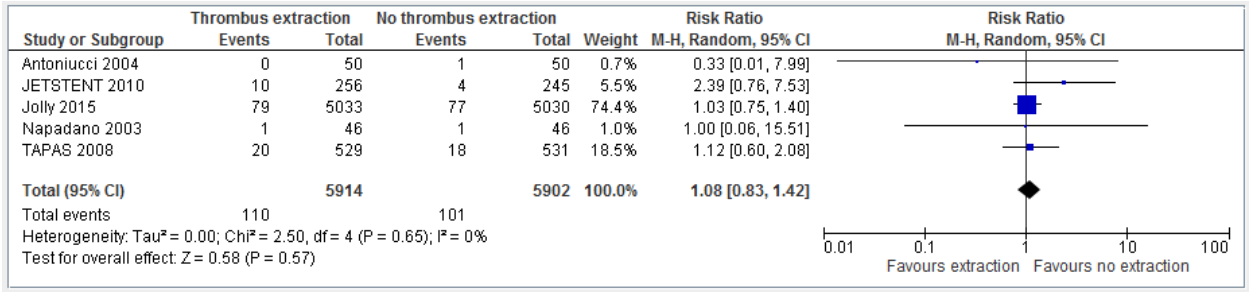
Re-infarction longer term



Stroke at 30 days



Revascularization – long term



Major Bleeding

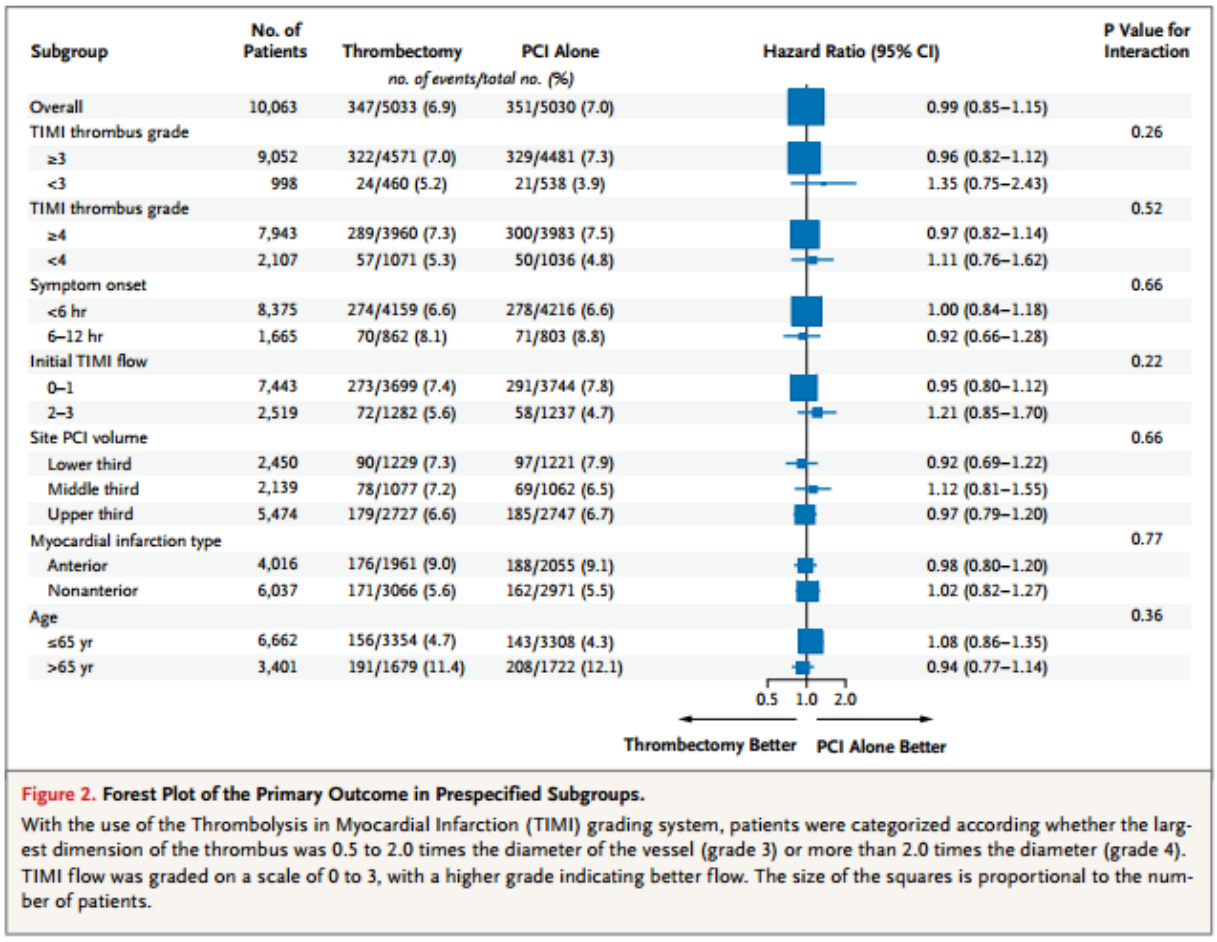
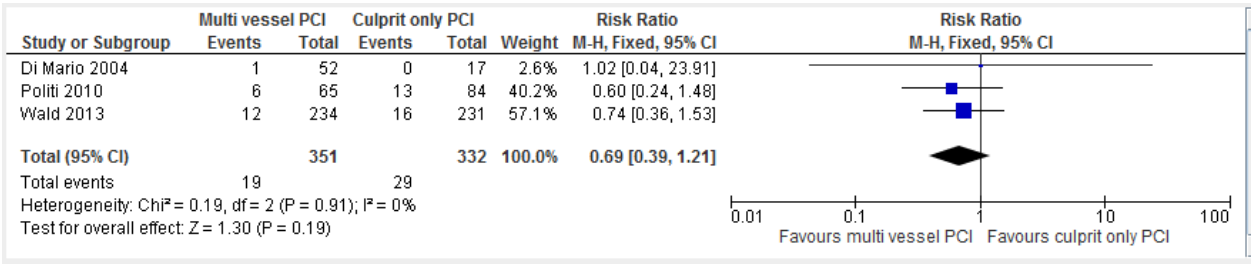


Figure 2. Forest Plot of the Primary Outcome in Prespecified Subgroups.

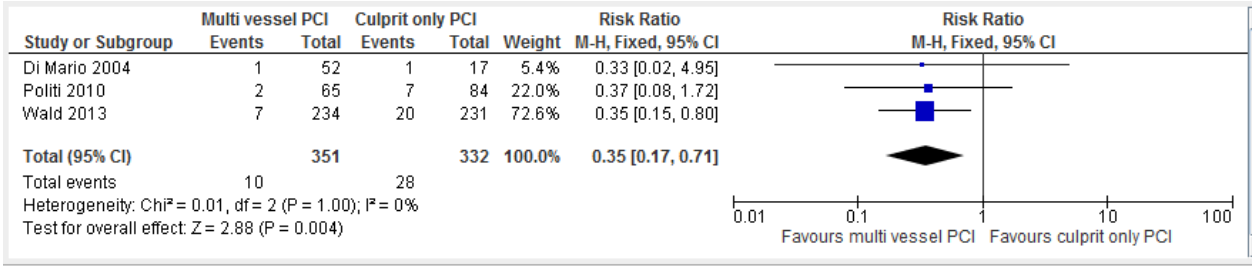
With the use of the Thrombolysis in Myocardial Infarction (TIMI) grading system, patients were categorized according whether the largest dimension of the thrombus was 0.5 to 2.0 times the diameter of the vessel (grade 3) or more than 2.0 times the diameter (grade 4). TIMI flow was graded on a scale of 0 to 3, with a higher grade indicating better flow. The size of the squares is proportional to the number of patients.

From: Jolly, S. S., et al. "Randomized Trial of Primary PCI with or without Routine Manual Thrombectomy." New England Journal of Medicine (ePub ahead of print March 16, 2015)

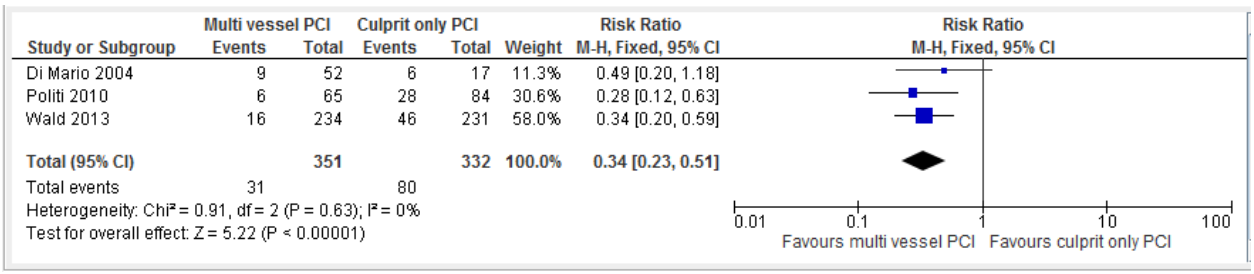
Guideline Question 4 Forest Plots: Should multi-vessel PPCI versus culprit only PPCI be used in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI?



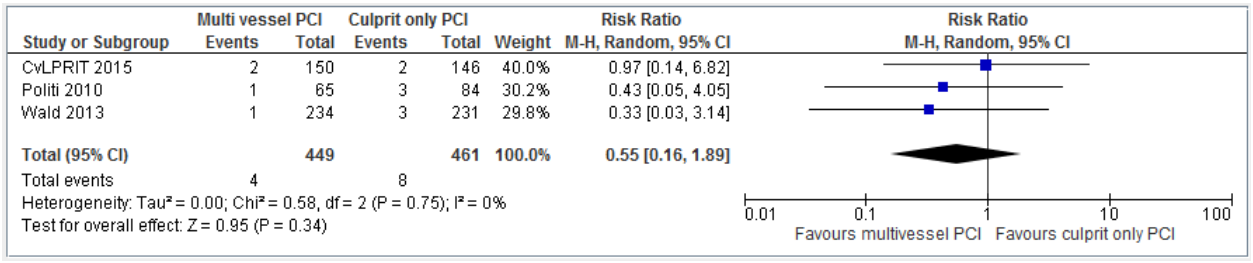
Mortality-long term



Reinfarction



Revascularization



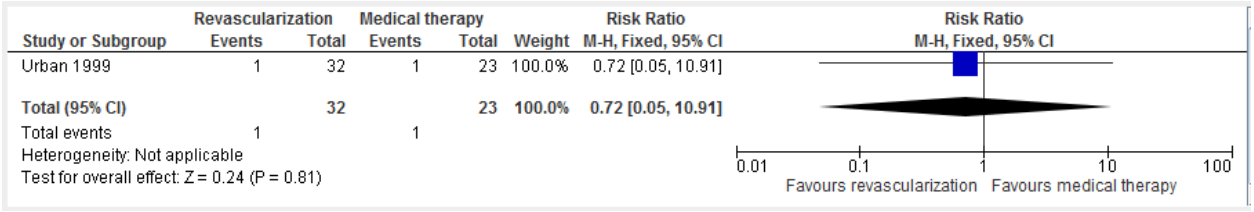
Contrast Induced Nephropathy (CIN). Definitions differ in the three trials that reported this outcome. Wald – CIN was defined as requiring dialysis reported in the supplement, Politi – CIN was defined as an absolute increase in serum creatinine values of 0.5mg/dl or greater or a 25% or greater increase from baseline within 72 hours following the procedure.

Guideline Question 5 Forest Plots: Should early revascularization versus medical stabilization be used in patients with cardiogenic shock due to STEMI?

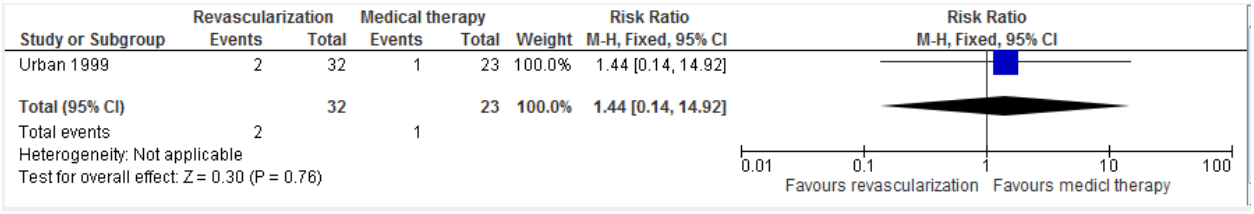
Mortality at 30 days

Mortality at 1 year

Stroke at 30 days



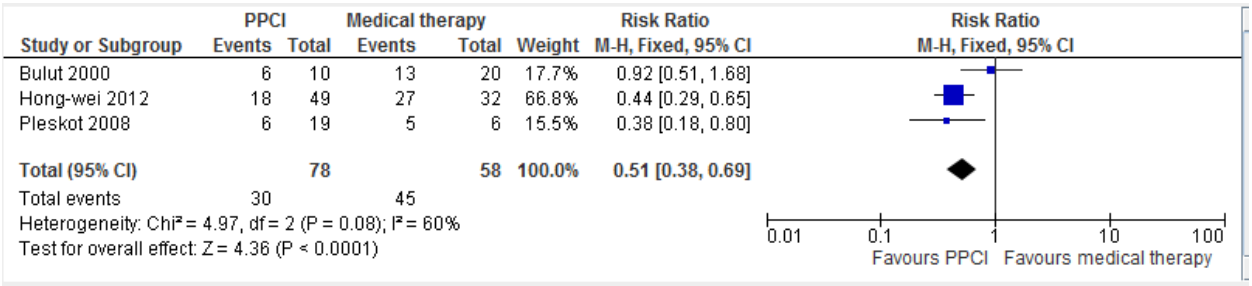
Re-infarction at 30 days



Unplanned revascularization at 30 days

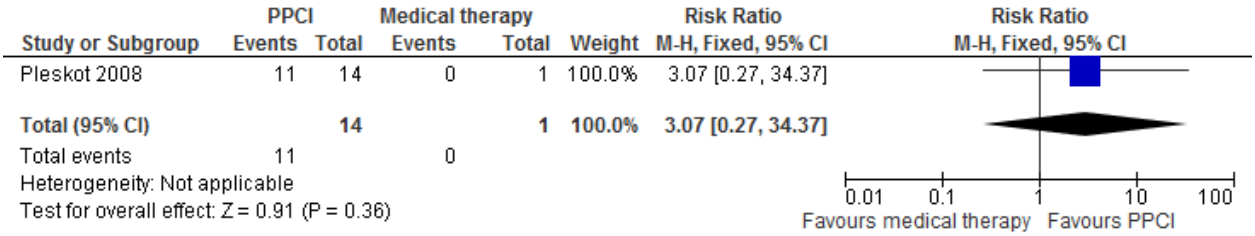
Class III/IV heart failure at 2 weeks

Guideline Question 6 Forest Plots: Should immediate angiography followed by PPCI where indicated be used in patients with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?



Mortality at 30 days

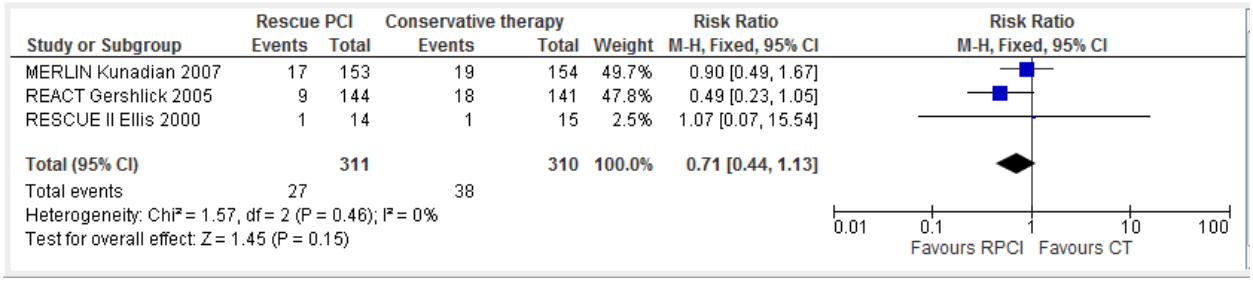
Stroke at 30 days



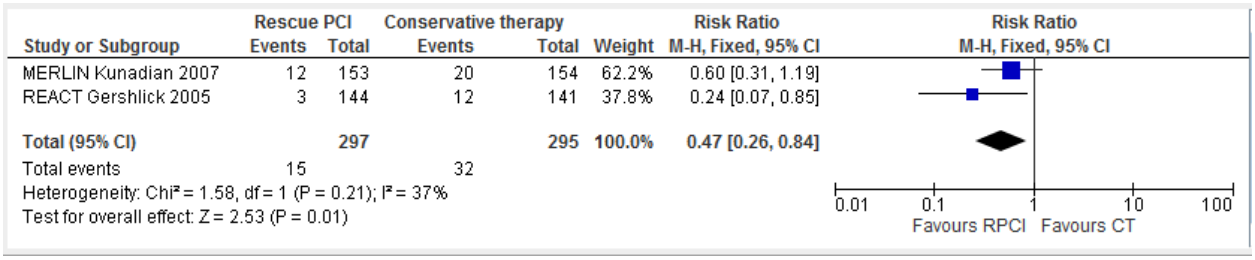
Good performance on CPC at hospital discharge

Guideline Question 8 Forest Plots: Should rescue PCI, repeat fibrinolysis, or conservative management be used in patients with STEMI who fail to reperfuse after fibrinolytic therapy?

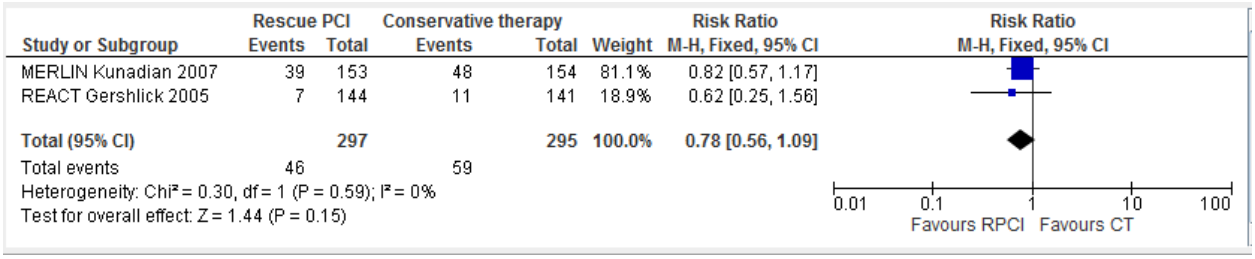
1. Rescue PCI versus conservative management:



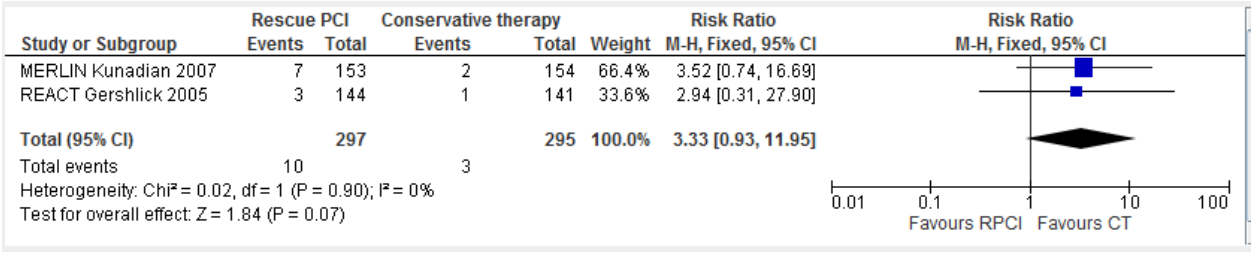
Mortality at 6 months



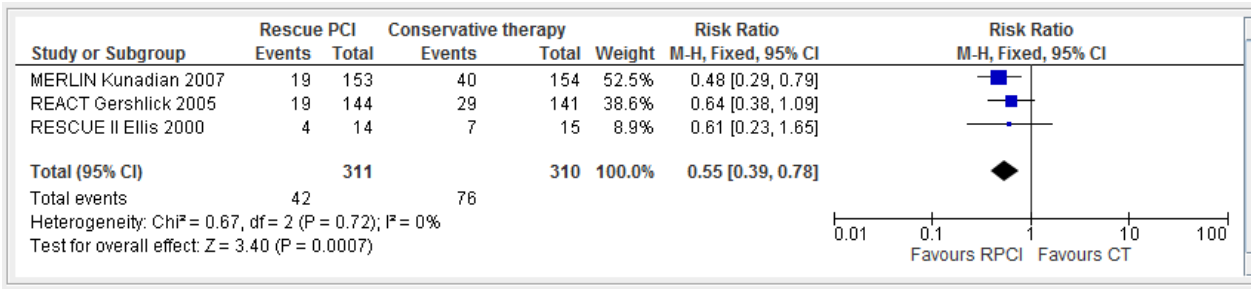
Reinfarction at 6 months



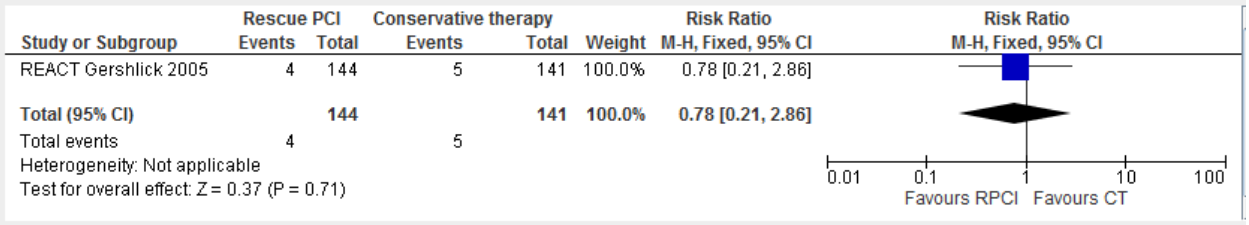
Heart Failure at 6 months



Stroke at 6 months

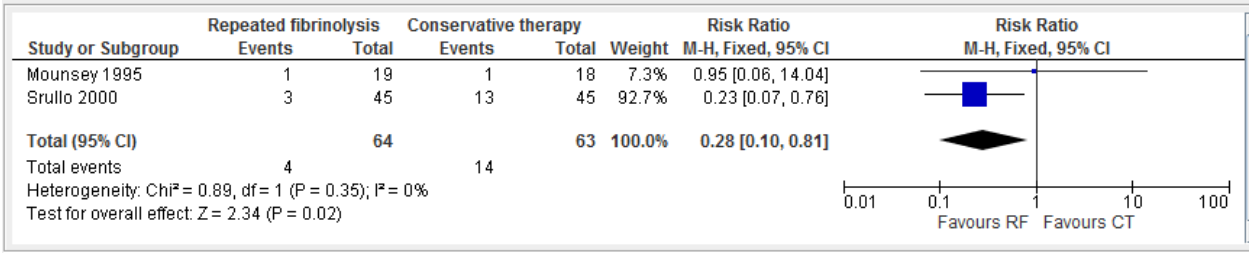


Unplanned revascularization at 6 to 12 months

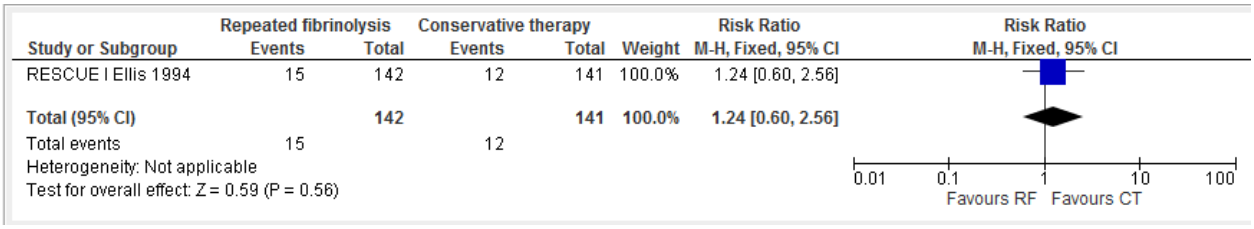


Major bleeding at 30 days

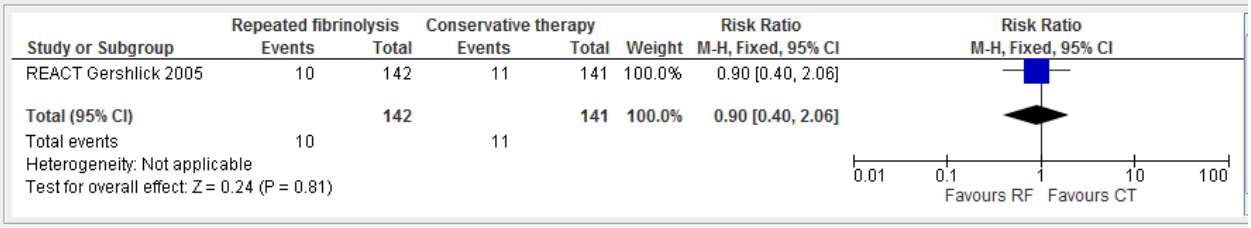
2. Repeat fibrinolysis versus conservative therapy



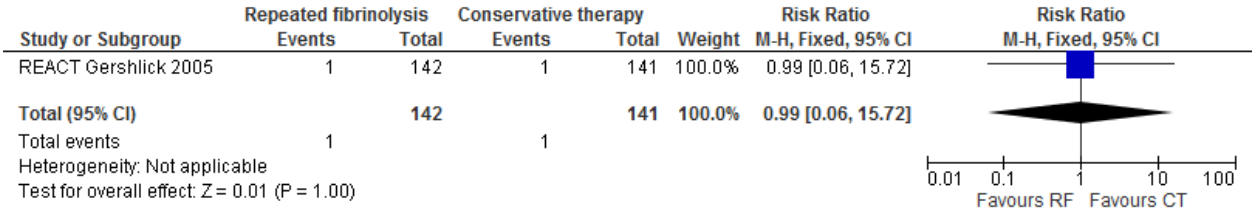
Mortality at 6 weeks



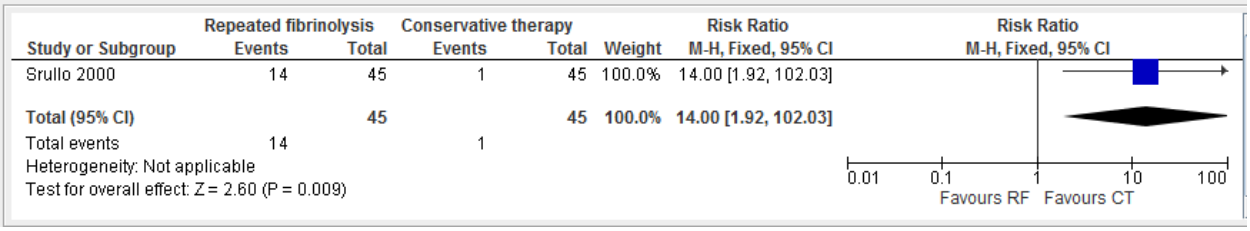
Reinfarction at 6 months



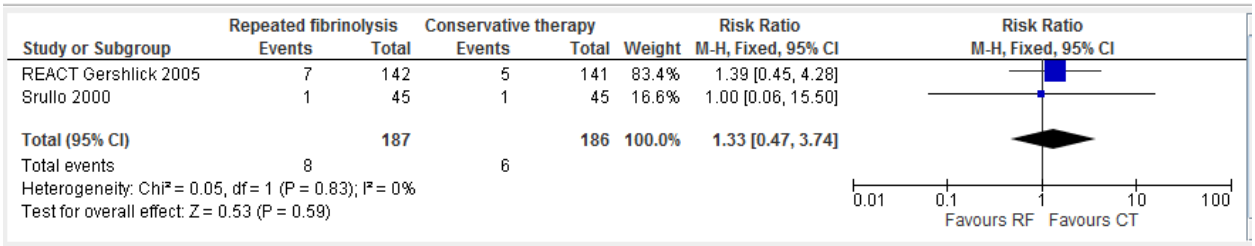
Heart Failure a 6 months



Stroke at 6 months

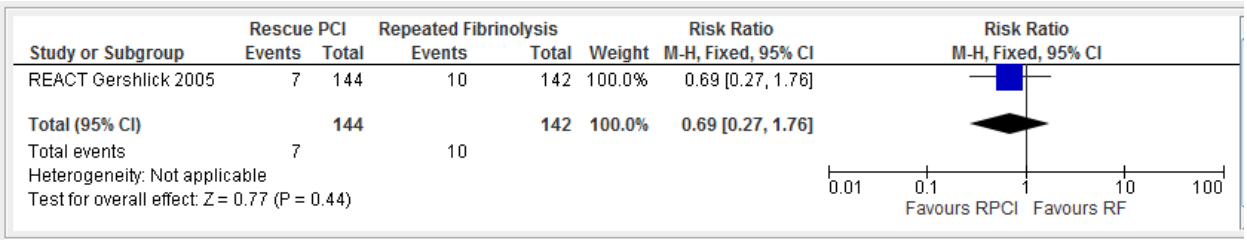


Unplanned revascularization before hospital discharge

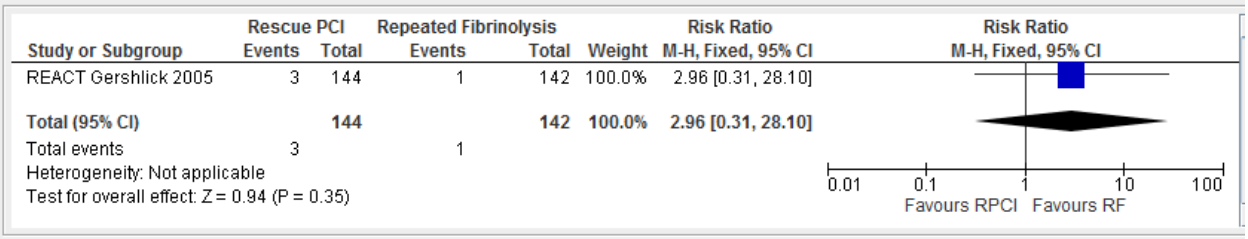


Major bleeding before hospital discharge

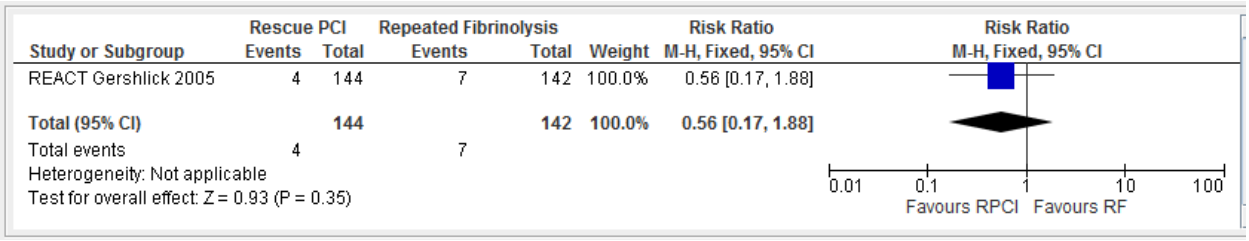
3. Rescue PCI versus repeat fibrinolysis



Heart Failure at 6 months

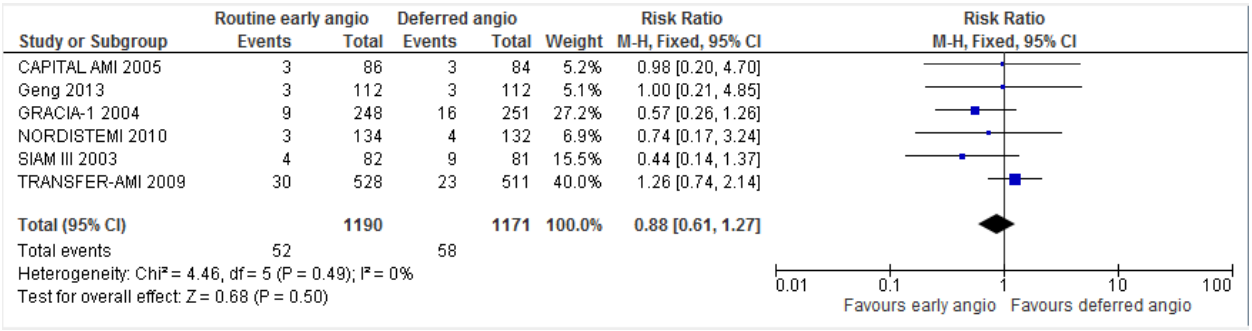


Stroke at 6 months

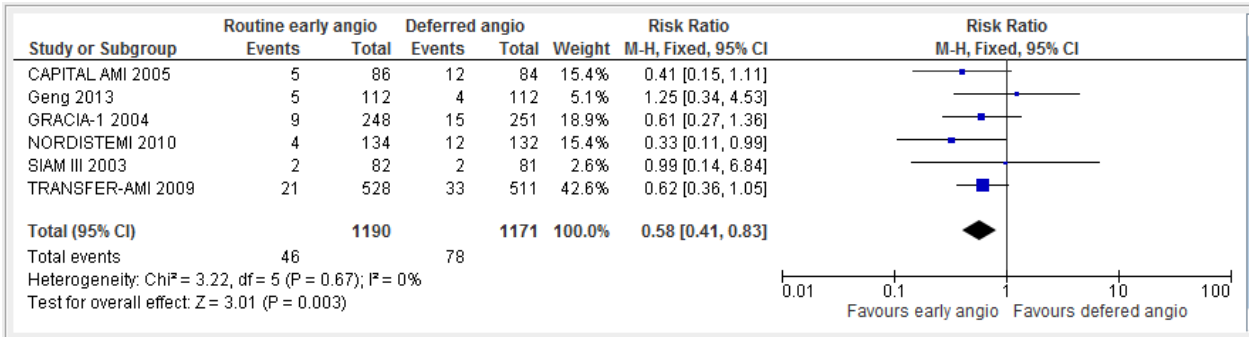


Major bleeding before hospital discharge

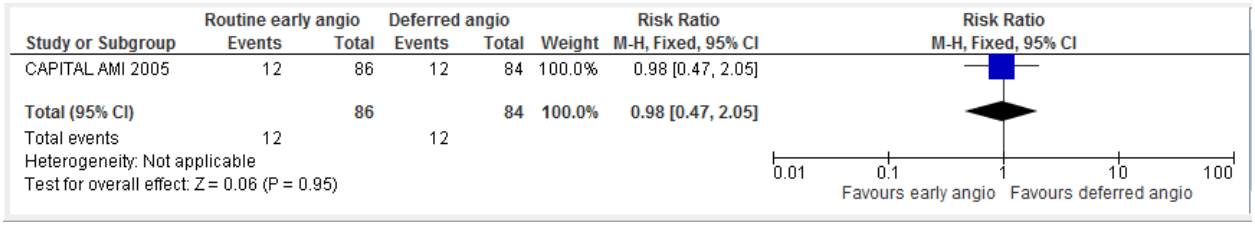
Guideline Question 9 Forest Plots: Should routine early angiography versus routine deferred or selective angiography be used for STEMI successfully treated by fibrinolysis?



Mortality at 6 to 12 months (different studies reported 6 or 12 months data; if both were available, the 12 month data was used for the meta-analysis)

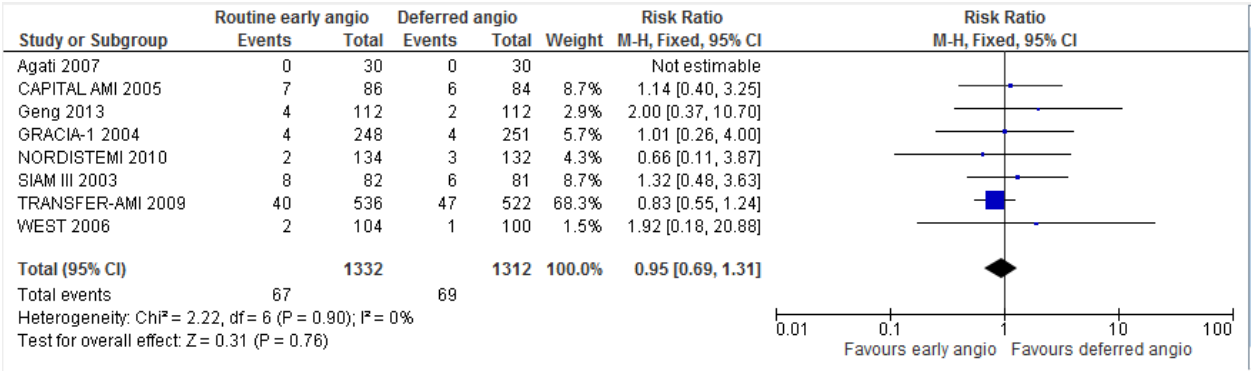


Reinfarction at 6 to 12 months

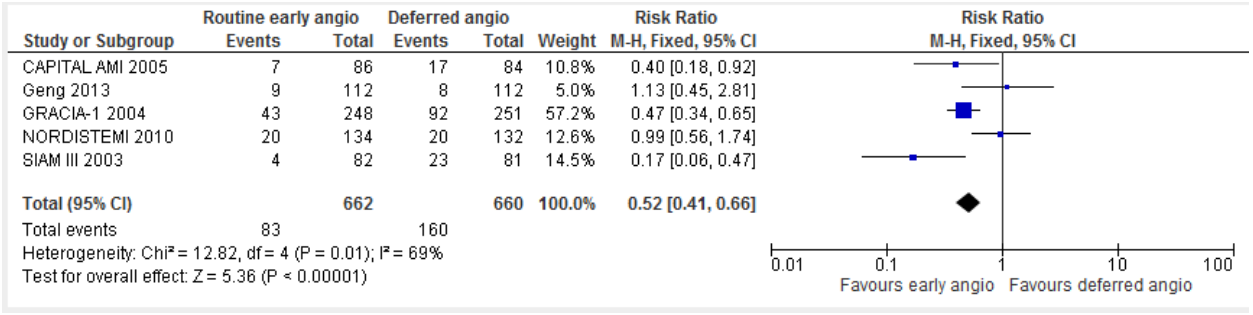


Heart failure at 6 months

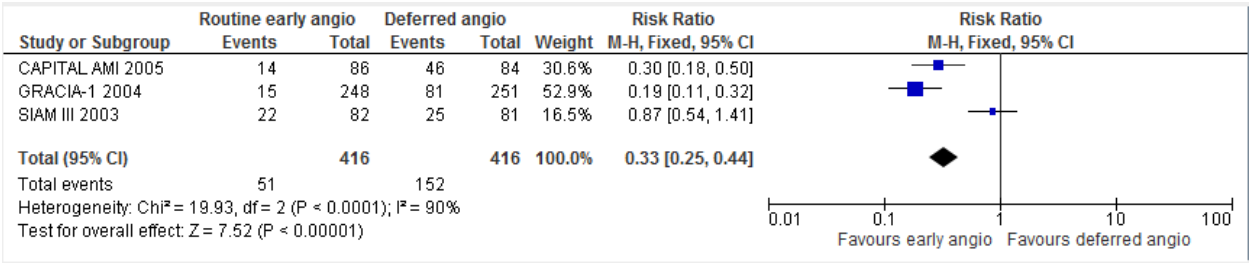
Stroke at 6 to 12 months



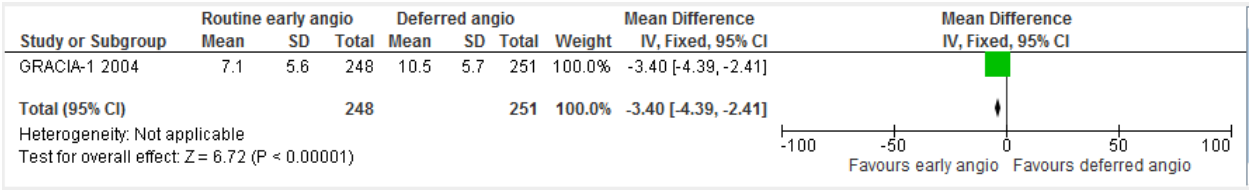
Major bleeding at 30 days



Recurrent ischaemia at 6 to 12 months



Unplanned revascularization at 6 months



Length of hospital stay – index admission