Authors' objectives
To update a 1997 report (see Other Publications of Related Interest no.1) that evaluated diagnostic tests for the identification of acute cardiac ischaemia (ACI) in the emergency department.

Searching
MEDLINE was searched for articles in the English language (1966 to December 1998); the search strategy was reported. All studies referenced in the 1997 report (see Other Publications of Related Interest no.1) were retrieved. Additional articles were identified through contact with technical experts and through examination of the bibliographies of published meta-analyses and selected review articles.

Study selection
Study designs of evaluations included in the review
No inclusion criteria for the study design were specified. The review included randomised controlled trials (RCTs), non-randomised controlled trials and diagnostic accuracy studies. Reports published only as abstracts were excluded.

Specific interventions included in the review
Studies evaluating technologies used to diagnose ACI in an emergency setting were eligible for inclusion. Studies of 12-lead electrocardiography (ECG) or thallium-201 scanning were excluded: 12-lead ECG is standard care and is part of the World Health Organization reference standard for diagnosing ACI, while thallium-201 has been superseded by other radioisotopes. The included studies were of ECG methods, biomarkers, imaging techniques and clinical decision rules.

Reference standard test against which the new test was compared
No reference standard of diagnosis was specified. Studies reporting the diagnosis of acute myocardial infarction (AMI) or unstable angina pectoris (UAP), as reported by the authors of the primary studies, appear to have been eligible for inclusion.

Participants included in the review
Studies of patients aged 18 years or older presenting to emergency settings (including settings such as cardiac care units where no other emergency setting data was available) with symptoms suggestive of ACI were eligible for inclusion. Studies with no clear reference to emergency department settings, or which were of patients with particular co-morbidities (e.g. renal disease), were excluded. Where reported, the mean age of the participants ranged from 37 to 69 years, and between 39% and 95% of them were male.

Outcomes assessed in the review
No inclusion criteria for the diagnostic outcome measures were specified. The review reported sensitivity and specificity values for diagnostic accuracy studies and measures of clinical impact for other study designs. The target condition of interest was ACI, including myocardial infarction and unstable angina.

How were decisions on the relevance of primary studies made?
Titles and abstracts of citations were screened and potentially relevant articles were retrieved for further examination. The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The validity of the included studies was assessed using two separate 3-point evidence scales (A to C): one for diagnostic accuracy studies and one for clinical impact studies. In addition to grading each included study, the authors presented an overall quality of evidence score for each technology. Study quality was assessed by one reviewer and checked by a
second, or performed independently by two reviewers, using a quality assessment form presented in the report. Any discrepancies were resolved by the centre director.

**Data extraction**

The data were abstracted directly into spreadsheets. The data extraction was either performed by one reviewer and checked by a second, or performed independently by two reviewers. Any discrepancies were resolved by the centre director. The studies were categorised according to the population recruited. Sensitivity and specificity were calculated for each diagnostic accuracy study. Time to thrombolysis, ejection fraction and mortality were extracted from each RCT and non-randomised study.

**Methods of synthesis**

How were the studies combined?

Diagnostic accuracy studies were combined, according to test, by:

- estimating pooled values for sensitivity and specificity using a random-effects model (where there was 'little variability in the test results');
- estimating a summary diagnostic odds ratio using a random-effects model; or
- estimating a summary receiver operating characteristic curve using the method of Moses and Shapiro, which accounts for the effects of differing diagnostic thresholds between studies.

Studies included in meta-analyses of clinical impact data were combined using a random-effects model. The risk ratio was reported for dichotomous data, and the mean time to event for continuous data.

How were differences between studies investigated?

The authors did not report a formal statistical method for investigating between-study heterogeneity in groups of studies for which pooled estimates were presented.

**Results of the review**

A total of 105 studies were included in the report.

Pre-hospital 12-lead ECG.

The pooled sensitivity and specificity values were 76% (95% confidence interval, CI: 54, 89) and 88% (95% CI: 67, 96), respectively, for ACI (11 studies). For AMI, the sensitivity was 68% (95% CI: 59, 76) and the specificity 97% (95% CI: 89, 92). The pooled risk ratio for mortality, derived from data from 9 RCTs, was 0.84 (95% CI: 0.73, 0.98).

Continuous or serial ECG.

The sensitivity was 21% (specificity 99%) and 25% (specificity 92%) for ACI (2 studies), and 39% (specificity 88%) for AMI (1 study).

Non-standard lead ECG.

The sensitivity for AMI (3 studies) ranged from 59% (specificity 93%) to 83% (specificity 76%), and the specificity from 76% (sensitivity 83%) to 93% (sensitivity 59%). The sensitivity for ACI (1 study) was 96% (specificity 40.7%).

Exercise stress ECG.

The sensitivity for ACI (2 studies) was 70% (specificity 82%) and 100% (specificity 93%).

Creatine kinase (CK) and creatine kinase subunit (CK-MB).
The pooled sensitivity and specificity values of initial CK for the diagnosis of AMI in the emergency department (11 studies) were 36% (95% CI: 29, 44) and 88% (95% CI: 80, 93), respectively. The sensitivity increased for serial CK measurements (2 studies): 99% (specificity 68%) and 69% (specificity 84%). One study reported a sensitivity of 23% (specificity 96%) for the diagnosis of ACI using initial CK.

The pooled sensitivity and specificity values of initial CK-MB for the diagnosis of AMI in the emergency department (11 studies) were 44% (95% CI: 35, 53) and 96% (95% CI: 94, 97), respectively. Both sensitivity and specificity increased for serial CK-MB measurements. The pooled sensitivity for serial CK-MB measurements (8 studies) was 80% (95% CI: 61, 91) and the pooled specificity was 96% (95% CI: 94, 98). One study reported a sensitivity of 31% (specificity 95%) for serial CK-MB measurements for the diagnosis of ACI in the emergency department.

Myoglobin.

The pooled sensitivity and specificity values of myoglobin for the diagnosis of AMI in the emergency department (10 studies) were 49% (95% CI: 41, 57) and 93% (95% CI: 88, 96), respectively. The sensitivity increased where serial myoglobin measurements were used. The pooled sensitivity and specificity values for serial myoglobin measurements (5 studies) were both 90% (95% CI: 78, 96) when simple numerical thresholds were used to diagnose AMI.

Troponin I and troponin T.

Two studies reported sensitivities of 23% (specificity 95%) and 66% (specificity 89%) when using troponin I to diagnose AMI. One study reported a sensitivity of 90% (specificity 96%) when serial troponin I measurements were used. The pooled sensitivity and specificity values of troponin T for the diagnosis of AMI in the emergency department (6 studies) were 44% (95% CI: 32, 56) and 92% (95% CI: 88, 95), respectively. Two studies reported sensitivities of 90% (specificity 80%) and 65% (specificity 93%) when serial troponin T measurements were used.

The use of combinations of biomarkers in series generally resulted in increased diagnostic accuracy for AMI.

Echocardiography.

The pooled sensitivity and specificity values of rest echocardiography for the diagnosis of AMI in the emergency department (3 studies) were 93% (95% CI: 81, 97) and 66% (95% CI: 43, 83), respectively. One study evaluated dobutamine stress echocardiography. This study reported a sensitivity of 90% (specificity 89%) for AMI.

Technetium-99m sestamibi imaging.

The pooled sensitivity and specificity values for the diagnosis of AMI (4 studies) were 92% (95% CI: 78, 98) and 67% (95% CI: 52, 79), respectively; for ACI (3 studies), they were 81% (95% CI: 74, 87) and 73% (95% CI: 56, 85), respectively.

Clinical decision instruments.

Two studies reported sensitivities of 86% (specificity 92%) and 95% (specificity 78%) for the ACI Time-Insensitive Predictive Instrument. Two studies reported sensitivities of 88% (specificity 74%) and 91% (specificity 70%) for the Goldman chest pain protocol for the diagnosis of ACI.

Accuracy data for a number of other, individually reported, diagnostic protocols and computer-based decision aids were reported.

Cost information

Based on diagnostic performance data, the combination of troponin T-echocardiography was the most cost-effective technology for the diagnosis of both ACI and AMI in the general emergency department population. When the results of clinical impact studies were considered, the ACI Time-Insensitive Predictive Instrument was the most cost-effective technology for diagnosing ACI in the general emergency department population. The cost-effectiveness of the relative technologies did not change with increasing prevalence.
Authors' conclusions
No single technology is able to identify all ACI patients whilst avoiding hospitalisation of many patients without ACI. Research was characterised by heterogeneity and poor reporting. Some technologies remain underevaluated and little research has been conducted on sequential or combination testing. The clinical impact of testing has been inadequately addressed.

CRD commentary
This review addressed a clearly stated question. Broad inclusion criteria were defined in respect of the technologies and study populations assessed. No inclusion criteria relating to the reference standard were specified, and a number of different definitions of disease appear to have been used in the included studies. Although a large number of studies were included, the restriction of the search to studies published in English as full papers and the searching of only one bibliographic database might have resulted in incomplete retrieval of the available data. Full details of the included studies and evidence grading were given in the report, and appropriate measures were taken to avoid the introduction of biases during the review process.

Given the apparent differences in key study characteristics (e.g. reference standard) and the lack of a reported method for assessing between-study heterogeneity, the presentation of pooled accuracy estimates may be of limited value. The authors' conclusions are suitably cautious given the limitations outlined.

Implications of the review for practice and research
Practice: The authors made no specific recommendations for practice.

Research: The authors stated that most studies evaluate a technology's performance in diagnosing AMI; future studies should also evaluate performance in diagnosing UAP. Echocardiography, sestamibi imaging, serial biomarkers and newer biomarkers remain underevaluated. Research is needed to determine the performance of combinations of tests.

There is a need for studies evaluating the impact of testing on clinical outcomes. Improvements in the methodological quality and the reporting of future diagnostic accuracy studies are also required.

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http://www.ahrq.gov/clinic/epcsums/cardsum.htm

Other publications of related interest

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