# WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

**Worksheet author(s)**

<table>
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<tr>
<th>Assoc/Prof. Darren Walters</th>
<th>Date Submitted for review:</th>
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<tbody>
<tr>
<td>Peter Morley</td>
<td>15/2/2010; final version 26 April 2010</td>
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</table>

**Clinical question.**

In patients with suspected ACS in various settings (eg. prehospital, emergency or in-hospital) (P), do specific historical factors, physical examination findings and test results (I), compared with normal (C), increase the accuracy of diagnosis ACS and MI?

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** diagnosis

**State if this is a proposed new topic or revision of existing worksheet.** Update of the worksheet from 2005:WS221

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No conflicts to declare relevant to the worksheet.

**Search strategy (including electronic databases searched).**

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27 oxygen consumption/ (73354)
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32 11 and 31 (2935)
33 hypotension/ (12345)
34 sweating/ (3796)
35 exp chest pain/ (32777)
36 exp dyspnea/ (7683)
37 nausea/ (8593)
38 vomiting/ (12838)
39 exp pain/ (169292)
40 dizziness/ (1754)
41 unconsciousness/ (2412)
42 syncope/ (5852)
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49 likelihood functions/ (6242)
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52 area under curve/ (7959)
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55 or/47-54 (931025)
56 46 and 55 (611)
57 limit 56 to all adult <19 plus years> (396)
58 56 not 57 (215)
59 limit 58 to all child <0 to 18 years> (6)
60 58 not 59 (209)
61 57 or 60 (605)
Studies including in the 2005 COSTR reviewed: search updated as outlined: 1076 studies returned from updated search.

One additional study included:


### State inclusion and exclusion criteria

Includes only; Human Subjects, 19+ (adults)

Excludes case reports and reviews

### Number of articles/sources meeting criteria for further review:

35 studies included.
# Summary of evidence

## Evidence Supporting Clinical Question

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<thead>
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## Level of evidence

A = Return of spontaneous circulation  C = Survival to hospital discharge  
B = Survival of event  D = Intact neurological survival  
E = Other endpoint  
Italics = Animal studies
### Evidence Neutral to Clinical question

<table>
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| Good              | Lee 1995 E  
Goodacre 2002 E  
Goodacre 2003 E  
Henrikson 2003 E  

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*

### Evidence Opposing Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
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E = Other endpoint  
*Italics = Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

The following summary review was provided by Andrzej Okreglicki from 2005:

Detailed summary of final evidence:

The symptoms and signs occurring in Acute Coronary Syndrome (ACS) and Acute Myocardial Infarction (AMI), which, although on their own may have limited diagnostic value (sensitivity and specificity), especially when not used in association with ECG and enzyme studies or when these are unavailable or still awaited, can have the following major clinical impact in the pre-hospital and emergency department (ED) setting and subsequently:

- By helping to make an as accurate presumptive initial diagnosis as possible (i.e before the further investigations and ECG). The symptoms and signs are, thus, important in the initial period, both pre-hospital and in hospital, for triage of patients on the basis of the possibility or risk-stratification of the diagnosis of ACS and AMI: high risk, medium risk, low risk.
- It follows that this will therefore influence:
  - Whether and what further investigations are performed, which will subsequently affect:
  - Use or wastage of resources
  - Hospitalization rates.
  - Inappropriate discharge from ED
  - Cardiac Care Unit vs Chest Pain Unit admission rates
  - Delay before definitive treatment instituted: time to thrombolysis or percutaneous coronary intervention
- Furthermore, the symptoms and signs will also influence the lag time from their onset to when emergency care is requested (the time prior to pre-hospital and ED management). (Grossman 2003)

All of these will have an impact on the final outcome: i.e. the symptoms and signs, their presence or absence, their correct interpretation or inadvertent overlooking may all have a direct bearing on and relationship to the prognosis of the patient with ACS and AMI.

In assessing the diagnostic value of the symptoms and signs one must be aware that these are rarely used in isolation clinically and normally form part of a diagnostic protocol. (Goldman 1988) (Goldman 1982) (Lau 2001) The symptoms and signs of ACS and AMI will for the most part be identical although it does appear that they may be more severe with more associated autonomic symptoms in AMI. (Herlihy 1987) Many of the older studies examining the predictive value of AMI, defined AMI according to old WHO diagnostic criteria. New cardiac markers for AMI and ACS are more sensitive and thus, in turn, affect the statistical assessment of the sensitivity and specificity of the signs and symptoms. In patients in whom the diagnosis of ACS is made, the distinction between signs and symptoms specific to myocardial infarction versus non-myocardial infarction in order to determine further management is not really relevant. Ideally, the diagnostic value of the signs and symptoms should be determined in ‘all-comers’ with any type of presentation of ACS and AMI (not even limited to patients with chest pain as this will exclude as significant proportion of patients who have absence of chest pain with ACS and AMI). (Lau 2001) Many of the studies assess the diagnostic value of various symptoms and signs in patients who have already been triaged, (Albarran 2002) (Boersma 2000) (Everts 1996) (Herlihy 1987) (Lee 1995) (Meischke 1998) and often in patients with undifferentiated chest pain. (Goodacre 2002) (Goodacre 2003) This group of patients would comprise those in whom ECG had excluded ACS or in whom the diagnosis of ACS is not clear. Limiting statistical analysis to these patients obviously affects the sensitivity and specificity of the symptoms and signs negatively.

Likelihood ratios are preferentially used in the statistical analysis of the value of signs and symptoms particularly by review articles. Some use and only report the results of variables in which the likelihood ratio is > or = 2.0, or , < or < 0.5. (Panju 1998)

Chest pain and its nature

Chest pain is the most frequent symptom in ACS and AMI. It is, however, very important it be aware that ACS occurs in patients who experience no chest pain at all and only what is regarded as atypical symptoms (Canto 2000) and may also be more rarely completely silent with regard to symptoms. Up to 33% of patients with AMI may not have pain on presentation to hospital. (Canto 2000) This may be higher in women; up to 43%. (McSweeney 2003) Clearly, this would predictably, by extrapolation, have a great clinical impact on admission to chest pain assessment units and also patient prognosis.

In those who do experience pain, studies have shown that particular characteristics have a higher predictive and diagnostic value in making the correct diagnosis of ACS and AMI. As pain alone is not specific enough, the various features of pain have been used to assist but with progressive diminution of sensitivity. The most specific pain would be chest pain that radiates to both arms, that
is crushing/pressing, associated with effort and not influenced by breathing (not pleuritic) and not reproduced by palpation or pressure on the chest wall. (Goodacre 2002) (Goodacre 2003) (Lee 1985) (Panju 1998) Unfortunately, it is shown that reliance on these clinical characteristics will result in missing the diagnosis in patients who may have less typical features. (Lee 1985) In the setting of emergency care management, pain needs to be interpreted according to the safety of making the diagnosis. Thus, in ED, the less frequently experienced indigestion symptoms and burning should be used to predict ACS rather than making a diagnosis of acute gastro-esophageal pain. (Goodacre 2002) (Goodacre 2003)

Pleuritic, sharp, stabbing, positional, pressure-reproducible pain decreases the probability of ACS (Panju 1998) but does not eliminate the possibility. As chest wall tenderness may predict a reduced likelihood of ACS, when combined with a low probability of AMI, some reviewers consider that this sign could effectively rule out the diagnosis of ACS. (Goodacre 2002) The absence of tenderness has little predictive value.

Duration of chest pain (<5min) is less usual in patients with ACS compared to those who are subsequently shown to have normal coronary arteries. (Cooke 1997)

Radiation of pain:
There is significantly more radiation of pain to the left and right shoulders or arms with patients with AMI compared to patients with out AMI. (Albarron 2002) (Kogan 2003)

Other sites of pain: jaw, neck
Radiation to the jaw was not found to be predictive of ACS. (Goodacre 2003)

Relief of pain with nitrates:
Relief of pain with nitrates has no predictive value with regard to the diagnosis of ACS. (Cooke 1997) (Day 1976) (Henrikson 2003)

Nausea, Vomiting
There is no agreement in the studies with regard to this symptom. Some state that vomiting increases the likelihood of the presentation of chest pain being due to ACS. (Panju 1998) (Goodacre 2003) In a study of 265 patients, nausea and vomiting had a sensitivity of 53% for detecting AMI and a specificity of 72%. (Herlihy 1987) Others report that it is not predictive. (Goodacre 2002). Nausea and vomiting is twice as common in women as compared to men. (DeVon 2002) (Goldberg 2000)

Sweating
This increases the likelihood of the presentation of chest pain being due to ACS. (Panju 1998) Others dispute this. (Goodacre 2002) Its presence alone, without chest pain, requires a high index of suspicion of ACS in elderly patients. (Milner 2001)

Respiratory symptoms and signs:
Breathlessness was shown to be not useful as it was present more frequently in patients without coronary artery disease than in patients with. (Cooke 1997) The signs of chest crackles and pulmonary edema are shown to be related to myocardial ischemia and if used alone or in combination with other signs (as part of the Killip classification) have a statistically significant clinical impact on the prognosis. (Antman 2000) (Boersma 2000) (Khot 2003)

Auscultatory cardiac signs:
Signs on clinical examination such as the presence of the third heart sound are not sensitive in diagnosing AMI but are reasonably specific for AMI as opposed to non-infarct presentations of ACS. (Panju 1998) (Antman 2000) There is also a problem with observer variability in detecting such difficult signs. (Panju 1998) Other cardiac signs, such as elevated heart rate and hypotension have significant clinical impact as they affect outcome and prognosis. (Eagle 2004)

Combination of clinical signs:
The signs that make up the Killip classification are valuable in combination as they are predictive of prognosis. The view that the observation of these signs has significant clinical outcome is supported by some studies (Khot 2003) (Kogan 2003) (Lopez de Sa 2002) and not by others. (Eagle 2004)

Clinical symptoms and signs in combination with ECG changes, as in the Goldman Computer Protocol, have significantly improved diagnostic power. (Goldman 1988) (Goldman 1982) (Lau 2001) However, this protocol, and by extrapolation, the signs and symptoms forming a component of this protocol, have not been shown to have significant clinical outcome, by not affecting the management of suspected ACS patients in the routine clinical setting. (Lee 1995)

Atypical presentations:
Awareness is needed that silent myocardial infarcts, AMI with absence of chest pain and with other atypical presentations of ischemia occur in diabetics, women, elderly and other high risk patients. (Cooke 1997) (Canto 2000) (McSweeney 2003) Atypical
symptoms include headache, tinnitus, vertigo, hiccups and belching. (Culic 2001) The clinical impact of the atypical symptoms is the tendency to longer lag times before treatment is sought. (Grossman 2003)

Gender differences:
Numerous studies of patients with ACS and AMI have shown differences between men and women to varying degrees with regard to the prevalence of symptoms, characteristics of pain, pain radiation and even signs. (Albarran 2002) (Kudenchuk 1996) (McSweeney 2003) (Meischke 1998) This affects the sensitivity and specificity of these clinical findings. It is well recognized that the prognosis in women with ACS and AMI is worse than in men. This may be influenced by the presence of ‘atypical’ symptoms of ACS resulting in misinterpretation by the patient herself and delayed lag time before calling for emergency care, later presentation, further delays in hospital and before starting definitive treatment. (Canto 2000) Women are more likely to have pain radiating to the back and neck. (Everts 1996) (Goldberg 2000) Awareness of the non-traditional presentations of women is needed to avoid delays.

Age:
Typical symptoms are less predictive of ACS in patients over the age of 70 years. There are no statistically significant symptoms predicting ACS in these elderly patients. (Milner 2001) Atypical symptoms e.g. fatigue also do not predict the diagnosis. Differences in localization of pain have been observed in older patients, thus again affecting sensitivity of the known typical presentation. (Everts 1996)

[Precision:
Precision refers to intra- and interobserver variability. This may play an important role in taking a history of pain, particularly in the emergency setting. Interpretation is open to subjective influences. Furthermore, subtle signs that may be of value may be missed or not appreciated in the stress of the emergency setting. This has been shown for the symptoms and signs in ACS such as for the more detailed attributes of pain and for clinical signs such as third heart sound. (k range: 0.14-0.37) (Panju 1998)]

Summary
Although, the likelihood of ACS and AMI is increased by the presence of any of the following clinical findings: patients presenting with chest pain that radiates to the left arm, radiates to the right shoulder or radiates to both arms, patients presenting with chest pain and sweating, S3 or hypotension. (Panju 1998), the various studies suggest that clinical characteristics (symptoms and signs) are an unreliable means for selecting patients for further investigations, admission, discharge or definitive therapy. (Goodacre 2003) A high index of suspicion together with a low threshold for diagnostic testing are required. No single clinical variable has sufficient sensitivity and specificity that can be used to rule in or rule out the diagnosis of myocardial ischemia / infarction. (Lee 1987) (Goodacre 2002). Awareness of presentations with absence of chest pain and also non-traditional presentations, more frequent in women and elderly, is needed. (Canto 2000) This awareness should not be only amongst emergency care givers but should also involve public awareness and teaching.

Additional Update since 2005:
The search since 2005 included the study by Thuresson 2005. This demonstrated that a relatively low proportion of patients with ACS actually present with the type of symptoms that are commonly associated with ACS. ST elevation was distinguished by more frequently having associated symptoms more often than patients without STEMI. They had higher pain/discomfort intensity and more frequently had pain with abrupt onset reaching maximum intensity within minutes. Even n this patients group symptom onset was only seen in less than half the patients with only 1 in 5 fulfilling all the criteria usually associated with a severe heart attack. Women had more pain/discomfort in the neck or jaw and back, vomiting, and scored their pain/discomfort slightly higher than men. Differences between age groups were minor and there was no difference between patients with and without diabetes.

Acknowledgements: COSTR worksheets 221A, 221B
Andrzej Okreglicki
David Andrew Lendrum, Laurie Morrison.
Citation List


Prospective cohort study of CCU admissions with chest pain.

Comparison of pain and radiation between MI and non-MI patients.
More radiation to L & R shoulder/arm significantly higher in MI group.
Statistical differences between men and women: women more in back and radiation to front of neck.

Limitations:
All CCU admissions with pain.
Compared AMI and not ACS.
No predictive statistics: indirect sensitivity.

LOE: D2 (CEBM 1b symptom prevalence study)
QOE: Good
Evidence: Sensitivity: pain radiation; differences gender.


Guidelines based on review of articles on ACS.

Risks of adverse events related to various symptoms and signs
Duration of ischemic pain >20min
Pulmonary edema related to ischemia
Angina with S3
Angina with hypotension.

LOE: D5 (CEBM 2b Prognosis study)
QOE: Good
Evidence: Clinical impact (by extrapolation): pain duration; signs: pulmonary edema, S3, hypotension


Retrospective analysis for predictors of outcome in patients with ACS (9461pts)

Chest crackles incidence very low (0.3-8%)
Chest crackles < 1/3 chest in 1% but presence gave up to a 5.85 OR (3.32-10.3) for 30d death.
Various admission Systolic BP and Heart rates related to outcome. Strong predictor of outcome.

Limitations:
All patients had ACS (PURSUIT study). Not all-comers. Only included ACS with non-ST elevation.

LOE: D2 (CEBM 2b Prognosis study)
QOE: Good
Evidence: Clinical impact: chest crackles, heart rate, systolic BP.


Prospective observational study of registry of 435000 patients with confirmed AMI at assess prevalence of presentation without chest pain.

33 % of patients did not have pain on presentation to hospital.
More common in elderly, women, diabetics, prior heart failure.
Longer lagtime to hospital presentation.
Less likely to get appropriate treatment for AMI.
Higher in-hospital mortality compared to patients with chest pain (OR for mortality 2.21 (2.17-2.26))

Limitation:
Only AMI pts

LOE: D2 (CEBM 1b Symptom prevalence study)
QOE: Good
Evidence: Clinical Impact: Chest pain-silent AMI prognosis, Lag time, Treatment institution. (Sensitivity by extrapolation: Chest Pain)


Matched case-control study- 65pts with coronary artery disease and chest pain and 65 without CAD. Compared chest pain characteristics by presence of normal or abnormal coronary angiography.

No important differences in chest pain: site, quality, radiation of pain.
Relief by nitrates: no difference between 2 groups overall; within 5 minutes OR=4.1
Shortness of breath: more in patients without coronary artery disease.
If no typical features and age < 55yrs : 2% chance of abnormal angiogram
If no typical features and age >55yrs: 12% chance.

3 symptoms had discriminatory value:
Pain consistently reproduced with exercise
Duration of pain (>5min, <30min)
Frequency of pain at rest.
If all 3 present: probability of CAD = 69% in <55 yrs group; =93% in >55yrs group.

Limitations:
Not ACS / AMI patients i.e. not in acute setting
Retrospective study of symptoms
Small number of pts.

LOE: D3 (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: chest pain; shortness of breath, age differences


Study of frequency of occurrence of presenting symptoms in patients with subsequently proven AMI.
Some link between infarction sites and specific groups of symptoms.
Many patients had non-specific / atypical symptoms of AMI: headache, tinnitus, vertigo, hiccups, belching.

Limitations:
All pts AMI.
Relative differences only between different groups of infarct sites.
No predictive statistics.

LOE: D5 (Extrapolation) (CEBM 2b Symptom prevalence study)
QOE: Good.
Evidence: Extrapolated Sensitivity: atypical symptoms in AMI.

Prospective small study of patients with normal coronaries

45 pts

60% had pain radiating to L arm/shoulder
22% had pain radiating to neck/jaw
18% had relief from nitrates <5 min

Shows (by extrapolation) that these signs have poor specificity.

Limitation: only included patients with normal coronary arteries
Small number.

LOE: D2 (By extrapolation 3) (CEBM 3b Symptom prevalence study)
QOE: Good
Evidence: Specificity (by extrapolation): site of pain, pain relief from nitrate; pain radiation neck/jaw.


Systematic review of 12 studies reviewing gender differences in symptoms of acute coronary syndromes.

ACS and AMI.

In some studies there were gender differences but much variability among studies.
Important to note that even though e.g nausea and vomiting 2 times more common in women, only 1/3 had this symptom.

Limitation:
No predictive statistics (no direct sensitivity or specificity).

LOE: D5 Review (by extrapolation) (CEBM 2a Symptom prevalence study)
QOE: Excellent.
Evidence: Sensitivity (by extrapolation): symptoms, atypical symptoms, gender.


Analysis of data from the multinational Grace registry of outcome of factors predicting mortality in ACS post discharge. Of 9 variables, 2 signs: increased heart rate and lower systolic BP at presentation were predictive of 6 month mortality.
Developmental and validation cohorts with 6 month F/U 15007 pts
Heart rate mean 79 +/- 20
Systolic BP: 143 +/- 29
Findings: HR increase >30: Hazard ratio 1.3 (1.2-1.5)
BP decrease >20 mmHg: 1.1 (1.06-1.17)
Killip class not one of variables by multivariate analysis.

Limitation: Postdischarge patients
Not ER or preED patients.

LOE: D1 (CEBM 1a Prognosis Study)
QOE: Good
Evidence: Clinical impact: Outcome: Supportive for Pulse, BP. Neutral for Killip class


Prospective study of localization of pain in patients admitted to CCU with suspected AMI. Pain in both right and left arms was more frequent in pts with AMI. Women with AMI, reported pain in the neck (p < 0.05) and in the back (p < 0.01) more frequently than did men.
Both patients with AMI and without had similar localization and therefore localization of chest pain of no predictive value.
Differences between men and women. Differences between younger and older.

Limitation: CCU patients.

LOE: D2 (CEBM 1b Symptom prevalence study)
QOE: Good


Retrospective analysis of symptoms in patients with AMI and ACS and comparison between genders, ages.

Study of prevalence of symptoms and signs showed no single sign or symptom present in > 51% of patients. Common atypical symptoms: dyspnea (49%), arm pain (46%), sweating (35%), and nausea (33%)

Nausea and radiation to back, neck and jaw more in women.

LOE: D2 (extrapolation) (CEBM 2b Symptom prevalence study)
QOE: Good
Evidence: Sensitivity (by extrapolation): atypical symptoms; pain radiation gender differences,


Prospective validation of computer protocol which included signs and symptoms but also ECG.

Limitation:
Protocol used and not individual signs and symptoms. ECG assessment part of protocol.
AMI prediction only.

LOE: D1 (CEBM 1b Diagnosis study)
QOE: Good
Evidence: Clinical impact (by extrapolation): signs and symptoms important component of diagnosis protocol.


Prospective evaluation and validation of a computer derived protocol including combination of clinical symptoms and signs and also ECG findings.

Assessment of specificity and sensitivity of protocols: sensitivity 91%; specificity 70%.

Protocol used:
pain radiation
local pressure causing pain
association with sweating.

Limitation:
Protocol used and not individual signs and symptoms. ECG assessment part of protocol.

LOE: D1 (CEBM 1b Diagnosis study)
QOE: Good
Evidence: Clinical impact (by extrapolation): signs and symptoms important component of diagnosis protocol.


Prospective observational cohort study in adults (893pts) assessing the diagnostic usefulness of clinical features in patients with chest pain and non-diagnostic ECGs.
Characteristics of pain (exertional, radiation to left shoulder or both arms, chest wall tenderness) were assessed and found to be statistically significant predictive value for AMI and ACS. Nausea/ vomiting/ sweating / response to nitrates/ type of pain/ radiation to sites other than shoulder and both arms were not predictive. The symptoms of pain radiating to the shoulder or both arms are predictive but have insufficient sensitivity and specificity to rule out or rule in diagnosis on own. Chest wall tenderness predicts a reduced likelihood of AMI and combined with a situation with low probability of AMI, this sign could effectively rule out the diagnosis. Absence of tenderness had little predictive value.

Limitation:
Only clinically stable patients with acute chest pain and no diagnostic ECG changes.
Only patients presenting to chest pain unit
Young patients (mean=52.6yrs)

LOE: D2 (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: support chest pain for diagnosis of ACS; not supportive for nausea, sweating, relief with nitrates


From a prospective study / RCT assessing standard routine care vs chest pain unit care, the presenting characteristics of 972 patients with ACS but with non-specific ECG were analyzed.

Independent predictors of ACS
- indigestion or burning type pain
- pain radiating to left or right arm
- vomiting

Not predictive were dyspnea, hypertension, pain radiating to neck, jaw, back.

Clinical characteristics are unreliable for selecting further diagnostic investigations.

Limitations:
Excluded all patients with ECG evidence of ACS, clear diagnosis of ACS
Young patients (mean=49.5yrs)
Not all patients presenting to the ED consented to be in study

LOE: D2 (by extrapolation) (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: Chest pain; Vomiting (supportive); Dyspnoea (not-supportive); Pain radiation to jaw (Not-supportive)


Prospective observational study of 374pts admitted to ED with suspected ACS and lagtimes before admission.. 73% had chest pain. 27% had atypical symptoms (abdominal pain/ back pain, shortness of breath, sweating, nausea, palpitations, syncope) Tendency to longer lag times if atypical symptoms or if older.

Limitations: Limited to ACS suspected pts; not all-comers
Indirect sensitivity/ specificity.

LOE: D2 (CEBM 1b Differential diagnosis/symptom prevalence study)
QOE: Good
Evidence: Clinical impact: atypical symptoms and longer lag time; Sensitivity; Specificity

Prospective study of patients with acute chest pain (459 consecutive pts)

Nitroglycerine relieved pain in:
- 35% of those with active CAD
- 41% of those without active CAD
Therefore, relief of pain after nitroglycerine treatment does not predict active CAD and should not be used to help / guide diagnosis.

Sensitivity and specificity

LOE: D2 (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: Pain relief from nitrates: non-supportive.


Prospective observational study relating nausea and vomiting to AMI.

All patients admitted to CCU.
Nausea and vomiting strongly predictive of AMI (P<0.0001)
Odds of having MI was 3.14 times with nausea and vomiting than without.
Sensitivity for detecting MI = 53%; Specificity = 72%

Limitations:
Sensitivity and specificity only for AMI from among ACS pts and not all-comers
Patients admitted to CCU not ED

LOE: D1 (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: nausea, vomiting.


Retrospective analysis from existing data in patients with NSTEMI trials looking at the prognostic value of signs of heart failure.

Signs incorporated in the Killip classification (evidence of heart failure: chest crackles, pulmonary edema and hypotension <90mmHg) are highly predictive of prognosis in patients who are diagnosed as having MI.

Limitation: All patients had MI
Signs not discriminatory for diagnostic purposes.

LOE: D1 validation of Killip classification (CEBM 2b Prognosis Study)
QOE: Good
Evidence: Clinical Impact: Signs (Killip Class) supportive.


Prospective study of the diagnostic features (clinical, ECG and enzymes) in patients with chest pain admitted or discharged from ED.
Although an epidemiological difference between those discharged and those admitted (more dyspnoea, sweating, weakness), the clinical factors were not discriminatory enough for diagnosis.
Pain attributes (on effort, radiation) affected admission decision.

Limitation: Small study
Sensitivity and specificity not for individual signs / symptoms but for combination of clinical, ECG and enzymes.
LOE: D1 validation of clinical, ECG and enzymes (CEBM 2b Diagnosis study)

QOE: Good


Retrospective cohort study comparing presentation, treatment and outcome by gender.
In AMI.

No difference in prevalence of symptoms or signs.
Chest pain in 99% (1086pts), dyspnoea 51%, sweating 72%, nausea 55%, epigastric discomfort 10%, clinical shock 1.5%

Limitations: Symptoms and signs not analysed for diagnosis or outcome. (Not used as a diagnostic test.)
AMI pts only.

Indirect sensitivity assessment

Level of Evidence: D2 (CEBM 2b Diagnosis study)
Quality of Evidence: Good


Systematic review and meta-analysis of diagnostic technologies for sensitivity, specificity and outcome.
In ACS.
Of all eligible ED patients.
Prevalence of AMI related to chest pain: 7-50%.
Goldman Chest pain protocol has 89-91% sensitivity for AMI, specificity 70-74%, diagnostic odds ratio 20-23. Only outcome tested was hospitalization - made no difference. Quality of evidence: A.

Level of Evidence: D1 (CEBM 1a Diagnosis study)
QOE: Good


Prospective study of 596 patients seen in ED with chest pain assessing the clinical variables.

Pain quality was predictive of AMI but no particularly sensitive or specific.
Pain reproduced by chest wall tenderness, combined with pleuritic / positional components was rare in AMI (5%) and UAP (3%) but did not exclude the diagnosis.
Pain quality 'sharp / stabbing' was most predictive of a diagnosis: 5% in MI group, 17% in UAP group and 78% in 'other' group.

Limitation: Old study.

LOE: D2 (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Sensitivity and specificity: chest pain quality (supportive)


Prospective study of the impact on care of patients with chest pain by physicians when they were provided information from the Goldman computer-based chest pain protocol.

No impact on care and no change in resource utilization was noted when the information was provided.
Limitation: Testing of protocol which together with signs, symptoms also evaluated ECG.
Only in AMI

LOE: D1 validation of Goldman computer-based chest pain protocol  by extrapolation (CEBM 2b Diagnosis study)
QOE: Good
Evidence: Clinical impact (by extrapolation): protocol with signs, symptoms and ECG (not-supportive)


Review of 35 patients sent home from ER with AMI and compared to 105 patients admitted.
Pressure pain in 40% of patients with AMI but misdiagnosed.
Radiation to left arm and jaw in 43%.
Sweating in 26%.

Data indicate that no single clinical variable can be used to exclude AMI.

Limitation
Small study

LOE: D3 Diagnostic case control study  (CEBM 2b Symptom Prevalence Study)
QOE: Good
Evidence: Sensitivity: Signs and symptoms (non-supportive)


Prospective study of patients with NSTEMI on admission assessing clinical and ECG variables for their prognostic value/prediction. (4115pts)

Only clinical sign by multivariate analysis was Killip Class > or = 2.
Outcome of Killip 1 = 3.1% 90d mortality
Outcome of Killip 2 or higher= 12.3% 90d mortality (p<0.0001)
RR of Killip 2 or more = 1.68 (1.4-2.01)

Limitation: NSTEMI i.e excluded ST seg elevation
Not all-comers: limited to patients with pain considered to be ischemic

LOE: D2 Derivation of a clinical decision rule  (CEBM 1b Prognosis Study)
QOE: Good
Evidence: Clinical Impact: Killip Class supportive


Study of women who were previously admitted with AMI to evaluate prodromal symptoms and AMI symptoms.

Acute chest pain absent in 43%.
Most frequent acute symptoms: SOB 57.9%, weakness 54.0%, fatigue 42.9%.
Main locations of chest pain: back 37%; high chest 21.7%

Limitations: Women only
AMI only
No 'predictive statistics'.

LOE: D2 CDR derived from a population  (CEBM 1b Symptom prevalence study)
QOE: Good
Evidence: Sensitivity and specificity: prevalence of chest pain: neutral; atypical symptoms: supportive


Retrospective observational study (4497pts)

Note the gender differences that occur in AMI symptoms.
Women: more nausea and SOB; less sweating.

Limitations:
Only AMI.

LOE: D2 CDR derived from a population (by extrapolation) (CEBM 2b Symptom Prevalence Study)
QOE: Good
Evidence: Sensitivity(by extrapolation): symptoms in AMI; gender differences.


Retrospective analysis of symptoms predictive of ACS, relating to their predictive value according to age <70 or >70yrs.

(531pts)

(ACS)

No symptoms significantly associated with ACS in older patients, whereas, in younger patients, presence of chest symptoms were significantly associated with ACS.
Atypical symptom: fatigue, was a significant positive predictor of ACS. (OR 2.52 CI: 1.10-5.81)

Limitation: Small no of >70yrs olds.

LOE: D2 CDR derived from a population (CEBM 2b Diagnosis study)
QOE: Good


Likelihood ratios: results presented only if LR > or =2.0, or < or =0.5

Amongst the most powerful features that increase the probability of MI are:
chest pain radiating to both arms simultaneously (LR=7.1)
presence of S3 (LR=3.2)
hypotension (LR=3.1)

Sensitivity of these signs is poor, their specificity for AMI is high.

Pleuritic, sharp, stabbing, positional and pressure-reproducible pain decrease the probability of MI

Also assessed precision (intra- and inter-observer variability). This depended on the observers (internist vs nurse) and also the specific attributes: the finding of pain radiating to left arm was obtained with less variability than 'sharp pain'.

With regard to physical signs and precision/observer variability: dyspnea agreement amongst observers was best (k=0.62-0.75); S3 and chest crackles were poor (k=0.12-0.31)

LOE: D1 Validation of a CDR (CEBM 1a Diagnosis Study)
QOE: Good
Evidence: Sensitivity, specificity: Chest pain, radiation, sweating, S3, hypotension; also precision of observation.

LOE: D2 CDR derived from a population
Fair
Evidence reinforces that symptoms and signs are unreliable (i.e., neither sensitive nor specific) diagnostic features of ACS.