Evidence Based Medicine

The 2017 International Joint Working Group recommendations of the Indian College of Cardiology, the Academic College of Emergency Experts, and INDUSEM on the management of low-risk chest pain in emergency departments across India

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ABSTRACT

There have been no published recommendations for the management of low-risk chest pain in emergency departments (EDs) across India. This is despite the fact that chest pain continues to be one of the most common presenting complaints in EDs. Risk stratification of patients utilizing an accelerated

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diagnostic protocol has been shown to decrease hospitalizations by approximately 40% with a low 30-day risk of major adverse cardiac events. The experts group of academic leaders from the Indian College of Cardiology and Academic College of Emergency Experts in India partnered with academic experts in emergency medicine and cardiology from leading institutions in the UK and USA collaborated to study the scientific evidence and make recommendations to guide emergency physicians working in EDs across India.

Key Words: Acute coronary syndrome, major adverse cardiac events, protocol

INTRODUCTION TO THE CONSENSUS STATEMENT

This consensus statement aims to assist in the identification and disposition of low-risk chest pain in adults. Our purpose is to enable emergency physicians to systematically and safely evaluate and discharge patients with low-risk chest pain from the emergency department (ED) with a risk of major adverse cardiac events (MACE) of <1%.

Evidence
We reviewed the literature regarding low-risk chest pain utilizing PubMed. To the best of our knowledge, there are no published studies from India addressing management of low-risk chest pain in the ED.

Disclaimer
The consensus panel consisted of emergency physicians and cardiologists from the US, UK, and India. The consensus statement represents the views of consensus panel members who developed this document after careful consideration of the available literature and medical evidence. This document proposes the use of an accelerated diagnostic protocol (ADP) for low-risk chest pain, with the understanding that data supporting any of the ADPs are lacking, and therefore not covered by any American or European guideline. When evaluating patients presenting with low-risk chest pain, physicians should consider this consensus statement, along with an individual patient's preferences, requirements, and values. The application of these recommendations is not binding, and it does not override the physician's responsibility to make decisions appropriate to the circumstances of a particular patient.

Scope of consensus statement
This consensus statement is intended for physicians working in the ED.

Inclusion criteria
The consensus statement applies to adult patients aged 18 years and older presenting to the ED with recent onset chest pain suggestive of acute coronary syndrome (ACS).

Exclusion criteria
The consensus statement is not intended to be used for pediatric patients.

DEFINITIONS

Characteristics of anginal chest pain
Several papers have attempted to delineate which factors are more suggestive of ACS.[1,2] A careful history and physical examination should be taken to determine the likelihood that a patient's presentation is suggestive of ACS. Anginal pain is described as episodic, lasting from 2 to 10 min.[1] A well-conducted review published in the Journal of the American Medical Association[2] found the following patient descriptions of pain to significantly increase the likelihood that a patient's chest pain was truly anginal in nature: Radiation to both arms; symptoms mimicking prior angina; provocation by exertion; and a change in pain pattern over 24 h. It is also important for the clinician to recognize that symptoms other than chest pain, which appear to be related to exertion, such as dyspnea, nausea, and vomiting, should raise concern for an anginal equivalent. Response to nitroglycerin, either positive or negative, was not found to be helpful. Factors that can lower clinical suspicion include a pleuritic nature to the pain as well as pain reproduced by palpation.

Definition of low-risk chest pain
Amsterdam *et al.* define patients at low risk for ACS as "those with no hemodynamic derangements or arrhythmias, a normal or near normal electrocardiogram (ECG), negative initial cardiac injury markers, and low likelihood of signs and symptoms suggestive of ACS."[1]

Definition of major adverse cardiac events
MACE is defined as development of any of the followings within a 30-day period:[3,4] non-ST-elevation myocardial infarction (STEMI), STEMI, emergency revascularization, cardiovascular death, cardiac arrest, cardiogenic shock, or high-grade atrioventricular block.

BACKGROUND

Chest pain is one of the most common chief complaints in patients presenting to the ED. Despite this fact, only a minority of these patients are ultimately found to have either an STEMI or ACS.[5] Given that Asian Indians have a mean onset of coronary artery disease (CAD) 5–10 years earlier than the western world, the burden of chest pain visits to EDs in India is likely much higher.[6] Approximately 10% of patients presenting to the ED with chest pain are ultimately

diagnosed with ACS.[7] Amsterdam *et al.* state that of patients that present to ED with chest pain, those with <5% probability of myocardial infarction (MI) can be identified simply from history and ECG.[1] Although there are no firm guidelines for what constitutes an acceptable threshold, Kline *et al.* calculated that a <2% missed ACS is acceptable in practice. They found that at this threshold, the risk of further testing outweighs the benefit of confirming ACS.[8]

An ideal risk stratification tool should be sensitive enough to delineate patients with ACS or other emergent conditions from those who can be safely discharged from the ED after an abbreviated evaluation. Basic clinical scoring systems such as thrombolysis in myocardial infarction (TIMI), HEART, and Emergency Department Assessment of Chest Pain Score (EDACS) have been developed to estimate cardiac risk. The use of ADPs, which incorporates a clinical risk score, has shown to decrease this risk even further.

Ultimately, a decision for early and safe discharge from the ED can be made in approximately 40% of all patients presenting with chest pain.[3,4] Patients who present with signs and symptoms suggestive of other emergent conditions, including but not limited to aortic dissection and pulmonary embolism, are not candidates for an ADP. Patients with dynamic ECG changes are similarly not candidates for an ADP. Using an ADP can significantly increase the proportion of patients with cardiac chest pain to be identified as low risk and can be safely discharged from ED within 2–6 h of presentation with a 30-day MACE rate of <1%.[3,4]

INITIAL EVALUATION

- The consensus panel recommends that a 12-lead ECG should be completed immediately on arrival to the ED. The patient should be placed on a monitor, intravenous (IV) access established, and blood for cardiac troponin levels should be sent to the laboratory for quantitative measurement in all patients with chest pain suggestive of ACS within 10 min of presenting to the ED[9,10]
- If the initial ECG is not diagnostic for STEMI and there is a high index of clinical suspicion of ACS, ECGs should be done serially and repeated if pain recurs[8]
- The consensus panel recommends that ECGs should be interpreted by qualified emergency physicians in the ED. ECGs should not routinely be taken to a cardiologist for interpretation nor should a cardiologist be asked to consult on every patient who presents to the ED with chest pain. Exceptions for emergent cardiology consultation include ECGs with borderline findings suggestive of a possible acute STEMI
- The triage nurse should mark the patient's chart or record for emergent evaluation through the appropriate ED patient flow processes and the patient's laboratory and radiographic studies should be expedited.

INITIAL MANAGEMENT OF PATIENTS WITH SUSPECTED ACUTE CORONARY SYNDROME

Antiplatelet therapy
Once ACS is suspected, 325 mg of chewable aspirin should be administered to the patient (unless allergic to aspirin).[11]

Pain control
Initial pain control should be attempted with sublingual or buccal nitrates. If this is not possible, an IV opioid should be used.[11,12] Contradictions to nitrate use include hypotension, use of phosphodiesterase inhibitors, signs of possible inferior/right ventricular ischemia, or aortic stenosis.

Oxygen use
The consensus panel recommends not administering oxygen to every patient presenting with chest pain suggestive of ACS. Rather, the decision to administer supplemental oxygen should be based on oxygen saturation using pulse oximetry obtained as soon as possible after presentation.[13]

Chest radiograph (chest X-ray) and point-of-care ultrasound
Although most patients with uncomplicated ACS will have a normal chest X-ray (CXR), a portable CXR and point-of-care ultrasound (where available) should be used to diagnose lung and heart pathologies mimicking ACS.[1]

DIFFERENTIAL DIAGNOSIS

The emergency physician should be cognizant of the fact that many other diagnoses, ranging from benign to life threatening, can present with chest pain and should be considered in the initial evaluation.

Table 1 shows the differential diagnosis for recent onset chest pain other than ACS.

Red flag signs
For all patients presenting to the ED with the chief complaint of chest pain, "red flag signs" must be kept in mind. Efforts should be made to rule them out, during the initial evaluation; by the time, the troponin levels are received from laboratory. The presence of any one of these red flag signs warrants an early admission and exclusion from low-risk pathway:
- STEMI on ECG
- Ischemic changes on ECG, new bundle branch blocks, or cardiac arrhythmias not demonstrated to be previous findings on the previous ECGs
- Ongoing chest pain
- Crescendo angina
- Aortic dissection
- Pulmonary embolism
- Acute abdominal pathology
- Other comorbidity as an indication for admission.

CARDIAC ENZYMES

- The consensus panel recommends using cardiac troponins in all patients with chest pain suggestive of ACS. The consensus panel does not recommend biochemical markers such as brain natriuretic peptides (BNPs), C-reactive protein (CRP), creatine phosphokinase-MB (CK-MB), or myoglobin to diagnose ACS in patients with chest pain suggestive of ACS
  - Troponin testing: Many different troponin assays are available. It is imperative that the ED physician is aware of the assay available at their institution and the limitations of various assays
  - Quantitative versus qualitative testing: The consensus panel recommends the use of quantitative troponin in the assessment of the low-risk patients suspected of ACS
  - Qualitative troponin tests: Qualitative troponin tests are used widely in India to diagnose acute myocardial infarction. The most commonly used test is troponin T card test that gives positive result at ≥100 ng/L, much higher than the recommended level to detect MI. The 3rd universal definition of MI has lowered the level for diagnosis of MI to 99th percentile of upper reference limits. For high-sensitive Troponin T, 99th percentile is 14 ng/L and for troponin I, it ranges from 20 to 70 ng/L depending on the manufacturer[14]
  - Qualitative troponin tests can be used when quantitative tests are not available to diagnose the presence of acute MI. It is important to emphasize, however, that a negative result does not rule out ACS
  - Repeat troponin: Given that the lower limit of detection for conventional troponins is not sensitive to detect MI at initial presentation, we recommend that troponins be repeated at 3 h of initial troponins
  - 3-h troponin: A negative troponin at 3 h has been shown to have high negative predictive value for ACS. A repeat troponin is not necessary in low-risk patients who present after 6 h of onset of chest pain
  - High-sensitive troponins: High-sensitive troponins have detection limit of 5–10 ng/L. These assays, when available, are more sensitive for the detection of MI.[15,16]

EVIDENCE-BASED ACCELERATED DIAGNOSTIC PATHWAYS FOR LOW-RISK CHEST PAIN

The panel evaluated the HEART protocol and the EDACS ADP and the ADAPT protocol (using TIMI scores) [Tables 2-4], which have both been studied extensively in an ED population outside of India and have been found to decrease MACE rates to <1%.[3,4,17]

It is important to note that none of these ADPs have been validated in India. Therefore, at this time, there is not enough evidence to strongly support one ADP over another. Importantly, because heart disease occurs in Indians 5–10 years earlier than

Table 1: Differential diagnosis of recent onset chest pain other than acute coronary syndrome

Cardiac
  Aortic dissection
  Pericarditis
  Pericardial effusion
Gastrointestinal
  Heartburn/GERD
  Dysphagia
  Pancreatitis
Musculoskeletal
  Costochondritis
  Chronic pain syndromes
  Rib fracture
Pulmonary
  Pulmonary embolism
  Pleurisy
  Pulmonary hypertension
Other causes
  Psychogenic
  Herpes Zoster, sympathomimetic drug induced

GERD: Gastroesophageal Reflux Disease

Table 2: Emergency department assessment of chest pain score

Clinical characteristics	Score
A) Age (please circle single best answer)	
18-45	+2
46-50	+4
51-55	+6
56-60	+8
61-65	+10
66-70	+12
71-75	+14
76-80	+16
81-85	+18
86+	+20
B) Male sex (please circle if true)	+6
C) This component is to be used only for ages 18-50 with either	
Known CAD (previous AMI, CABG, or PCI in men <55 years or women <65 year)	OR
≥3 risk factors present (family history premature CAD, diabetes, hypertension, dyslipidemia, and current smoker)	+4
D) Signs and symptoms (circle each that present)	
Diaphoresis (in association with pain)	+3
Pain occurs or worsened with inspiration	−4
Pain radiates to the arm or shoulder	+5
Pain reproduced by palpation	−6
EDACS total (please add score of all circled figures)	[ ]

EDACS: <16 (Low Risk), 16-21 (Intermediate Risk), ≥21 (High Risk). EDACS: Emergency Department Assessment of Chest Pain Score, CAD: Coronary Artery Disease, CABG: Coronary Artery Bypass Graft, PCI: Percutaneous Coronary Intervention, AMI: Acute Myocardial Infarction

in Western nations, care should be extended when interpreting the age cutoffs in these scoring systems. The EDACS risk score uses a wider age range for scoring and was thus found by the consensus panel to be possibly more suitable for Indian settings. The HEART protocol and ADAPT ADP are both evidence based, validated, and available for application on Indian

Table 3: Heart score and pathway

Variables	Score
History	
Highly suspicious	2
Moderately suspicious	1
Slightly suspicious	0
ECG	
Significant ST-depression	2
Nonspecific repolarization disturbance	1
Normal	0
Age (years)	
≥65	2
45-65	1
<45	0
Risk factors	
≥3 risk factors or history of atherosclerotic disease	2
1 or 2 risk factors	1
No risk factors known	0
Troponin	
≥3x normal limit	2
1-3x normal limit	1
≤ Normal limit	0

THE HEART SCORE: LOW RISK=0-3; HIGH RISK=4 OR GREATER. RISK FACTORS INCLUDE HYPERCHOLESTEROLEMIA, HYPERTENSION, DIABETES MELLITUS, SMOKING, FAMILY HISTORY OF CAD, OBESITY (BMI >30), OR HISTORY OF SIGNIFICANT ATHEROSCLEROSIS. HEART PATHWAY: (a) LOW RISK + NEGATIVE SERIAL TROPONINS=EARLY DISCHARGE, (b) HIGH RISK + NEGATIVE SERIAL TROPONINS=ADMIT TO OBSERVATION OR INPATIENT + STRESS TESTING OR CARDIAC IMAGING, (c) POSITIVE SERIAL TROPONINS IRRESPECTIVE OF HIGH OR LOW RISK=CARDIOLOGY CONSULT AND INPATIENT OR OBSERVATION + STRESS TESTING OR CARDIAC IMAGING. BMI: BODY MASS INDEX, CAD: CORONARY ARTERY DISEASE, ECG: ELECTROCARDIOGRAM

Table 4: Accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponin

The ADAPT ADP

All parameters have to be negative for the ADP to be considered negative and for the patient to be identified as low risk

Cardiac troponin levels at 0 and 2 h below institutional cutoff for an elevated troponin concentration

No new ischemic changes on the initial ECG

TIMI score=0

ADP: ACCELERATED DIAGNOSTIC PROTOCOL, ECG: ELECTROCARDIOGRAM; TIMI: THROMBOLYSIS IN MYOCARDIAL INFARCTION; ADAPT: ACCELERATED DIAGNOSTIC PATHWAYS FOR CHEST PAIN

patients. While we acknowledge that EDACS ADP advocates for a troponin to be drawn at the 0 and 2 h mark, we recognize this quick turnaround time may not be possible in many EDs in India. With this in mind, we consider a 3 h troponin to be an acceptable alternative.

- The consensus panel recommends using an adapted EDACS ADP to stratify the chest pain with no "red flag sign" into low, intermediate, or high-risk categories [Table 2 and Figure 1]
- EDACS ≥16: The consensus panel recommends that patients with EDACS ≥16 should not be considered low risk despite negative ECG and cardiac troponins. These individuals are at an increased risk for MACE and thus require hospitalization for further diagnosis and management [Figure 1]
- EDACS <16: The consensus panel recommends a 3-h troponin for patients presenting with low-risk chest pain when the initial troponin is below 99th percentile of upper

reference limit. A second troponin level should be obtained 3 h after the initial troponin. If the second troponin is also below the 99th percentile of upper reference limit, it allows for early discharge from ED. In individuals who present after 6 h of pain onset, a single value of cardiac troponin below the 99th percentile of upper reference allows for early discharge from ED [Figure 1]

- The consensus panel recommends that busy hospitals consider development of a chest pain unit, within the ED, which centralizes work-up of chest pain patients.

Table 5 describes decisions based on troponin I and T levels done within or after 6 h of chest pain onset.

Table 6 shows 99th percentile values given by various manufacturers of troponin assays in India.

SPECIAL SITUATIONS

- Left circumflex artery occlusion may present with normal ECG. The availability and interpretation of cardiac troponins as described in this statement becomes very important in such lesions[18]
- Chest pain after cocaine or other stimulant use: ECG changes are common among cocaine users. Chances of developing MI are highest within 1–3 h of cocaine abuse.[19] The consensus panel recommends that cocaine users with chest pain suggestive of ACS be managed similarly to nonusers
- Repeated visits to ED with chest pain after discharge utilizing an ADP: The consensus panel recommends performing repeat evaluation for a possible missed diagnosis or an acute cardiac event in a patient representing with chest pain after recent discharge
- Chest pain in pregnant women: The consensus panel recommends that evaluation of chest pain during pregnancy remains the same as for nonpregnant females. Of note, these patients may have a greater risk for acute pulmonary embolism, coronary artery dissection, and postpartum cardiomyopathy.

DISPOSITION AND FOLLOW-UP

All patients discharged from ED with a diagnosis of low-risk chest pain should receive confirmatory testing within 72 h.[1,20] Patients with a previous diagnosis of CAD should be advised to follow up with their cardiologist for specialized diagnostic testing.

LIMITATIONS

In this consensus statement, we attempted to present and propose a practical application of current ADPs for chest pain patients in India, to guide ED physicians to better risk-stratify patients, and determine which patients may require further diagnostic studies, focused management, and who may be safely discharged home. Nonetheless, there are a few limitations to
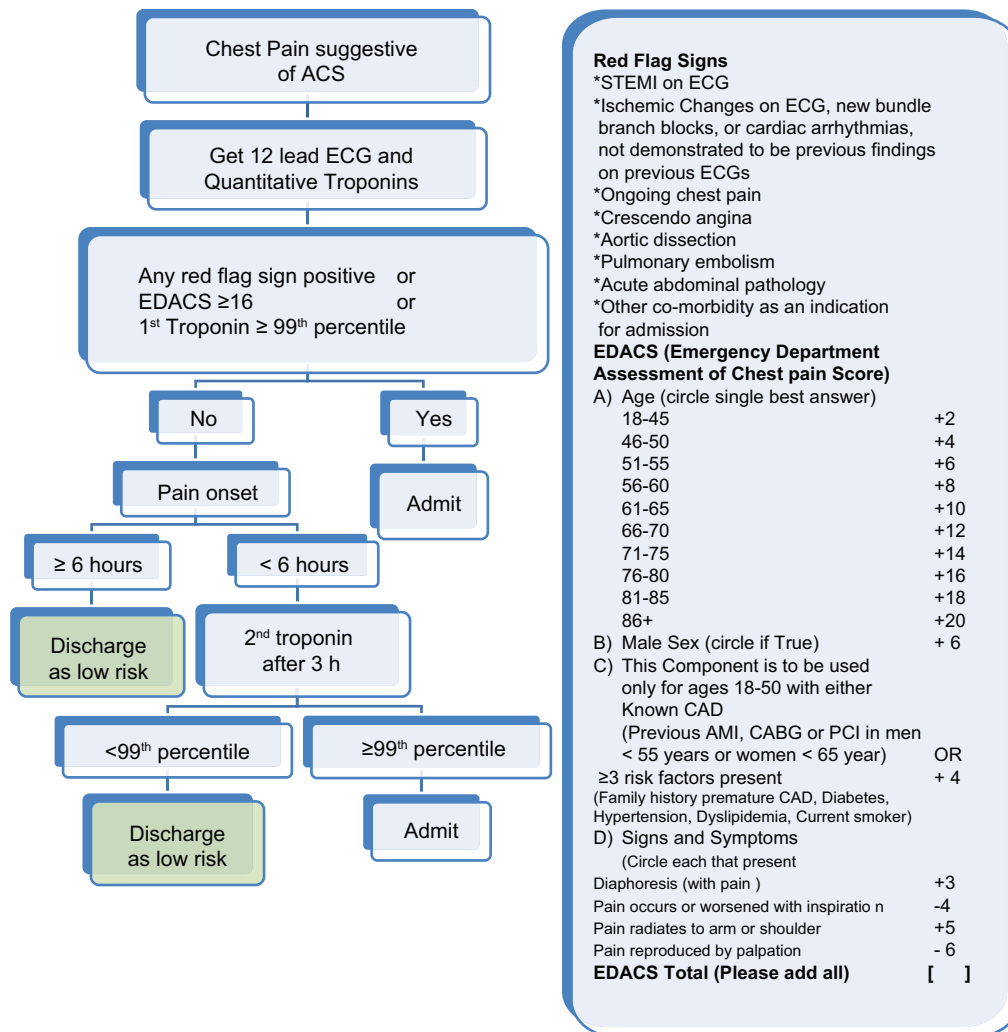
Figure 1: Low-risk chest pain pathway (Indian College of Cardiology-INDUSEM). Adapted Emergency Department Assessment of Chest Pain Score accelerated diagnostic protocol

Table 5: Interpretation of 3-h troponin for troponin T and I		
High-sensitive troponin T	3-h troponin T	Interpretation
<14 ng/L (≥ 6 hours of onset)	Not to be done	Discharge
<14 ng/L (within 6 h of onset)	<14 ng/L	Discharge
	≥14 ng/L	Admit
≥14 ng/L	Not to be done	Admit
Troponin I	3-h troponin I	Interpretation
<99th percentile (>6 h of onset)	Not to be done	Discharge
<99th percentile (<6 h of onset)	<99th percentile	Discharge
	≥99th percentile	Admit
≥99th percentile	Not needed	Admit

this statement. First, although there are a number of chest pain risk stratification scores available, none have been validated for an Indian patient population presenting to the ED. Therefore, the recommendations made in this document are limited by the lack of validation studies and paucity of data pertinent to Indian patients. We encourage studies using the above-mentioned scores on Indian patients so that we have data to use for future updates. Second, this guideline does not reflect multiple factors

including: rural versus urban settings; insured versus uninsured patients; private versus public institutions; delays and modes of transportation to the hospital; diagnostic testing and technology accessibility; inpatient bed availability; and long-term follow-up. Clearly, further studies are needed in the Indian population.

KEY RECOMMENDATIONS

- The consensus panel recommends that a 12-lead ECG should be completed immediately on arrival to the ED. The patient should be placed on a monitor, IV access established, and blood for cardiac troponin levels should be sent to the laboratory for quantitative measurement in all patients with chest pain suggestive of ACS within 10 min of presenting to the ED

- The consensus panel recommends that ECGs should be interpreted by qualified emergency physicians in the ED. ECGs should not routinely be taken to a cardiologist for interpretation nor should a cardiologist be asked to consult on every patient who presents to the ED with chest pain

Table 6: The 99th percentile levels of various troponin assays available in India*

Name of test	99th percentile or cutoff limit (ng/L)	Limit of detection (ng/L)
Roche troponin T high sensitive	14	5
ADVIA Centaur TnI-Ultra® Assay Siemens	40	6
Siemens Stratus CS Troponin I (POC)	70	30
Alere Triage Troponin I test (POC)	20	10
AQT90 Flex Troponin I (POC)	23	10
AQT90 Flex Troponin T (POC)	17	10

*INFORMATION FROM MANUFACTURERS. POC: POINT OF CARE

- This consensus panel recommends the use of quantitative troponin in the assessment of chest pain suggestive of ACS [Table 5]
- The consensus panel recommends using cardiac troponins in all patients with chest pain suggestive of ACS. The consensus panel recommends not using biochemical markers such as BNP, CRP, CK-MB, or myoglobin to diagnose an ACS in patients with chest pain suggestive of ACS
- The consensus panel recommends using an adapted EDACS ADP to stratify the chest pain with no "red flag sign" into low, intermediate, or high-risk categories [Table 2 and Figure 1]
- EDACS ≥16: The consensus panel recommends that patients with EDACS ≥16 should not be considered low risk despite negative ECG and cardiac troponins. These individuals are at an increased risk for MACE and thus require hospitalization for further diagnosis and management
- EDACS <16: The consensus panel recommends a 3-h troponin for patients presenting with low-risk chest pain when the initial troponin is below 99th percentile of upper reference limit. A second troponin level should be obtained 3 h after the initial troponin. If the second troponin is also below the 99th percentile of upper reference limit, it allows for early discharge from ED. In individuals who present after 6 h of pain onset, a single value of cardiac troponin below the 99th percentile of upper reference allows for early discharge from ED
- All patients discharged from ED with a diagnosis of low-risk chest pain should receive confirmatory testing within 72 h
- These recommendations are a decision aid and not a substitute for clinical judgment.

Conflicts of interest

There are no conflicts of interest.

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