ABSTRACT

Objective: We sought to determine the diagnostic accuracy of clinical prediction rules to exclude acute coronary syndrome (ACS) in the emergency department (ED) setting.

Methods: We searched MEDLINE, EMBASE, Web of Science and the Cochrane Database of Systematic Reviews. We contacted content experts to identify additional articles for review. Reference lists of included studies were hand searched. We selected articles for review based on the following criteria: 1) enrolled consecutive ED patients; 2) incorporated variables from the history or physical examination, electrocardiogram and cardiac biomarkers; 3) did not incorporate cardiac stress testing or coronary angiography into prediction rule; 4) based on original research; 5) prospectively derived or validated; 6) did not require use of a computer; and 7) reported sufficient data to construct a $2 \times 2$ contingency table. We assessed study quality and extracted data independently and in duplicate using a standardized data extraction form.

Results: Eight studies met inclusion criteria, encompassing 7937 patients. None of the studies verified the prediction rule with a reference standard on all or a random sample of patients. Six studies did not report blinding prediction rule assessors to reference standard results, and vice versa. Three prediction rules were prospectively validated. Sensitivities and specificities ranged from 94% to 100% and 13% to 57%, and positive and negative likelihood ratios from 1.1 to 2.2 and 0.01 to 0.17, respectively.

Conclusion: Current prediction rules for ACS have substantial methodological limitations and have not been successfully implemented in the clinical setting. Future methodologically sound studies are needed to guide clinical practice.

Keywords: acute coronary syndrome, myocardial infarction, unstable angina, diagnosis, emergency medical services

RÉSUMÉ

Objectif : Nous avons cherché à déterminer l'exactitude diagnostique des règles de prévision clinique visant à exclure le syndrome coronarien aigu (SCA) dans les salles d'urgence.
Introduction

Chest pain is a diagnostic dilemma for the emergency physician. Data from the United States suggest that 2.1% of patients with acute myocardial infarction and 2.3% of patients with unstable angina are misdiagnosed,1 with slightly higher rates reported in a recent Canadian study (4.6% and 6.4%, respectively).2 Information obtained from the history, the initial 12-lead electrocardiogram (ECG), and a single set of cardiac markers does not have sufficient sensitivity to identify those patients who are safe for early discharge.3,4

To assist the American College of Cardiology and American Heart association (ACC/AHA) in developing guidelines for the diagnosis and treatment of unstable angina, the Agency for Healthcare Research and Quality (AHRQ) produced an evidence report that summarized the literature on the prediction of risk for patients with unstable angina.5 The evidence report consisted of 3 systematic reviews: the first evaluated the diagnostic value of the clinical history, physical exam and ECG; the second evaluated cardiac troponin; and the third assessed chest pain units and emergency department (ED) protocols. Despite these 3 systematic reviews, neither the 2007 ACC/AHA Guidelines for the Management of Patients with Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction,6 nor the practical implementation of the 2002 AHA guidelines for the ED7 identify a subset of patients at very low risk for acute coronary syndrome (ACS) who can be safely discharged from the ED without cardiac stress testing. As a result, many patients at low risk for ACS may undergo prolonged ED observation or extensive outpatient investigation, resulting in a greater likelihood of false positive cardiac stress testing and significant cost to the health care system.

Clinical prediction rules are clinical tools that are designed to be used at the bedside to assist physician decision-making.8 They are derived from original research and incorporate variables from the history, physical examination, ECG and cardiac biomarkers. We conducted a systematic review to summarize the diagnostic accuracy of clinical prediction rules that incorporate these variables in decision-making. This review was designed to answer the question: In patients who present to the ED with chest pain, what is the diagnostic accuracy of clinical prediction rules to exclude ACS?

Methods

A protocol (available upon request) was written with input from both content experts (A.S.J. and I.G.S.) and 1 systematic review methodology expert (V.M.M.). This report adheres to the Quality of Reporting of Meta-analyses (QUORUM) guidelines as applicable to diagnostic accuracy reviews.10
**Search strategy**

The search strategy was designed and conducted by an expert reference librarian (P.E.) with input from the clinical lead. Given that clinical prediction guides are variably indexed in the literature as clinical prediction rules, clinical decision rules, risk scores, algorithms and risk stratification tools, we incorporated medical subject heading keywords and a highly sensitive validated search filter for retrieving methodologically sound clinical prediction guides in the search strategy (Appendix 1). A second information specialist reviewed the search strategy and Boolean logic of the combination for errors. The electronic search included the following databases: MEDLINE (1950 to May 2007), EMBASE (1988 to 2007 week 05), Web of Science (1993 to February 2007) and Cochrane Database of Systematic Reviews (fourth quarter, 2006). The Ovid interface was used for searching MEDLINE and EMBASE. No language restrictions were applied. Adjustments were made to the search strategy to account for differences in indexing between databases.

Conference proceedings from the Canadian Association of Emergency Physicians and the Society for Academic Emergency Medicine from 2005 to 2007 were hand searched to identify abstracts that had not yet been indexed in electronic bibliographic databases. We consulted content experts (A.S.J. and J.E.H.) to identify additional published or other unpublished reports. Reference lists of included studies were searched to identify other relevant studies.

**Eligibility criteria**

The purpose of this review was to identify prediction rules of sufficient methodological rigour that would warrant consideration for use in clinical practice. To safeguard against intrusion of bias, inclusion criteria were chosen according to published methodological standards for clinical prediction rules, and are listed in Box 1.

We included studies that incorporated information from commonly available tests (ECG and cardiac biomarkers) since clinicians rely on these basic investigations in conjunction with their history and physical examination in bedside decision-making. Moreover, the limitations of variables from the history, physical examination and ECG for detecting ACS are well-established. Studies incorporating cardiac stress testing or coronary angiography as part of the prediction rule were excluded to reduce the risk of incorporation bias. Prediction rules that were not prospectively derived or validated were excluded. Prediction rules requiring use of a computer to generate diagnostic probabilities were excluded because an in-depth review of artificial neural networks was beyond the scope of this review.

**Study selection**

Study retrieval was conducted in duplicate by 2 independent reviewers in 2 phases. In phase I, we screened titles and abstracts to identify potentially relevant articles. In phase II, we obtained the full articles and assessed them for eligibility. We determined the degree of interobserver agreement for each phase and reported \( \kappa \) values based on the following: for phase I “potentially eligible yes/no” agreement; for phase II, “eligible yes/no.” After making independent assessments, we resolved disagreements by consensus.

**Assessment of methodological quality**

Although methodological criteria for clinical decision rules have been published, they have not been validated for use in systematic reviews. As such, QUADAS (Quality Assessment of Diagnostic Accuracy Studies), a validated quality assessment tool, was used. Two reviewers (E.P.H. and V.T.), working independently, assessed the quality of included studies. We calculated \( \kappa \) values based on the total number of QUADAS criteria met and subsequently resolved all disagreements by consensus. We dichotomized answers as “yes” and “no/unclear” for \( \kappa \) calculations.

When assessing the methodological quality of clinical prediction rules, it is useful to classify studies based on the hierarchy of evidence for clinical prediction rules. In this classification, prediction rules that have been derived but not validated constitute the lowest level of evidence (level 4), followed by studies that have been validated in only 1 narrow prospective sample (level 3), studies that have been validated broadly in multiple settings (level 2) and studies that have undergone impact analysis (level 1).

**Data extraction**

Working independently and in duplicate using a standardized data extraction form, we recorded the following descriptive data from every study: year and journal of publication, patient population (e.g., age, sex, cardiac risk factors
and medical history), percentage of patients in whom ECGs, cardiac biomarkers and stress tests or coronary angiograms were obtained, clinical prediction rule characteristics, duration of follow-up and outcome definitions. We extracted the necessary data to construct 2 × 2 contingency tables. If data from the primary report were unclear, we contacted the corresponding author for clarification. If the corresponding author did not respond, we entered consensus data into each cell of the contingency table. Data were entered into a Microsoft Excel database (Microsoft Corp.).

**Data synthesis**

Sensitivity and specificity were calculated from 2 × 2 contingency tables. Forest plots of sensitivity and specificity, and positive and negative likelihood ratios were constructed using Meta-DiSc software (Unit of Clinical Biostatistics of the Ramón y Cajal Hospital).14

**Results**

**Study selection**

Figure 1 describes the flow of candidate and eligible articles. The initial search strategy produced 720 records. After removing 46 duplicates, 674 records remained for screening in phase I. Eighty potentially eligible records were identified for further review based on review of the title and abstracts (κ = 0.95). Review of the full articles in phase II identified 8 that met inclusion criteria (κ = 0.85).15–21 Two additional articles were selected for further review from the bibliographies of selected articles.22,23 On full text review these were excluded because one retrospectively analyzed data that was originally collected from 2 large clinical trials22 and the other required the use of a computer to generate diagnostic probabilities.23 One potentially relevant article was identified through consultation with content experts. The article did not incorporate variables from the history or physical examination into the prediction tool and was therefore excluded.24 Data were available to construct 2 × 2 contingency tables for all 8 articles that met inclusion criteria. The 8 articles included in the review represent 5 different clinical prediction rules.

**Characteristics of included studies**

The studies included in the review were published from 2003 to 2007 and included 7937 patients in total (Table 1).15–21,23. There were 3 studies conducted in the United States, 2 in the United Kingdom, 1 in Canada, 1 in Spain and 1 in Brazil. With the exception of 1 study that enrolled adults between 24 and 39 years of age,19 and 2 studies that did not report cardiac risk factors,18,20 the remaining studies reported approximately comparable baseline characteristics and cardiac risk factors.

**Quality assessment**

Assessment of quality based on QUADAS criteria count had an interobserver agreement of 89.3% (κ = 0.79) (Table 2).15–21). None of the studies verified the results of their index test (prediction rule) against a reference standard of diagnosis (cardiac stress testing or coronary angiography) on either the whole study population or random sample thereof. A proxy reference standard of close patient follow-up for the development of adverse events was used in 7 studies.16–21 The reference standard was not reported in 1 study.15 Of the 8 studies, 6 did not clearly specify that the index test was interpreted without knowledge of results of the reference standard,15,17,18,20,21,23 nor did it specify that the reference standard was interpreted without knowledge of the results of the index test. Table 2 lists quality assessment

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**Fig. 1. Flow diagram of study selection process. ECG = electrocardiogram; ED = emergency department.**
scores, diagnostic testing and prevalence of disease for each study.

Three of the prediction rules were derived but not validated (level 4 in hierarchy of evidence). Bassan and colleagues classified the type of chest pain according to the likelihood of ACS and based subsequent diagnostic testing on this assessment. This increased the risk of verification bias (i.e., failure to use the same gold standard on all patients), potentially overestimating diagnostic performance. In addition, it is unclear whether outcomes were assessed without knowledge of the chest pain classification and vice versa (i.e., the lack of blinding). Fernandez Portales and colleagues used cardiology residents to select patients for enrolment based on a presumed diagnosis of ACS thus reducing the generalizability of their results. The clinical decision rule derived by Christenson and colleagues, on the other hand, adhered to established methodology for clinical prediction rules. All patients with a primary complaint of chest pain were potentially eligible, reducing the risk of selection bias. Study assistants

<table>
<thead>
<tr>
<th>Study (and no. of patients enrolled)</th>
<th>Clinical prediction guide</th>
<th>Variables included in prediction guide</th>
<th>Duration of follow-up</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Bassan et al. (1003)                | Classification diagnostic tree | chest pain type, history of CAD, history of diabetes, CK-MB level, ST depression or T-wave inversion on ECG | Not reported | • AMI  
• Unstable angina |
| Chase et al. (1481)                 | Risk score                | age ≥ 65 yr, known CAD, ≥ 3 cardiac risk factors, ST-segment deviation, ≥ 2 anginal events in past 24 hr, aspirin use in past 7 d, elevated cardiac biomarkers | 30 d          | • All-cause mortality  
• AMI  
• Revascularization |
| Christenson et al. (819)            | Clinical prediction rule  | Age < 40 yr, normal or T-wave flattening on initial ECG, initial CK-MB < 3.0 ng/mL, or initial CK-MB > 3.0 ng/mL with no change in ECG, rise in CK-MB, or rise in troponin I 0–12 hr after arrival | 30 d          | • AMI  
• Unstable angina |
| Conway Morris et al. (1000)         | Risk score                | age ≥ 65 yr, known CAD, ≥ 3 cardiac risk factors, ST-segment deviation, ≥ 2 anginal events in past 24 hr, aspirin use in past 7 d, elevated cardiac marker levels | 30 d          | • All-cause mortality  
• ST-segment elevation myocardial infarction  
• AMI  
• Troponin-positive acute coronary syndrome  
• Revascularization  
• Recurrent ischemia  
• Death  
• Heart failure |
| Fernandez Portales et al. (321)    | Risk score                | 6 hr troponin T > 0.04 ng/mL, age > 70 yr, cardiac history, prolonged chest pain in past 15 d, chest pain on presentation without ST-segment depression, chest pain on presentation with ST-segment depression, 6 hr troponin T > 0.04 ng/mL without ST-segment depression, 6 hr troponin T > 0.04 ng/mL with ST-segment depression | 15 d          | AMI  
• Troponin-positive acute coronary syndrome  
• Revascularization |
| Lyon et al. (1000)                 | Risk score                | age, pulse rate at presentation, systolic blood pressure at presentation, serum creatinine level at presentation, Killip score, ST-segment depression on presenting ECG, elevated initial serum cardiac biomarker level, cardiac arrest on admission | 30 d          | • All-cause mortality  
• ST-segment elevation myocardial infarction  
• AMI  
• Troponin-positive acute coronary syndrome  
• Revascularization |
| Marsan et al. (1077)               | Clinical prediction rule  | Absence of cardiac history, no cardiac risk factors, normal ECG, CK-MB < 5 ng/mL, troponin I < 0.3 ng/mL | 30 d          | • AMI  
• Unstable Angina |
| Tong et al. (1236)                 | Risk score                | age ≥ 65 yr, known CAD, ≥ 3 cardiac risk factors, ST-segment deviation, ≥ 2 anginal events in past 24 hr, aspirin use in past 7 d, elevated cardiac marker level | 30 d          | • All-cause mortality  
• AMI  
• Revascularization  
• Unstable Angina |

AMI = acute myocardial infarction; CAD = coronary artery disease; CK-MB = creatine kinase; ECG = electrocardiogram.
assessed potential predictor variables without knowledge of the outcome and vice versa (adequate blinding).

Two prediction rules have been prospectively validated in 1 narrow sample (level 3).\textsuperscript{19,20} Marsan and colleagues\textsuperscript{19} enrolled only adults from 24 to 39 years of age, limiting the study’s generalizability. Lyon and colleagues\textsuperscript{20} enrolled all patients with chest pain, decreasing the likelihood of selection bias. However, outcome was determined from routinely available data rather than close prospective follow-up, increasing the risk of misclassification for some patients.

The Thrombolysis in Myocardial Infarction (TIMI) risk score has been prospectively validated by 3 studies (level 2).\textsuperscript{17,18,25} Chase and colleagues\textsuperscript{17} enrolled all patients with nontraumatic chest pain in whom an ECG was obtained, decreasing the likelihood of selection bias. However, they did not report whether the score was assessed while blinded to the outcome diagnosis and vice versa. Conway Morris and colleagues\textsuperscript{18} validated the TIMI score in patients with chest pain deemed to be potentially cardiac in origin by the treating physician, potentially introducing selection bias. Also, the outcome relied on discharge diagnosis rather than prospective follow-up. Finally, Tong and colleagues\textsuperscript{25} enrolled all patients with presumed cardiac chest pain that persisted longer than 30 minutes, but 237 (19\%) patients were either lost to follow-up or had uninterpretable reference standard test results, potentially biasing the estimates of diagnostic performance.

**Heterogeneity**

We observed substantial heterogeneity between studies with regard to the variables incorporated in each clinical prediction tool, the cardiac biomarker assays used, the pretest probability of disease and the outcome measures. With the exception of 3 studies that validated the TIMI risk score,\textsuperscript{17,18,25} each study incorporated different variables into the prediction model. The study by Bassan and colleagues\textsuperscript{15} used CK-MB, 5 studies used cardiac troponin alone,\textsuperscript{17,18,20,21,25} and 2 studies used both CK-MB and cardiac troponin.\textsuperscript{16,19} Only 2 of the studies\textsuperscript{16,19} reported the actual assay used to measure the biomarker as recommended by reporting guidelines.\textsuperscript{26} The pretest probability of disease varied between studies, potentially contributing to variability in diagnostic performance. The outcome measures in each

<table>
<thead>
<tr>
<th>Study; stage of development</th>
<th>No. of QUADAS criteria met</th>
<th>Test; no. (and %) of patients</th>
<th>Probability of disease; no. (and %) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bassan et al.;\textsuperscript{15} derivation</td>
<td>10</td>
<td>ECG 556 (100)</td>
<td>Cardiac markers 443 (78.3)</td>
</tr>
<tr>
<td>Chase et al.;\textsuperscript{17} validation</td>
<td>10</td>
<td>ECG 1458 (100)</td>
<td>Cardiac markers 1293 (85)</td>
</tr>
<tr>
<td>Christenson et al.;\textsuperscript{16} derivation</td>
<td>10</td>
<td>ECG 769 (100)</td>
<td>Cardiac markers 769 (100)</td>
</tr>
<tr>
<td>Conway Morris et al.;\textsuperscript{18} validation</td>
<td>9</td>
<td>ECG — (100)</td>
<td>Cardiac markers — (100)</td>
</tr>
<tr>
<td>Fernandez Portales et al.;\textsuperscript{21} derivation</td>
<td>8</td>
<td>ECG 321 (100)</td>
<td>Cardiac markers 321 (100)</td>
</tr>
<tr>
<td>Lyon et al.;\textsuperscript{28} validation</td>
<td>9</td>
<td>ECG — (100)</td>
<td>Cardiac markers — (100)</td>
</tr>
<tr>
<td>Marsan et al.;\textsuperscript{19} validation</td>
<td>11</td>
<td>ECG 1023 (100)</td>
<td>Cardiac markers — (100)</td>
</tr>
<tr>
<td>Tong et al.;\textsuperscript{25} validation</td>
<td>9</td>
<td>ECG 957 (100)</td>
<td>Cardiac markers 957 (100)</td>
</tr>
</tbody>
</table>

ECG = electrocardiograms; GRACE = Global Registry of Acute Coronary Events; QUADAS = Quality Assessment of Diagnostic Accuracy Studies; TIMI = Thrombolysis in Myocardial Infarction; — = not reported.

*Percentages were calculated based on the total number of patients analyzed in each study.
study, as well as their definitions, also varied. For these reasons, the study data were not pooled.

**Diagnostic performance**

Figure 2 shows a forest plot of sensitivity. Two studies reported sensitivities of 100%, with the remainder ranging from 94% to 99%. The forest plot for specificity is displayed in Figure 3. Substantial variation between specificity estimates is evident, with most estimates falling well below the 50% range. Figures 4 and 5 display forest plots of positive and negative likelihood ratios. Given that clinical prediction rules prioritize sensitivity over specificity, the positive likelihood ratios are near 1 (little diagnostic information), while the negative likelihood ratios are small. As a result, patients who are prediction-rule negative have a low posttest probability of disease.

**Discussion**

We conducted a systematic review of prospective clinical decision rules that exclude ACS in ED patients with chest pain. Of the 8 risk prediction rules, 5 have been prospectively validated and thus could be considered for use in clinical practice. Although the diagnostic performance of the TIMI and Global Registry of Acute Coronary Events (GRACE) scores was sufficient for incorporation into clinical practice, the performance of the TIMI risk score varied between studies and the GRACE score required data that was not available in all ED patients. We did not identify any prediction tool that was appropriate for incorporation into clinical practice.

All 8 studies had methodological weaknesses that could have led to the introduction of bias. Deficiencies in reference standard testing, follow-up and blinding could have led to overestimation of diagnostic performance.

We observed considerable heterogeneity between the studies with regard to the variables incorporated in each clinical prediction tool, the cardiac biomarkers and cutoff values selected, the prevalence of disease, the outcome studied and the diagnostic performance.

Likelihood ratios (LRs), unlike positive and negative predictive values, are independent of disease prevalence, and thus useful for comparing diagnostic tests between...
populations. A negative LR less than 0.1 is generally con-
sidered clinically useful. The upper bound of the 95% 
confidence interval for the negative LR in each study in-
cluded 0.1, suggesting that none of the prediction rules ex-
clude ACS with enough certainty to be clinically useful.

Numerous risk stratification tools for ED patients with 
chest pain have been published. In the 1980s, Goldman 
and colleagues derived and validated a computer pro-
tocol to predict myocardial infarction. However, much 
like other computer-derived prediction tools in emer-
genous medicine, it has not been broadly adopted by 
emergency physicians. The Acute Cardiac Ischemia 
Time-Insensitive Predictive Instrument (ACI-TIPI) de-
designed by Selker and colleagues is another prediction 
tool that has been commonly used. A multicentre con-
trolled clinical trial found that its use reduced hospitaliza-
tion among ED patients with chest pain. The ACI-TIPI 
instrument, however, defines low risk as less than a 10% 
risk for ACS, which is not low enough to forego cardiac 
stress testing. Also, it does not incorporate the results of 
cardiac biomarkers.

There is limited evidence to suggest what miss rate clin-
cians would consider acceptable. It is conceivable that this 
may differ between Canadian and American emergency 
physicians. In Canada, few ED-based observation units ex-
ist, and patients are often managed on an individualized 
basis.2 Given the miss rate of 5.3%, and the cost implica-
tions of broadly adopting ED observation units, a clinical 
 prediction rule that decreases the rate of misdiagnosis in a 
fiscally efficient manner is likely to be acceptable to cli-
cians. A survey of Canadian emergency physicians indi-
cated that most (94%) would use a clinical prediction rule 
for ACS, provided that it did not increase the miss rate 
above 2%.4 In the United States, however, physicians’ 
triage decisions may be influenced more by perceived 
medical and legal risk, and it is not known what miss rate 
would be acceptable to most US physicians.

In the course of the review we did not identify a predic-
tion tool to recommend for use in clinical practice. Future 
studies in this area are needed to guide clinical practice 
and should be carefully designed to prevent intrusion of 
bias, to take into account current guidelines by the Euro-
pean Society of Cardiology and by the American College 
of Cardiology and standardized reporting guidelines for 
ED studies, and to use the most sensitive cardiac troponin 
assays available.

<table>
<thead>
<tr>
<th>Positive likelihood ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fernandez Portales et al.</td>
<td>1.79</td>
</tr>
<tr>
<td>Conway Morris et al.</td>
<td>1.39</td>
</tr>
<tr>
<td>Lyon et al.</td>
<td>1.14</td>
</tr>
<tr>
<td>Tong et al.</td>
<td>1.20</td>
</tr>
<tr>
<td>Bassan et al.</td>
<td>2.24</td>
</tr>
<tr>
<td>Chase et al.</td>
<td>1.46</td>
</tr>
<tr>
<td>Christenson et al.</td>
<td>1.46</td>
</tr>
<tr>
<td>Marsan et al.</td>
<td>1.42</td>
</tr>
</tbody>
</table>

Fig. 4. Forest plot of positive likelihood ratios. Horizontal bars represent the 95% confidence interval (CI).

<table>
<thead>
<tr>
<th>Negative likelihood ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fernandez Portales et al.</td>
<td>0.05</td>
</tr>
<tr>
<td>Conway Morris et al.</td>
<td>0.01</td>
</tr>
<tr>
<td>Lyon et al.</td>
<td>0.03</td>
</tr>
<tr>
<td>Tong et al.</td>
<td>0.12</td>
</tr>
<tr>
<td>Bassan et al.</td>
<td>0.06</td>
</tr>
<tr>
<td>Chase et al.</td>
<td>0.17</td>
</tr>
<tr>
<td>Christenson et al.</td>
<td>0.04</td>
</tr>
<tr>
<td>Marsan et al.</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Fig. 5. Forest plot of negative likelihood ratios. Horizontal bars represent the 95% confidence interval (CI).
Limitations

Our review is primarily limited by the methodological quality of the primary studies and the relatively small number of studies meeting inclusion criteria. None of the studies verified the results of the prediction rule by using a reference standard of diagnosis on the whole sample or random selection of the sample, increasing the risk of verification bias. Although only 8 studies met inclusion criteria, we conducted a thorough literature search that was unrestricted by language. In addition, we hand searched recent conference abstracts and consulted content experts thus minimizing the potential for publication bias.

Conclusion

Chest pain is a diagnostic dilemma for the emergency physician. Current prediction rules are heterogeneous, have substantial methodological limitations and have not been successfully implemented in the clinical setting. Future methodologically sound studies are needed to guide clinical practice.

Acknowledgements: We would like to thank Dr. Maria Fernanda Bellolio Avaria for her assistance in translation. This project was conducted as part of a course on systematic reviews and meta-analysis at the University of Ottawa Epidemiology master’s program. We are grateful for the assistance of Drs. David Moher and Dean Fergusson, co-teachers of the course.

Competing interests: None declared.

Funding: This study was jointly funded by the American Heart Association, the Emergency Medicine Foundation and the Society for Academic Emergency Medicine.

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Appendix 1. Search strategy for MEDLINE

1. *chest pain/ or chest pain/bl, di, et, en, ep, pa, ra or (chest adj pain).mp. or chestpain.mp. [mp=title, original title, abstract, name of substance word, subject heading word] 16582
2. (emergency(adj2 (center$ or centre$ or unit$1 or room$1 or department$1 or service or physician$ or medicine or care or ward$1)).mp. 56706
3. emergency service, hospital/ or emergency medical services/ or triage/ 47137
4. 1 and (2 or 3) 2054
5. limit 4 to “clinical prediction guides (optimized)”* 415
6. exp angina pectoris/di, co, et, ep, ra or exp myocardial ischemia/di, ra, co, et, ep 123391
7. (acute adj (coronary or cardiac or myocardial or heart) adj (syndrome$ or infarct$)).mp. 40383
8. 4 and (6 or 7) 1265
9. diagnosis, differential/ or diagnostic errors/ or missed.mp. or patient discharge/ or patient readmission/ or outcome$.mp. 977299
10. 8 and 9 581
11. decision support techniques/ or multivariate analysis/ or probability/ or logistics model/ or algorithms/ or likelihood functions/ or neural networks$.mp. 168322
12. 10 and 11 89
13. 8 and 11 155
14. 5 or 12 or 13 496