**TITLE**: Systematic review of clinical decision support systems for pre-hospital acute coronary syndrome identification.

**Authors**

Charles Richard Knoery (MHChB)\*1,2

Janet Heaton (PhD)\*1

Rob Polson (MSc)\*3

Raymond Bond (PhD)\*4

Aleeha Iftikhar (MSc)\*4

Khaled Rjoob (MSc)\*4

Victoria McGilligan (PhD)\*5

Aaron Peace (PhD)\*5,6

Stephen James Leslie (PhD)\*1,2

**Affiliations**

1. Division of Rural Health and Wellbeing, University of the Highlands and Islands, Centre for Health Science, Old Perth Road, Inverness, UK, IV2 3JH

2. Cardiac Unit, NHS Highland, Inverness, UK, IV2 3BW

3. Highland Health Sciences Library, University of the Highlands and Islands, Centre for Health Science, Old Perth Road, Inverness, UK, IV2 3JH

4. Ulster University, Jordanstown Campus, Shore Road, Newtownabbey, Northern Ireland, UK, BT37 0QB

5.Centre for Personalised Medicine, Ulster University, Londonderry BT47 6SB, Northern Ireland, UK

6. Cardiac Department, Altnagelvin Hospital, Northern Ireland, UK, BT47 6SB

**Author for correspondence:** Charles Knoery, Division of Rural Health and Wellbeing, University of the Highlands and Islands, Centre for Health Science, Old Perth Road, Inverness, UK, IV2 3JH

Email: [Charles.knoery@uhi.ac.uk](mailto:Charles.knoery@uhi.ac.uk)

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**ABSTRACT**

Objective

Timely pre-hospital diagnosis and treatment of acute coronary syndrome (ACS) are required to achieve optimal outcomes. Clinical decision support systems (CDSS) are platforms designed to integrate multiple data and can aid with management decisions in the pre-hospital environment. The review aim was to describe the accuracy of CDSS and individual components in the pre-hospital ACS management.

Methods

This systematic review examined the current literature regarding the accuracy of CDSS for ACS in the pre-hospital setting, the influence of computer-aided decision making and of four components: electrocardiogram, biomarkers, patient history and examination findings. The impact of these components on sensitivity, specificity, positive and negative predictive values was assessed.

Results

A total of 11,439 articles were identified from a search of databases, of which 199 were screened against the eligibility criteria. Eight studies were found to meet the eligibility and quality criteria. There was marked heterogeneity between studies which precluded formal meta-analysis. However, individual components analysis found that patient history led to significant improvement in the sensitivity and negative predictive values. CDSS which incorporated all four components tended to show higher sensitivities and negative predictive values. CDSS incorporating computer-aided electrocardiogram diagnosis showed higher specificities and positive predictive values.

Conclusions

Although heterogeneity precluded meta-analysis, this review emphasises the potential of ACS CDSS in pre-hospital environments that incorporate patient history in addition to integration of multiple components. The higher sensitivity of certain components, along with higher specificity of computer-aided decision-making, highlights the opportunity for developing an integrated algorithm with computer-aided decision support.

**INTRODUCTION**

Despite a decline in coronary heart disease deaths by more than 50% between 1961 and 2016, coronary heart disease is still a leading cause of mortality in the United Kingdom1. In Scotland, acute coronary syndrome (ACS) is a major cause of mortality with 6,697 deaths in 2016 2. ST elevation myocardial infarction (STEMI) is the most acutely critical subtype of ACS with highest 30-day mortality3–5. Time is critical for STEMI management as mortality increases with treatment delays4,6. Pre-hospital STEMI identification has been shown to reduce treatment delays and improve mortality7,8.

The importance of timely pre-hospital recognition of STEMI is well established7, yet there are still recognised difficulties. Pre-hospital difficulties include the absence of complete medical records and lack of diagnostic support tools, such as imaging, which increases the risk of ACS misdiagnosis and creates a low positive predictive value for pre-hospital ACS diagnosis9. A low positive predictive value increases inappropriate treatment of ACS including cardiac catheterisation laboratory (‘cath-lab’) activation10. Over activation of the cath-lab is a potentially avoidable strain on a valuable clinical resource. False mobilisation increases workload of the cath-lab team and often requires unnecessary redirection of emergency medical services to deliver patients to cath-lab centres outside their normal operating zones.

Conversely, under-diagnosis of STEMI has obvious negative consequences. Delayed presentation of STEMI has significantly decreased long-term survival rates (73% survival with late presenters versus 93% survival with early presenters)11 and even late treatment of STEMI via reperfusion of the culprit occluded artery has no benefit in mortality compared to conservative medical therapy12. In addition, subtypes of ACS such as non-ST elevation myocardial infarction (NSTEMI) and unstable angina can be just as critical as a STEMI as ST elevation on the ECG is not exclusive for acute coronary artery occlusion13 i.e. a proportion of NSTEMI are actually caused by an occluded coronary artery.

Clinical decision support systems (CDSS) are platforms that combine multiple clinical data inputs (termed “components” in this review) to produce a single output, which can be a diagnosis, clinical advice or risk stratification, that can help clinicians with difficult decision making9. For instance, CDSS have already been developed for use in the emergency department for ACS14,15, where these tend to focus on a high negative predictive value to prioritise safe discharge. In the community, there is increased difficulty for out-of-hospital practitioners, like general practitioners (especially those in remote and rural communities) and ambulance crews, to make triage decisions in patients with ACS without the clinical diagnostic tools that are available in the hospital. These difficulties are compounded with suspected ACS that presents without obvious ST elevation as a non-diagnostic ECG creates further ambiguity. This challenge has been the target of CDSS-related research to assist pre-hospital clinicians to manage patients who have suspected ACS16.

With great interrogation of technology into healthcare, there is a large potential for computer-aided diagnosis of ACS in the pre-hospital setting. Computer-aided decision support has already been shown to be beneficial determining allocation for level of life support in the emergency department17. In addition, computer-aided ECG interpretation algorithms have been developed to improve pre-hospital and emergency department ACS identification to reduce the delay or misdiagnosis of ACS associated with prolonged door-to-balloon time18.

However, computer-aided ECG interpretation is still limited by ECG artefact and other non-ischaemic causes of ST elevation such as early-repolarisation and thus interpretation of the ECG should be done in combination of other components such as symptoms and medical history19,20.

In the pre-hospital environment, there are concerns that CDSS can cause delays compared to standard care9 and that these systems might reduce the autonomy of clinicians21. However, previous studies have shown the benefit of pre-hospital CDSS for patients with stroke22 and spinal injury23. One review looked at pre-hospital CDSS for ACS but excluded tests using computer-aided decision systems and biomarker tests24. With advances in computer technology and point-of-care testing, the use of these components is now increasingly realistic in a pre-hospital setting.

The aim of this systematic review was to describe the accuracy of CDSS and their individual components in the pre-hospital management of ACS.

**METHOD**

The search strategy followed the guidelines set by the preferred reporting items for systematic review and meta-analysis (PRISMA)25. The review protocol was designed with guidance from the PRISMA-Protocol statement and was registered with Prospero (registration number**:**116600)26.

**Search strategy**

The search strategy was designed and executed by the first author. Five databases were searched: EMBASE, Medline, Cochrane library, Web of Science and CINAHL. The searches were performed between December 2018 and January 2019. Grey literature was also reviewed for any additional sources. The search terms used are in *appendix 1*.

**Study selection and eligibility**

Abstracts and titles were screened and selected if they were adjudged to be relevant to the review aim. Duplicates were excluded. The review focused on the use of CDSS in a pre-hospital setting where patients presented with symptoms suggestive of ACS. Definitions for ACS included STEMI, NSTEMI or unstable angina as per ESC guidelines27. Pre-hospital was defined as contact with first emergency responders (including paramedics, medical dispatch callers, general practitioners). Studies carried out in the hospital environment or emergency department were excluded. Patient history was defined as subjective symptoms reported by the patient (e.g. chest pain, shortness of breath and clamminess), while vital signs/examination were defined as objective non-invasive clinical measurements obtained by clinical staff (e.g. heart rate, blood pressure and oxygen saturations).

Inclusion criteria:

1. Published source
2. Data on patient diagnosis or outcome such as major adverse cardiovascular events
3. Set in a pre-hospital setting
4. Use of CDSS as an intervention
5. Patients with suspected ACS
6. English language

Exclusion criteria

1. No data on outcomes
2. Inclusion of emergency department/in-hospital decision aids
3. Inclusion of non-suspected acute coronary syndrome patients
4. No definition of Myocardial Infarction (MI)
5. Not in English language

Full-text versions of the papers selected were obtained and analysed. Papers were then included or excluded based on the criteria. A second reviewer judged the selection process and analysed the eligible papers separately by the criteria for consensus. Any disagreements were resolved by discussion between the two reviewers to reach a consensus. Cohen’s kappa co-efficient was performed between the reviewers to analyse the rate of agreement.

**Assessment of quality and risk of bias**

Quality assessment was conducted using the QUADAS 2 tool28. Papers were analysed to ensure there was no obvious missing data and that patients progressed through the study as described. Studies were excluded from analysis where there was a high or unclear risk of bias. They were then ranked according to level of evidence as determined by published hierarchy of evidence, which takes into account any validation and impact analysis of CDSS29.

**Data extraction**

Data were extracted using a data extraction tool that was piloted with two initial studies and subsequently refined. The datatypes that were extracted are outlined in *appendix 2*. The primary outcome recorded from studies was a final diagnosis of ACS accuracy.

**Data analysis**

Data analysis was performed using statistical analysis software SPSS 24.0 (SPSS Inc., Chicago, IL). The sensitivity, specificity, positive predictive value and negative predictive value of CDSS were examined. The results were reported as percentages and analysed as continuous data. Whether a history, examination/vital signs, ECG and biomarker components were included in the study, then this was described as binary (yes or no) and treated as categorical data. Independent-samples t-test was used to analyse the difference of mean accuracy (percentage) between CDSS with and without components. A p-value equal to or less than 0.05 was considered to be statistically significant. Because of the considerable heterogeneity between the papers selected, formal meta-analysis was deemed not possible.

**RESULTS**

**Study selection and quality assessment**

**Figure 1** outlines the search and selection process for this review. The titles and abstracts for 11,439 articles were screened. A total of 199 articles were initially identified through this process and reviewed. Of these, 182 articles did not fulfil eligibility criteria, leaving 17.

The studies were assessed for their quality using the QUANDAS 2 tool28. Four studies were rejected from the study due to high risk of bias. A further five studies were assessed to have some minimal or moderate bias, all with patient selection, as would be expected with non-randomised prospective and observational studies20,30–33. Only two studies had validation phases for their CDSS and there was no impact analysis with any of the 17 articles thus undermining of the potential quality of evidence as judged by the pre-defined hierarchy31,33. Ideally, validation and impact analysis would be required before any CDSS could be judged suitable for implementation in other health localities. The second reviewer screened the 17 selected studies and Cohens kappa coefficient for inter-observer agreement between the two reviewers was calculated at k=0.46, which equates to moderate agreement. Following collaboration with the second reviewer and QUANDAS 2 tool quality control, nine studies from the 17 were excluded, leaving eight studies that were included in the analysis16,20,30–35.

**Study Characteristics**

Seven of the eight studies were prospective in nature, with use of CDSS performed ‘on-site’ by either a general practitioner, emergency medical services staff or medical dispatcher16,30–35. Two studies were retrospective analyses of patients and included either computer-aided ECG interpretation and decision-making20,34.**Table 1** displays the demographic characteristics of the patients in the eight studies. A total of 354,259 patients were in the studies combined; however, one study contributed 347,989 patients making up 98% of the total population. The average number of patients excluded was 69, the majority being from one study which only had data on 15% of patients30. Mean age was 65 years and 54% of participants were male. Half of the studies were conducted in the Netherlands, with a further two in the United States and the remainder in Sweden and Japan. Five studies involved emergency medical services, two involved general practitioners and one involved a medical call dispatch team.

**Heterogeneity**

There was a large degree of heterogeneity in the eight studies. The first study was published in 1996, and the last 22 years later in 201816,33. As noted above, seven of the studies were prospective and one was retrospective in design. The composition of the CDSS components differed, with seven studies involving patient history16,30–35; six involving pre-hospital ECG interpretation16,20,31,33–35; five involving examination and vital signs16,31–33,35; and two involving a pre-hospital biomarker test16,35. The last two studies were the only ones to develop CDSS that incorporated all four components16,35. With regards to the outcomes measured, three reported ACS (MI including unstable angina)30,32,33; three others reported STEMI20,31,34; one reported NSTEMI16; and one reported a major adverse cardiovascular event35(defined as any MI, primary PCI, coronary artery bypass graft or any cause of mortality). The definition of MI also differed between studies, with three30,32,34 using the universal guidance on the diagnosis of MI36, two other studies16,35 used the third universal definition of MI37, while the final three used a combination of ECG findings, biomarkers and history to diagnose ACS20,31,33. The incidence of the ACS also was widely different between the studies, ranging from 0.02% to 50%.

**Statistical analysis**

The results of the analysis of the outcomes, sensitivities, specificity, positive predictive value and negative predictive value of the studies are described in **Table 2**. The sensitivity between the studies varied from 100% to 58%, with specificity varying from 100% to 10%, positive predictive value between 100% and 7%, and negative predictive value between 100% and 30%. **Table 3** shows that only the inclusion of patient history was found to have a significant impact on improving accuracy of sensitivity and negative predictive value of CDSS.

**DISCUSSION**

The utility of CDSS for ACS in pre-hospital settings is yet to be established. This systematic review of the literature, the first to be conducted on the topic, found considerable variations in the components of CDSS that were examined in existing studies. The extent of the heterogeneity precluded a formal meta-analysis, however, a comparison of which components were key in successful CDSS was performed.

This review found that the use of the patient history component in CDSS remains highly important in diagnosis with significant improvement on the sensitivity (p = 0.002) and negative predictive value (p<0.001). These findings highlight the potential of CDSS that incorporate patient history in a ‘rule-out’ capacity for an ACS diagnosis. The significant impact of patient history in this review, may have been due to patient history being the most prevalent tool in CDSS with it being included in seven of the eight studies reviewed16,30–35. In comparison, pre-hospital ECG was used in six of the eight studies16,20,31,33–35, vital signs and examinations were used in five studies16,31–33,35, and biomarkers were used in just two studies16,35.

Interestingly, in the two studies16,35 that used all four components (the ECG, a point-of-care biomarker, patient history and vital signs/examinations), both achieved high sensitivity (100% and 96%) and negative predictive value (100% and 97%) but poor specificity (43% and 29%) and positive predictive value (29% and 21%). However, both studies excluded patients with clear ST elevation, thus focusing on the risk stratification of patients between ACS and non-ACS rather than triage of patients with NSTEMI or STEMI. Three of the studies20,31,34 looked exclusively at the identification of STEMI and had a larger range of specificity (88% to 100%) and positive predictive value (7% to 100%). The heterogeneity of the findings appears to be dependent on the aim of a pre-hospital CDSS to differentiate between a ‘rule-in/out’ for ACS, or between NSTEMI and STEMI.

Recent advances have allowed the use of high-sensitivity troponins to achieve a high degree of sensitivity in the diagnosis of ACS, leading to the reduction of unstable angina diagnosis38. One of the studies reviewed demonstrated that there is the capability of the traditional point-of-care troponin to be used in CDSS16. However, there were issues reported with the test used in this study, including device errors, inability to obtain blood, and the risk of false negatives when samples were taken shortly after symptom onset. The study was also limited by the use of a single troponin value in isolation, where clinicians are unable to observe any trends and a raised troponin does not always indicate myocardial ischaemia but may be a result of myocardial injury27. A computer-based machine learning algorithm for the diagnosis of MI has been developed with a paired troponin, analysing the rate of change of troponin along with age and sex showing strong sensitivity at 97.8% and specificity of 92.2%39. However, the study required a second troponin at 1-3 hours following the initial troponin measurement and therefore would not be feasible in the pre-hospital environment. The value of an isolated troponin in the pre-hospital situation maybe more apparent in combination with other components of CDSS such as patient history and suggestive ECG features. In addition, the use of pre-hospital high-sensitivity troponin tests in comparison to the in-hospital test may aid in the sensitivity when identifying ACS where shorter time from symptom onset to test can reduce sensitivity40.

The use of contemporary risk stratification algorithms for MI has been shown to be effective following hospital admission, with examples like the HEART, TIMI, and GRACE scores41–43. Two studies16,35 used the HEART score as the clinical decision algorithm to aid in ACS risk stratification, with one study35 modifying the score with the use of a high-sensitivity troponin rather than the conventional fourth-generation troponin measurement. Although there was excellent sensitivity (100%) and negative predictive value (100%) for the modified HEART score algorithm, specificity (43%) and positive predictive value (29%) were less accurate. This could be due to the designation of intermediate and high values in the modified HEART scores as a ‘positive’ score in this review. When adjusting for only the high scores on the modified HEART algorithm then specificity increases to 87% and positive predictive value to 51%. As the authors acknowledge, the main objective of the HEART score is to rule-out rather than rule-in ACS, however, the risk stratification element could aid the rapid transfer of high-risk patients to specialist cardiac facilities35.

The greatest area for future development in CDSS is with computer-aided interpretation. Three of the CDSS in this review incorporated computer-integration for either ECG interpretation or for the final clinical decision20,30,34. The accuracy of MI diagnosis is seen in the two studies that utilised computer-aided interpretation of ECG, with high specificity (100% and 99%) and positive predictive value (100% and 83%)20,34,44. However, one study which looked only at the digital ECG for the decision support had lower sensitivity (58%) and negative predictive value (30%)20. The use of computer-aided decision making is a rapidly-developing field with advances in radiology and pathology especially45. However, the role of computer-aided decision making in ECG interpretation has been previously reported with varying sensitivity and specificity46,47. Deep learning techniques for ECG interpretation have enormous potential to improve ECG ACS detection with the ability to detect subtle signs of ischaemia and continually learn from their findings48.

Computer aided decision making was not only limited to ECG interpretation. One study looked at the use of a computer-aided decision system for medical dispatch to patients presenting with chest pain, with the only component being patient history, and it found good sensitivity (92%) and negative predictive value (97%) but poor specificity (41%) and positive predictive value (17%)30. The use of a computer-aided decision system can help assimilate a large amount of data when assessing a patient and help prioritise patients dependent on certain features in the history and risk-factors. Innovations in computerised ACS diagnosis highlight the potential of machine learning where constant refinement of the algorithm accuracy can produce increasingly accurate decisions39.

This use of computer-aided decision systems in the pre-hospital setting can be advantageous, where often there is no experienced cardiologist present and paramedic crews, with limited training, may have to interpret the clinical situation and ECG alone47. The one study which had the computer ECG interpretation with combination of a clinical screening tool led to high sensitivity (86.9%) and specificity (98.5%) suggesting that an integrated approach with other components could be beneficial34.

**Limitations**

There are several important limitations with this study. Due to the high volume of ACS research, and in combination with the broad-search strategy, there is a possibility that some literature has been missed.This search strategy was employed to aid the identification of studies that examined principle components, such as patient history within CDSS, before the adoption of new technologies, such as pre-hospital ECG and biomarkers.

The considerable heterogeneity in CDSS which limited the statistical analyses that could be done, particularly with one study contributing 98% of the population for statistical analysis, hence the results must be taken with caution. In addition, MI was variously defined using the published universal definitions of MI16,30,32,34,35, a combination of an ECG and biomarker criteria31,33 or by ECG alone20. There was a notable variation in the incidence of ACS, ranging from 0.02%31 to 50%20. This was due to patient selection for analysis, with the first study having included all patients presenting to emergency services (n=347,989), whereas the second study focussed exclusively on pre-hospital transmitted ECGs suspected of STEMI (n=200) and therefore targeted a select patient group with a higher incidence of ACS.

Despite this, the review was able to document the nature and extent of the heterogeneity of the studies, including the components of CDSS and the methods used to examine them. It also provided the opportunity to examine what components were important in the pre-hospital diagnosis of ACS, and to compare the value of individual components and combinations thereof.

**Further research**

Further research would be useful to assess the accuracy of the high sensitivity of CDSS involving multiple components combined with the high specificity of computer-aided decision systems. CDSS research requires further validation in different clinical environments before CDSS are deployed for widespread use. In addition, impact analysis also helps judge whether the beneficial effects of CDSS would remain once fully incorporated into clinical use. Other effects that CDSS have on users need to be explored, including automation bias where the clinician can over-trust the decision aid 49. The user interface design of CDSS is another area that needs further research. Human factors and interaction design guidelines are often ignored in designing CDSS50. However, one study used human-computer interaction design principles to design CDSS to aid ECG interpretation51. They used eye tracking analysis of ECG interpretation52 and their understanding of human cognition and working memory to breakdown the ECG interpretation process into manageable tasks on CDSS to eventually present multiple automated diagnoses in order to prevent automation bias and to encourage differential decision making. Whilst CDSS are mostly concerned with the provision of algorithmic text-based suggestions, future work may also involve better use of intelligent dynamic graphics as part of the algorithmic output for depicting more spatiotemporal data to augment the decision support53. Finally, new studies that evaluate diagnostic CDSS would ideally focus on sensitivity, specificity, positive predictive value and negative predictive value of CDSS algorithms and use consistent definitions of MI. Studies that also use consistent definitions and outcomes between them, would help with the development of a successful CDSS algorithm that integrate multiple components to provide an effective clinical aid.

**Summary**

CDSS are increasingly prevalent in healthcare and in combination with computer-aided decision and point-of-care biomarkers, they could provide a way of improving the accuracy of pre-hospital diagnosis and outcomes of treatment. With risks associated with delayed treatment of ACS and, alternatively, pressures on hospital resources such as cardiac cath-lab activation, there is an opportunity to create an efficient and safe diagnostic pathway prior to hospital admission. This review has highlighted the importance of patient history in diagnosis but also the potential for combining components such as biomarkers and computer-aided decision ECG interpretation in the integration of CDSS for suspected ACS.

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**Figure legends:**

**Figure 1**. Flow chart of literature search and selection process

**Table 1.** Study characteristics

**Table 2.** Results of the analysis of the outcomes, sensitivities, specificity, positive

Predictive value and negative predictive value of the individual studies.

**Table 3**. Mean of combined clinical decision support systems accuracy with incorporated components

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study |  | Study type | CDSS model | Year | Mean age | No. patients | Location | Prehospital setting\*\*\* | Type of ACS analysed\* | Use of ECG | | Use of history | Use of biomarker | Use of vital signs\*\* | Bias |
| Grijseels et al.[33] |  | Prospective  two-phase | Questionnaire and ECG algorithm | 1995 | 65.6 | 977 | Netherlands | GP | ACS | Yes | Yes | | No | Yes | At risk of bias |
| Bruins et al.[32] |  | Prospective multi-centre | GP-based clinical decision rule | 2010 | 66 | 336 | Netherlands | GP | ACS | No | Yes | | No | Yes | At risk of bias |
| Bhalla et al.[20] |  | Retrospective cross-sectional | Computer-based ECG algorithm | 2012 | no info | 412 | USA | EMS | STEMI | Yes | No | | No | No | At risk of bias |
| Wilson et al.[34] |  | Retrospective cross-sectional | Clinical toolkit with ECG | 2013 | 56.8 | 310 | USA | EMS | STEMI | Yes | Yes | | No | No | Low risk of bias |
| Gellerstedt et al.[30] |  | Prospective  cross-sectional | Telephoned based Questionnaire | 2016 | 70.5 | 2,285 | Sweden | Emergency dispatch | ACS | No | Yes | | No | No | At risk of bias |
| Sakai et al.[31] |  | Prospective  case control | ECG transmission flow chart | 2017 | 69.4 | 347,989 | Japan | EMS | STEMI | Yes | Yes | | No | Yes | At risk of bias |
| Ishak et al.[35] |  | Prospective cross-sectional | Modified HEART score | 2018 | 63.8 | 1,127 | Netherlands | EMS | MACE^ | Yes | Yes | | Yes | Yes | Low risk of bias |
| Van Dongen et al.[16] |  | Prospective observational | Modified HEART score | 2018 | 63.6 | 823 | Netherlands | EMS | NSTEMI | Yes | Yes | | Yes | Yes | Low risk of bias |

**Table 1.** Study characteristics

\* ACS includes STEMI ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction and unstable angina. \*\*Defined as either respiratory rate, oxygen saturations, heart rate, blood pressure, conscious level, or temperature. \*\*\* EMS, Emergency Medical services; GP, General Practitioner MI, myocardial infarction; ACS, acute coronary syndrome, ECG electrocardiogram. ^ MACE, major adverse cardiovascular event; defined as death (all cause), MI, primary cutaneous intervention, coronary artery bypass grafting or all-cause mortality.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study | Primary Outcome | Sensitivity | Specificity | PPV | NPV |
| Grijseels et al.[33] | Diagnosis of ACS | 97.0% | 13.0% | 52.0% | 92.0% |
| Bruins et al.[32] | ACS diagnosis | 97.0% | 10.0% | 23.0% | 92.0% |
| Bhalla et al.[20] | STEMI diagnosis | 58.0% | 100.0% | 100.0% | 30.0% |
| Wilson et al.[34] | STEMI diagnosis | 86.9% | 98.5% | 83.3% | 98.6% |
| Gellerstedt et al.[30] | ACS | 92.2% | 41.0% | 17.0% | 97.0% |
| Sakai et al.[31] | STEMI diagnosis | 83.3% | 88.1% | 6.7% | 99.8% |
| Ishak et al.[35] | MACE | 100.0% | 43.0% | 28.5% | 100.0% |
| Van Dongen et al.[16] | MACE within 45 days | 96.0% | 29.0% | 21.0% | 97.0% |

**Table 2.** Results of the analysis of the outcomes, sensitivities, specificity, positive

Predictive value and negative predictive value of the individual studies.

\* MACE, major adverse cardiovascular event; defined as death (all cause), MI, primary cutaneous intervention, coronary artery bypass grafting or all-cause mortality.

PPV, positive predictive value; NPV, negative predictive value; ACS, acute coronary syndrome; STEMI, ST elevation myocardial infarction.

**Table 3**. Mean of combined clinical decision support systems accuracy with incorporated components

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Involved ECG | | Involved History | | Involved Biomarkers | | Involved Examination/vital signs\* | |
|  | Mean ±SD (%) | p-value | Mean ±SD (%) | p-value | Mean ±SD (%) | p-value | Mean ±SD (%) | p-value |
| Sensitivity | 86.9 ±15.5 | 0.531**\*** | 93.2 ±6.1 | **0.002\*\*** | 98.0 ±2.8 | 0.306**\*** | 94.7 ±6.5 | 0.122 |
| Specificity | 61.9 ±38.2 | 0.262**\*** | 46.1 ±34.7 | 0.197**\*** | 36.0 ±9.9 | 0.274 | 36.6 ±31.6 | 0.117**\*** |
| PPV | 48.6 ±36.8 | 0.339**\*** | 33.1 ±26.1 | 0.054**\*** | 24.7 ±5.3 | 0.462**\*** | 26.2 ±16.5 | 0.101**\*** |
| NPV | 86.2 ±27.7 | 0.703**\*** | 96.6 ±3.4 | **0.000\*\*** | 98.5 ±2.1 | 0.526**\*** | 96.1 ±4.0 | 0.256 |

**\***Equal Variance assumed by Levene’s test for heteroscedasticity

**\*\***Statistical significance (2-tailed) for component accuracy in model inclusion compared to omission.

ECG, electrocardiogram; SD, standard deviation; PPV, positive predictive value; NPV negative predictive value.

**Figure 1**. Flow chart of literature search and selection process

A close up of a logo

Description automatically generated

Supplementary material

**APPENDIX**

**Appendix 1**. Search terms

|  |
| --- |
| OVID (Medline and EMBASE) |
| Clinical decision support systems |
| 1. Clinical? decision? support? systems\* |
| 1. Algor#thm |
| 1. Diagnos\* |
| 1. Diagnos\* adj(accuracy or differential\* or decision\* or tool\*) |
| 1. Predict\* |
| 1. Clinical? adj(pathway? or tool? or decision?) |
| 1. Triage.mp |
|  |
| Pre-Hospital |
| 1. Pre-hospital\* |
| 1. Pre?hospital\* |
| 1. Emergency care.mp |
| 1. Point of care test\* |
| 1. Point-of-care systems/ |
| 1. Early?diagnosis.mp |
| 1. Out?of?hospital\* |
| 1. Emergency Medical Services/ |
|  |
| Myocardial infarction |
| 1. exp.Acute coronary syndrome\* |
| 1. acs.mp |
| 1. coronary adj(event\* or disease\* or arter\*) |
| 1. myocard\* infarct\* |
| 1. myocard\* isch?emia.mp |
| 1. STEMI.mp |
| 1. ST elevation adj(acute coro\* syndrome or myocard\* infarc\*) |
| 1. NSTEMI.mp |
| 1. Non-ST elevation adj(acute coro\* syndrome or myocard\* infarc\*) |
| 1. Steacs.mp |
| 1. Nsteacs.mp |
| 1. Heart adj(attack or pain or arrest) |
| 1. Heart arrest\* |
| 1. Chest pain.mp |
| 1. Unstable angina.mp |
| 1. UA.mp |
| 1. Cardiac\* |
| 1. Ischaem\* |

|  |
| --- |
| Web of Science search terms |
|  |
| 1. TS=(“acute coronary syndrome\*” OR “acs” OR “coronary adj(event\* OR disease\* OR arter\*)” OR “myocard\* infarct\*” OR “myocard\* isch?emia” OR “STEMI” OR “STEACS” OR “ST elevation adj(acute coro\* syndrome OR myocard\* infarc\*)” OR “NSTEMI” OR “Non-ST elevation adj(acute coro\* syndrome OR myocard\* infarc\*)” OR “NSTEACS” OR “heart attack”) |
| AND |
| 1. TS=(“Clinical? decision? support? systems\*” OR “Algor$thm” OR “Diagnos\* adj(accuracy OR differential\* OR decision\* OR tool\*)” OR “Predict\* adj(tool? OR pathway?)” OR “Clinical? adj(pathway? OR tool? or decision?))” |
| AND |
| 1. TS=(“Pre-hospital\*” OR “Pre?hospital\*” OR “Emergency care” OR “Point of care test\*” OR “Point-of-care systems/” OR “Early?diagnosis” OR “Out?of?hospital\*” OR “Emergency Medical Services/”) |
|  |
| REFINE: English language, WEB of Science Core Collection, Research areas ( CARDIOVASCULAR SYSTEMS CARDIOLOGY, HEALTH CARE SCIENCES SERVICES, EMERGENCY MEDICINE, GENERAL INTERNAL MEDICINE, CRITICAL CARE MEDICINE, AUTOMATION CONTROL SYSTEMS) |

|  |
| --- |
| CINAHL Search terms |
|  |
| Myocardial Infarction |
| 1. TX Acute coronary syndrome\* |
| 1. TX acs |
| 1. TX coronary N1 event\* or disease\* or arter\* |
| 1. TX myocard\* infarct\* |
| 1. TX myocard\* isch?emia |
| 1. TX stemi |
| 1. TX st elevation N1 acute coro\* syndrome or myocard\* infarc\* |
| 1. TX nstemi |
| 1. TX non st elevation N1 acute coro\* syndrome or myocard\* infarc\* |
| 1. TX steacs |
| 1. TX nsteacs |
| 1. TX Heart N1 attack or pain |
| 1. TX Chest pain |
| 1. TX Cardiac\* |
| 1. TX Isch#em\* |
|  |
| Pre-hospital |
| 1. TX Prehospital\* |
| 1. TX Pre#hospital\* |
| 1. TX Emergency#care |
| 1. MH point-of-care Testing |
| 1. TX Early$diagnosis |
| 1. TX Out$of$hospital\* |
| 1. MH Emergency Medical Services |
|  |
| Clinical decision support systems |
| 1. MH Decision Support Systems, Clinical |
| 1. MH Algorithms |
| 1. Algor#thm |
| 1. TX Diagnos\* w1 accuracy or differential\* or decision\* or tool\* |
| 1. TX Predict\* n1 tool\* OR pathway\* |
| 1. TX Clinical? n1 pathway\* or tool\* or decision\* |

|  |
| --- |
| Cochrane Search Terms |
|  |
| Myocardial Infarction |
| 1. “Acute (coronary or cardiac) syndrome?” |
| 1. “Acs” |
| 1. “coronary NEAR(event? or disease? or arter\*)” |
| 1. “myocard\* infarct\*” |
| 1. “myocard\* isch\*emia” |
| 1. “stemi” |
| 1. “st elevation NEAR (acute coro\* syndrome or myocard\* infarc\*)” |
| 1. “Nstemi” |
| 1. “Non st elevation NEAR(acute coro\* syndrome? or myocard\* infarc\*)” |
| 1. “Steacs” |
| 1. “Nsteacs” |
| 1. “Heart NEAR(attack or pain)” |
| 1. “Chest pain” |
| 1. “Cardiac\*” |
| 1. “Ischaem\* heart disease\*” |
|  |
| Pre-Hospital |
| 1. “Pre-hospital\*” |
| 1. “Emergency care” |
| 1. “Point of care test\*” |
| 1. “Point-of-care system?” |
| 1. “Early diagnosi\*” |
| 1. “Out of hospital” |
| 1. “Emergency Medical Services” |
|  |
| Clinical decision support systems |
| 1. “Clinical decision support systems?” |
| 1. “Computeri?ed decision support systems?” |
| 1. “Algor\*thm” |
| 1. “Diagnos\*” |
| 1. “Diagnos\* NEAR(accuracy or differential\* or decision\* or tool\*)” |
| 1. “Predict\*” |
| 1. “Predict \* NEAR (pathway? or tool? or decision?)” |
| 1. “Clinical? NEAR (pathway? or tool? or decision?)” |
| 1. “Triage” |

**Appendix 2.**

|  |
| --- |
| Data Extraction form template. |
| 1. Study number |
| 1. Date of extraction |
| 1. Extractor name |
| 1. Title |
| 1. First Author |
| 1. Publication type |
| 1. Study type |
| 1. Language |
| 1. Study Year |
| 1. Location |
| 1. Setting |
| 1. Funding |
| 1. Participant location |
| 1. Study length |
| 1. Age greater than 18? |
| 1. Pre-hospital? |
| 1. Clinical decision support systems involved Examination/Vital signs? |
| 1. Clinical decision support systems involved Biomarkers? |
| 1. Clinical decision support systems involved ECG |
| 1. Clinical decision support systems involved patient history |
| 1. Name of clinical decision support systems involved |
| 1. Decision maker (GP/Paramedic/Computer etc.) |
| 1. Myocardial infarction definition |
| 1. Type of ACS examined (e.g. STEMI/NSTEMI/all ACS) |
| 1. Enrolment period |
| 1. Sampling Method |
| 1. Length of time for outcome study |
| 1. Number of Participants |
| 1. Number lost to follow-up |
| 1. Mean age |
| 1. Gender percentage |
| 1. Outcome 1 type |
| 1. Outcome 1 percentage |
| 1. Outcome 1 number |
| 1. Outcome 2 type |
| 1. Outcome 2 percentage |
| 1. Outcome 2 number |
| 1. Independent predictors |
| 1. Sensitivity |
| 1. Specificity |
| 1. Positive Predictive Value |
| 1. Negative predictive Value |
| 1. c-Statistic |
| 1. Validation? |
| 1. Notes |
| 1. Quality of Evidence (QUADAS) |
| 1. Include in study? |
| 1. Reasoning if not |