Misdiagnosis of acute myocardial infarction: A systematic review of the literature

Short running title: Misdiagnosis of acute myocardial infarction

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Abstract

Despite the availability of tests to diagnose acute myocardial infarction (AMI), cases are still missed. We systematic reviewed the literature to determine how missed AMI has been defined, the reported rates of misdiagnosed AMI, the outcomes patients with misdiagnosed AMI have, what diagnosis was initially suspected in missed AMI cases, and what factors are associated with misdiagnosed AMI. We searched MEDLINE and EMBASE in September 2020 for studies that evaluated missed AMI. Data was extracted from studies that met the inclusion criteria and the results were narratively synthesized. A total of 15 studies were included in this review. The number of patients with missed AMI in individual studies ranged from 64 to 4,707. There was no consistently used definition for misdiagnosed AMI but most studies reported rates of approximately 1-2%. Compared to AMI that was recognized, one study found no difference in mortality for misdiagnosed AMI at 30 days and 1 year. The common initial misdiagnoses that subsequently had AMI were ischemic heart disease, non-specific chest pain, gastrointestinal disease, musculoskeletal pain and arrhythmias. Reasons for missed AMI include incorrect electrocardiogram interpretation and failure to order appropriate diagnostic tests. Hospitals in rural areas and those with a low proportion of classical chest pain patients that turned out to have AMI were at greater risk of missed AMI. Misdiagnosed AMI is an unfortunate part of everyday clinical practice and better training in electrocardiogram interpretation and education about atypical presentations of AMI may reduce the number of misdiagnosed AMI.

Keywords: Acute myocardial infarction; misdiagnosis; prognosis

Introduction

Acute myocardial infarction (AMI) is a significant global cause of adult death and disability. In the United States, there are more than 800,000 cases of myocardial infarction each year[1] and in the United Kingdom there are more than 100,000 hospital admission each year for AMI.[2] Missing cases of AMI is potentially disastrous for patients as they can have ventricular arrhythmias causing cardiac arrests or sudden death,[3] heart failure[4] or structural heart problems such as ventricular septal rupture, papillary muscle rupture and catastrophic ventricular free wall rupture.[5]

Despite current clinical practice where there are multiple investigations available for the diagnosis of AMI (such as electrocardiogram, plasma troponins, coronary imaging with or without intervention), there are still misdiagnosed AMI. This is likely because patients may not present with chest pain[6] and as such do not receive these tests despite their availability in emergency settings. Furthermore, patients may present to other healthcare professionals including primary care[7] where their symptoms may not be initially recognized and diagnostic test are less accessible.

Several studies have been conducted to evaluated misdiagnosis of AMI. These studies vary in methodology from single center reports[8-11] to large multicenter database studies.[12-14] They take place in different settings including emergency departments[8,9,12,15] and primary care.[10,11] As misdiagnosis of AMI has potential serious medicolegal consequences, there are also reports from malpractice claim reports.[11,16] In view of the importance of diverse literature on missed AMI we conducted a systematic review of the literature to determine how misdiagnosis of AMI has been defined, the reported rates of misdiagnosed AMI, the outcomes experienced by patients with misdiagnosed AMI, what was initially suspected in cases that were missed, and what factors are associated with misdiagnosed AMI.

Methods

Eligibility criteria

We selected studies that evaluated misdiagnosis of AMI. The studies had to report one or more of the following: i) the number of misdiagnosis of AMI cases within a defined population, ii) factors that differ between misdiagnosed AMI and recognized AMI, iii) outcomes associated with misdiagnosed AMI or iv) reasons for misdiagnosed AMI. There was no restriction on the definition of misdiagnosis of AMI and it was one of the aims to determine how it was defined in the literature. Outcomes included cardiovascular events, rehospitalization and mortality. In addition to clinical studies, reports from medicolegal claims were included provided they reported the required methodology and outcomes in sufficient detail. There was no restriction based on study design, cohort type or language of the report but original data had to be presented.

Search strategy

We searched MEDLINE and EMBASE using OVID with no date or language restriction in September 2020. The exact search terms were: (missed acute myocardial infarction or missed myocardial infarction or missed acute coronary syndrome) OR (Missed diagnos* adj3 (acute myocardial infarction or myocardial infarction or acute coronary syndrome)) OR (unrecogni* adj1 (acute myocardial infarction or myocardial infarction or acute coronary syndrome). We reviewed the bibliography of relevant studies and reviews for additional studies that met the inclusion criteria.

Study selection and data extraction

Two reviewers (CSK and SB) screened all titles and abstracts retrieved from the search for studies that met the inclusion criteria. The studies that potentially met the inclusion criteria were reviewed and the final decision to include or exclude studies was made by consensus. The data extraction was carried out by CSK and checked by ZA and VW independently. Data was

collected on study design, country of study origin, year, sample size, mean age, % male, inclusion criteria, definition of missed AMI/acute coronary syndrome (ACS), rate of missed AMI/ACS, patient outcomes, initial misdiagnosis and factors associated with misdiagnosis.

Risk of bias assessment

Methodological quality assessment of the included studies was based on the risk of bias assessment tool by Hayden et al.[17] This was conducted with consideration of the following: i) study design, ii) definition of AMI/ACS, iii) presence of a control group, iv) loss to follow up, v) adjustments in the statistical analysis and vi) generalizability to a contemporary AMI cohort. For the definition of AMI/ACS studies were considered high quality if they evaluated whether the cause for initial admission was potentially related to AMI. For the presence of control, patients should have been patients with AMI diagnosis that were not missed or those with chest pain. This was done by one reviewer (CSK) and checked independently by another reviewer (ZA).

Data analysis

Data was extracted into pre-designed and piloted tables. Study findings were narratively synthesized. Considerable heterogeneity in the study methodology meant that we did not perform statistical pooling or meta-analysis.

Results

Description of included studies

A total of 15 studies[8-16,18-23] were included in the review after excluding studies that did not meet the inclusion criteria (Figure 1).

Table 1 shows the study design, patient characteristics and inclusion criteria for the included studies. There were two prospective cohort studies, two case-control studies, ten retrospective cohort studies and one cohort study of unclear design. These studies took place

in the Hong Kong, United States, Canada, Italy and Australia between 1979 and 2017. The number of patients among the included studies ranged from 64 cases of missed AMI to 4,707 cases of missed AMI out of 371,638 cases of AMI that were not missed. The mean age ranged from 47.8 years to a median of 80 years and the average proportion of patients that were male ranged from 36.1% to 70.4%.

Quality assessment of included studies

The methodological quality assessment of included studies is shown in Supplementary Table 1. Two of the included studies were prospective in nature while seven studies had low risk of bias related to definitions for missed AMI and nine studies used reliable control groups. Ten studies had low risk of bias for loss to follow up or missing data and only two of the studies adjusted for confounders in their statistical analysis. Four studies analyzed data from a cohort in the last 10 years.

Definitions and rates for missed AMI

Many definitions were used to define missed AMI/acute coronary syndrome (ACS). Chan et al considered whether patients had an ED diagnosis that matched the final hospital diagnosis of AMI. [8] Other studies considered patients with an admission with a diagnosis of AMI and whether they presented in the preceding 7 or 30 days to an emergency department for any reason or a presentation that may be consistent with myocardial ischemia.[9,12-15,19,20] Jaffery et al considered missed AMI as any physician encounter not necessarily ED 30 days prior to hospitalization with AMI.[10] Another type of missed AMI were those that were identified from malpractice claims from insurance companies as described by Pelberg et al and Sequist et al.[11,18] Williams et al used the criteria of failure for STEMI patients to receive reperfusion therapy within 4 hours[22] while Singer et al considered the patients classified as low risk based on predictions tools who eventually had a final diagnosis of AMI as missed AMI.[21]

The rate of missed AMI varied considerably across the studies. The rates of missed AMI were as high as 27.0% in the small retrospective study in Hong Kong by Chan et al[8] but as low as 0% in the prospective study of 1,116 patients in Canada by Scheuermeyer et al.[19] Several studies report rates that were around 1-2%[12,13,15,20,23] including 1.3% reported by the largest study of over 300,000 Medicare patients by Wilson et al.[14]

Outcomes associated with missed AMI

Mortality with missed AMI was not higher than that reported in the control arm for several studies.[9,12,13] However, other studies suggest high mortality rates for patients with missed AMI (Wilson et al 24.0%, McCarthy et al 25.0%, Rusnak et al 81.5%). The only adjusted estimate for mortality found no difference at 30 days and 1 year.[13] Chan et al reported greater angina (20.9% vs 14.7%), recurrent non-fatal myocardial infarction (4.7% vs 3.4%), heart block (23.3% vs 14.7%) and heart failure (46.5% vs 40.5%). Readmission rates are also high for missed AMI; McCarthy et al found that 95.0% were readmitted and Wilson et al. found that 24% were readmitted within 30-days. The financial implications of missed AMI are also significant; even in the oldest studies from 1989 indemnity payments from malpractice occurred in 36.0% of cases which were up to $500,000[18] and the average insurance loss was £113,806.[16]

Initial misdiagnosis for missed AMI

Table 4 shows the initial diagnosis for patients who later went on to have a missed AMI. The common initial diagnoses included non-AMI ischemic heart disease, non-specific chest pain, abdominal pain/esophageal reflux/gastritis/duodenitis, musculoskeletal pain and arrhythmias. Less common initial misdiagnoses were non-specific symptoms such as dizziness or vertigo, syncope, malaise and fatigue and anxiety.

Factors associated with missed AMI

Many factors have been described to be associated with missed AMI as shown in Supplementary Table 2. Sharp et al found that women (OR 1.3 95%CI 1.2-1.5, p<0.001) and black ethnicity (OR 1.3 95%CI 1.1-1.6, p=0.0077) patients were overrepresented among missed AMIs. McCarthy et al found that 40% of the 20 cases of missed AMI had incorrect electrocardiogram (ECG) interpretation of which five had ST-elevation and three had ST changes that were read as normal.[15] In the series of malpractice claims by Pelberg et al, the reason for misdiagnosis of AMI included a failure to order diagnostic tests (18.7%), misdiagnosis (14.7%) and improper management (14.7%). In the study by Sequist et al, ECG misinterpretation was significantly increased in the group with missed AMI compared to controls (27.8% vs 0%, p<0.001);[11] Williams et al reported that failure to identify STEMI on ECG was a major contributor to missed AMI.[22] The only study that used multivariable adjustments to determine factors associated with missed AMI found that rural hospital (OR 2.61 95%CI 1.84-3.70) and public hospitals (OR 1.33 95%CI 1.08-1.61) were associated with greater missed AMI and that the most protective hospital characteristic for missed AMI was having above a minimum level of chest pain acuity (which was defined as hospitals where greater than 1.5% of all chest pain had AMI) (OR 0.23 95%CI 0.19-0.27).[14]

Discussion

Our review has several key findings. First, there is no consistent definition for missed AMI as most studies consider ED diagnosis compared to hospital diagnoses at a later point in time. However, patients do not always present first to ED and there may be other missed opportunities to diagnose AMI in healthcare settings such as primary care. Second, rates of missed AMI are infrequent representing in most studies 1-2% of cases in emergency departments. Third, the evidence is inconsistent regarding harm associated with missed AMI. Fourth, there are probably opportunities to reduce the number of missed AMI with better

education about atypical symptoms and improved training of ECG interpretation. Finally, a substantial portion of the evidence on missed AMI is not generalizable to contemporary practice because they took place more than ten years ago where current practice of early electrocardiogram, rapid access to highly sensitive troponins and emergency revascularization when needed were not widely practiced.

An important review finding is the significant methodological heterogeneity in the studies that evaluate missed AMI. One of the key issues is that there is no definition for missed AMI. Many of the included studies center the initial evaluation of patients from ED and consider missed AMI as those who are discharged from ED and subsequently are readmitted with AMI. The most interesting group of patients are those with an initial admission to ED should have been for a complaint that could be a typical or atypical feature of AMI as the initial visit may have been an opportunity to detect the AMI before it was detected at a later time as the patient may have been admitted for an unrelated reason. It should also be considered that a patient may develop AMI at any time, for example, despite negative diagnostic testing in ED, subsequent plaque rupture and AMI can occur after discharge. The other source of heterogeneity is the timing between ED discharge and evaluation of AMI readmission. Most studies use seven days as the time from ED discharge to readmission with AMI, and a few studies used 30 days. The longer the time interval between ED discharge and follow-up for AMI, the weaker the association between initial presentation and missed AMI given the potential for many precipitating factors to occur over time between ED discharge and the AMI event. Furthermore, ED may not be the first setting where patients present to healthcare professionals with AMI. There is dearth of contemporary evidence regarding the presentation of patients to primary care, missed diagnosed and subsequent missed AMI. Another important source of information about missed AMI is from the medicolegal literature. Many of the early studies identified from this review were from medical claims, and these studies reduced in

frequency in the more recent published literature. This may be the case that in more recent times, there may be reluctance for hospitals to admit fault and disclose information about cases where AMI are missed and would rather settle cases out of court when there are concerns about malpractice. However, the data from these individual cases are valuable as case notes and patient care are reviewed in detail so that reasons for the clinical decisions and outcomes could be determined.

An unexpected finding of this study was the lack of consistent evidence to suggest that patients with missed AMI were associated with increased risk of harm. One reason for this relates to selection bias where only patients who survive the missed myocardial infarction can go on to be diagnosed in hospital. The ones who died from out-of-hospital cardiac arrest are not captured in the studies. We found no studies that described out-of-hospital arrests after initial review in ED or primary care. Should patients die from sudden cardiac arrest outside of hospital, the patient may not be considered as a case of missed AMI which, in most literature, is measured by rehospitalization for AMI. In the second case where patients develop heart failure, the patient may go on to present weeks or months later and the missed AMI may be undetected until the workup for the etiology for heart failure.

The care of patients with AMI has changed from the time when many of the earlier studies took place and this has major implications. The current practice of 24 hours a day seven days a week access to emergency revascularization with primary percutaneous coronary intervention and routine use of electrocardiogram and high sensitivity troponins in the assessment of chest pain has significantly improved outcomes for patients with AMI. This is reflected in the study in Vancouver, Canada which reported no cases of missed AMI.[19] However, not all healthcare centers that manage patients who present acutely with chest pain have access to these tests, especially rural hospitals where there may be less frequent experience with management of chest pain and AMI. As highlighted by Wilson et al which

used a large population of Medicare patients, the factor most associated with missed AMI was rural hospitals and the most protective hospital characteristic for missed AMI was a hospital who regularly saw patients presenting with AMI.[14]

The findings of this review have several clinical implications. Firstly, cases of missed AMI may be reduced with better training in ECG interpretation for junior or less experienced staff. Secondly, while we expect in contemporary practice that most patients with chest pain will have an ECG and troponin test, better education regarding the atypical or non-chest pain presentation for AMI especially in high risk groups such as women or diabetic patients may reduce the cause of missed AMI attributed to a failure to order diagnostic tests. This is particularly important in patients for whom AMI has not been excluded and diagnoses such as non-specific chest pain, esophageal reflux, gastritis/duodenitis or musculoskeletal pain have been made. Thirdly, this review highlights the need to consider missed AMI on a local organizational level, especially when this is occurring more than may be expected. Fourthly, there is a need for more data from current practice about missed AMI in order to improve patient care. Finally, missed diagnosis of AMI in patients presenting to primary care requires further investigation.

There are several limitations with this review. We were unable to statistically pool the results because there was significant methodological heterogeneity. Many of the studies are out-of-date as some took place more than 20 years ago and the population with AMI and the clinical practice in the community, emergency departments and hospital has changed. Most of the literature appears to center on ED department as the setting where AMI is missed, which does not reflect clinical practice where patients may present to primary care or directly to outpatient clinics where their AMI is missed.

In conclusion, missed AMI is an unfortunate part of clinical practice. It is challenging to understand because there is no consistent definition and it is important because it represents

a barrier to delivering good care to all patients. While much of the literature focuses on misdiagnoses in ED department, patients may also have unrecognized AMI in the primary care setting which is less well understood. Better training in ECG interpretation and education about non-chest pain or atypical presentations of AMI may reduce the number of missed AMI.

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Table 1: Study design, patient characteristics and patient inclusion criteria

Study ID	Design; Country; Year	Sample size	Mean age	% male	Inclusion criteria
Chan 1998	Retrospective cohort study; Hong Kong; 1995.	43 with undiagnosed AMI out of 159	67.2	70.4	Patients admitted to the coronary care unit with diagnosis of AMI.
Chang 2019	Retrospective cohort study; Dallas-Fort Worth, USA; 2009 to 2015.	766 had missed ACS at 7 days, 2,117 had missed ACS at 30 days out of 24,914	64.0	60.1	Patients diagnosed with acute coronary syndrome who were seen and discharged from ED 7 and 3 days before visit to Dallas-Fort Worth Hospital.
Jaffery 2007	Retrospective cohort study; Detroit, USA; 2004.	68 had encounter out of 303 AMI cases	66.8	59.1	Patients admitted with AMI to a US tertiary center with Health Alliance Plan medical insurance.
McCarthy 1993	Post-hoc analysis of prospective study and case-control study; New England, USA; 1979-1981.	20 missed AMI in 1050 cases	-	p	Patients were admitted with AMI to one of six New England hospitals.
Moy 2015	Retrospective cohort study; 9 states in USA; 2007.	993 missed AMI in 112000 cases	-	-	Patients age 18 years or older with AMI index admission between February and December 2007.
Pelberg 1989	Retrospective cohort study; Pennsylvania, USA; 1977-1987.	64 missed AMI	60	70	Patients in the files of the Pennsylvania Hospital Insurance Company with legal action alleging a missed diagnosis of myocardial infarction in the emergency room.
Prattichizzo 1996	Cohort study; Italy; 1992-1994.	16 missed AMI in 1,237 cases	-	-	Patients with cardiovascular diseases admitted to a Division of Internal Medicine.
Rusnak 1989	Case-control study; USA; 1981-1985.	65 undiagnosed AMI and 65 controls	-	-	Patients had closed medical malpractice claims against St. Paul Fire and Marine Insurance Company and Spectrum Emergency Care with a diagnosis of AMI that was missed in the emergency department.
Scheuermeyer 2012	Prospective cohort study; Vancouver, Canada; 2006.	0 missed AMI out of 1,116 patients	54.7	60.0	Patients in the emergency department with potential ischemic chest pain.

Schull 2006	Retrospective cohort study; Ontario, Canada; 2002-2003.	419 missed AMI out of 19,663 cases	68.3	63.0	Patients with AMI admitted to an Ontario hospital.
Sequist 2005	Case-control study; USA; 1986-2002.	18 missed AMI out of 62 cases	47.8	36.1	Patients with no previous history of coronary heart disease presenting to primary care physician practices with potential cardiac ischemia.
Sharp 2020	Retrospective cohort study; USA; 2009-2017.	2,874 had ED visit within 30 days, 574 were probable missed AMI out of 44,473 cases	68.0	63.3	Patients with AMI hospitalization who were age 18 years or older with Kaiser Permanente health plan.
Singer 2017	Prospective cohort study; USA; Unclear.	434	Median 57	58.0	Patients age 21 and older with chest pain presenting to one of seven emergency departments.
Williams 2019	Retrospective cohort study; Australia; 2011-2016.	100 missed AMI out of 1,392 STEMI.	64.1	70.0	Patients with STEMI admitted to one of 37 hospitals in the health district services in Australia.
Wilson 2014	Retrospective cohort study; USA; 2004-2005.	4,707 cases with ED visit within 7 days out of 371,638 cases of AMI.	Median 80	48.0	Patients with age 65 years or older with AMI who presented to the emergency department.

Table 2: Definition and rate of missed acute myocardial infarction/acute coronary syndrome

Study ID	Definition of missed AMI/ACS	Rate of missed AMI/ACS
Chan 1998	Patient with ED diagnosis did not match the final diagnosis of AMI.	Missed AMI: 43/159 (27.0%)
Chang 2019	Patient with discharged 7 or 30 days from ED before an admission with ACS diagnosis.	Missed ACS within 7 days: 766/24914 (3.2%). Missed ACS within 30 days: 2117/24914 (8.8%).
Jaffery 2007	Patients with physician encounter 30 days prior to AMI.	Physician encounter within 30 days: 68/303 (22.4%).
McCarthy 1993	Patients in the ED with chest pain or other symptoms suggestive of ischemia that were sent home and subsequently returned to hospital with AMI.	Missed AMI 20/1050 (1.9%).
Moy 2015	Patients who visited an ED with chest pain or cardiac condition that were related from the ED and subsequently returned to hospital within 0 to 7 days with a principal diagnosis of AMI.	Missed diagnosis of AMI: 993/112000 (0.9%).
Pelberg 1989	Patients with missed myocardial infarction that resulted in legal action alleging a missed diagnosis of myocardial infarction in the emergency room.	75 cases of missed AMI.
Prattichizzo 1996	Unclear definition for missed AMI.	Missed AMI: 16/1237 (1.3%).
Rusnak 1989	Patients with closed malpractice claims against St Paul Fire and Marine Insurance Company and Spectrum Emergency Care Inc with at least $1,000 spent on legal fees and claims of the failure to diagnose or the improper treatment of an AMI that occurred in ED that were reported by either physicians or hospitals.	65 cases of missed AMI and 65 controls.
Scheuermeyer 2012	Patients with chest pain of potential cardiac origin that were triaged either to a monitored bed or a waiting room chair who had been discharged and had acute coronary syndrome within 30 days.	Missed ACS: 0/1116.
Schull 2006	Patient with a diagnosis of the previous visit to ED within 7 days matched a list of symptoms or illnesses and patient presented again with AMI.	Missed AMI 419/19663 (2.1%).
Sequist 2005	Patients with missed myocardial infarction from malpractice claims files of the Controlled Risk Insurance Company.	18 cases of missed AMI and 54 controls with chest pain diagnosis.

Sharp 2020	Patients with diagnostic error defined by patients given a non-AMI ED treat-and-release discharge diagnosis who returned within 30 days with an AMI hospitalization.	Missed AMI from look back analysis 573/44473 (1.3%)
Singer 2017	Patients classified as low risk based on several predictions who had a final diagnosis of AMI.	Missed AMI in low risk patients based on: HEART-2: 3.6% (1.3%-8.7%) HEART-1: 4.3% (1.8%-9.5%) TIMI: 0% (0%-14.1%) GRACE: 6.3% (0.3%-32.3%) EDACS: 0.9% (0.2%-3.5%) Unstructured impression without cTn: 5.7% (2.7%-11.2%) Unstructured clinical impression with serial cTn: 0% (0%-3.9%)
Williams 2019	Patients with STEMI who failed to receive reperfusion therapy within 4 hours.	Missed AMI: 100/1392 (7.2%)
Wilson 2014	Patients with AMI hospital admission within 7 days of an ED discharge for a condition suggestive of cardiac ischemia.	Missed AMI: 4774/371638 (1.3%)

ED=emergency department, AMI=acute myocardial infarction, ACS=acute coronary syndrome, STEMI=ST-elevation myocardial infarction

Table 3: Outcomes for patients with missed acute myocardial infarction

Study ID	Missed AMI and identified AMI outcomes
Chan 1998	Missed vs identified AMI: Death: 6/43 (14.0%) vs 19/116 (16.4%) Transfer to another hospital: 5/43 (11.6%) vs 5/116 (4.3%) Home: 32/43 (74.4%) vs 92/116 (79.3%) Recurrent angina: 9/43 (20.9%) vs 17/116 (14.7%) Recurrent non-fatal myocardial infarction: 2/43 (4.7%) vs 4/116 (3.4%) Ventricular tachycardia/fibrillation: 3/43 (7.0%) vs 5/116 (4.3%) 2°/3° heart block 10/43 (23.3%) vs 17/116 (14.7%) Heart failure 20/43 (46.5%) vs 47/116 (40.5%)
McCarthy 1993	Missed AMI: Readmission rate: 19/20 (95.0%). Death rate: 5/20 (25.0%). Mortality for missed AMI: 10% (1.2%-30.9%).
Moy 2015	Nearly half of probable misdiagnoses were admitted on the first day after discharge. Mortality rate for missed AMI vs not missed AMI: 42/993 (4.23%) vs 7413/110980 (6.68%).
Pelberg 1989	Indemnity payments from malpractice insurance 27/75 (36.0%). Settle without payment 17/75 (22.7%). Indemnity payments ranged from $1,667 to $500,000 and expense per case $58.00 to $73,135.
Rusnak 1989	Died 53/65 (81.5%) vs 2/65 (3.1%). Average insurance loss £113,806±178,330.
Schull 2006	Missed AMI and risk of mortality at: 30 days: OR 0.90 (0.3-1.3). 1 year: OR 1.03 (0.8-1.3).
Williams 2019	Missed AMI mortality: 24/100 (24%). Missed vs identified AMI: Length of stay: 5.5±4.5 days vs 4.3±3.7 days. 30-day readmission: 24/100 vs 43/1292.

AMI=acute myocardial infarction, OR=odds ratio

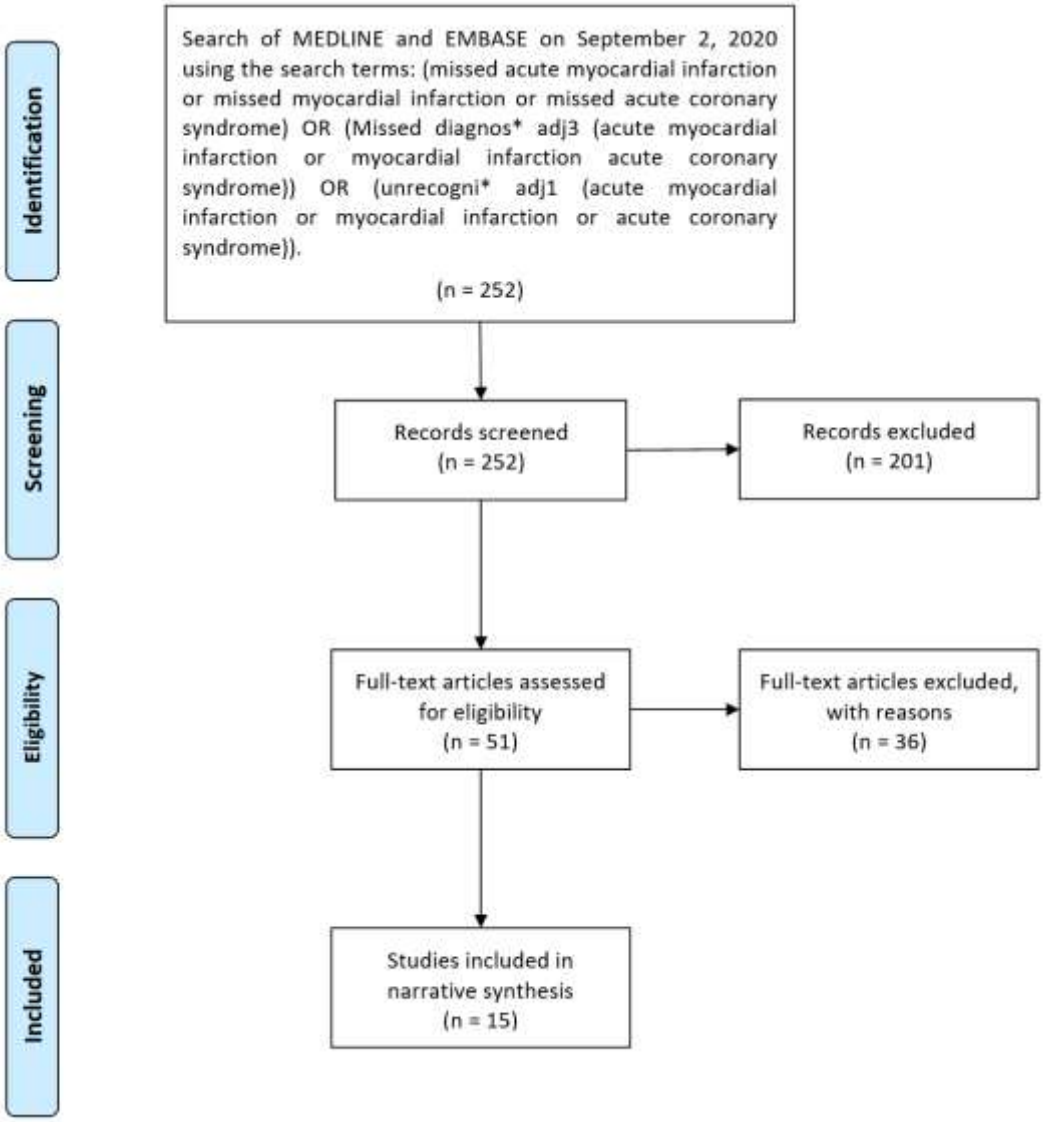
Table 4: Initial misdiagnosis for patients with missed acute myocardial infarction/acute coronary syndrome

Study ID	Initial misdiagnosis
Chan 1998	Unstable angina: 10/43 (23.3%) Ischemic heart disease: 6/43 (14.0%) Chest pain: 8/43 (18.6%) Heart failure: 8/43 (18.6%) Heart block/bradycardia: 3/43 (7.0%) Epigastric pain: 2/43 (4.7%) Chest infection/septicemia: 2/43 (4.7%) Vertigo: 2/43 (4.7%) Cerebrovascular accident: 1/43 (2.3%) Diabetes mellitus with poor control: 1/43 (2.3%)
Chang 2019	Diagnosis at 7 days:

	Chest pain: 442/766 (57.7%) Atherosclerotic disease: 149/766 (19.5%) Heart failure: 98/766 (12.8%) Painful respiration: 23/766 (3.0%) Syncope: 22/766 (2.9%) Esophageal reflux: 7/766 (0.9%) Epigastric pain: 7/766 (0.9%) Old MI: 2/766 (0.3%) Abnormal ECG: 1/766 (0.1%) Diagnosis at 30 days: Chest pain: 1117/2117 (52.8%) Atherosclerotic disease: 364/2117 (17.2%) Heart failure: 411/2117 (19.4%) Painful respiration: 64/2117 (3.0%) Syncope: 77/2117 (3.6%) Esophageal reflux: 36/2117 (1.0%) Epigastric pain:18/2117 (0.1%) Old MI: 2/2117 (0.1%) Abnormal ECG: 2/2117 (0.1%) Esophageal disorder: 5/2117 (0.2%)
McCarthy 1993	Gastrointestinal disease: 4/20 (20.0%) Chest pain of unknown etiology: 4/20 (20.0%) Musculoskeletal pain 2/20: (10.0%) Pulmonary disease 1/20: (5.0%) Arrhythmia: 1/20 (5.0%) Congestive heart failure: 1/20 (5.0%) Ischemic heart disease: 7/20 (35.0%)
Moy 2015	Misdiagnosis: Nonspecific chest pain 549/1427: (45.5%) Coronary atherosclerosis and other heart disease: 220/1427 (15.4%) Other lower respiratory disease: 127/1427 (8.9%) Abdominal pain: 94/1427 (6.6%) Congestive heart failure: 77/1427 (5.4%) Cardiac dysrhythmias: 47/1427 (3.3%) Esophageal disorder: 36/1427 (2.5%) Syncope: 32/1427 (2.5%) Other gastrointestinal disorders: 30/1427 (2.2%) Essential hypertension: 30/1427 (2.1%) Malaise and fatigue: 25/1427 (1.8%) Dizziness or vertigo: 24/1427 (1.7%) Acute myocardial infarction: 20/1427 (1.4%) Gastritis and duodenitis: 16/1427 (1.1%)
Sequist 2005	Gastrointestinal related: 7/18 (38.9%) Upper respiratory infection/pneumonia/pleurisy: 5/18 (27.8%) Anxiety: 1/18 (5.6%) Musculoskeletal: 1/18 (5.6%) Angina: 2/18 (11.1%)
Sharp 2020	Reason for ED treat-and-release Nonspecific chest pain: 465/2874 (16.2%) Other lower respiratory tract infection: 239/2874 (8.3%)

	Abdominal pain: 161/2874 (5.6%) Spondylosis, intervertebral disc disorder, other back problem: 119/2874 (4.1%) Urinary tract infection: 98/2874 (3.4%) Other injury due to external cause: 97/2874 (3.4%) Superficial injury, contusion: 94/2874 (3.3%) Other gastrointestinal disorder: 92/2874 (3.2%) COPD and bronchiectasis: 91/2874 (3.2%) Cardiac dysrhythmias: 88/2874 (3.1%) Other connective tissue disease: 86/2874 (3.0%) Malaise and fatigue: 80/2874 (2.8%) Other non-traumatic joint disorder: 78/2874 (2.7%) Congestive heart failure: 76/2874 (2.6%) Diabetes mellitus with complication: 71/2874 (2.5%) Unclassified: 64/2874 (2.2%) Conditions associated with dizziness and vertigo: 62/2874 (0.22%) Genitourinary symptoms and ill-defined conditions: 59/2874 (2.1%) Fluid and electrolyte disorder: 59/2874 (2.1%) Headache including migraine: 58/2874 (2.0%)

Figure 1: Flow diagram of study inclusion



Supplementary Table 1: Quality assessment of included studies

Study ID	Study design	Definition of AMI/ACS	Presence of control group	Loss to follow up	Statistical analysis for outcomes	Generalizable to contemporary practice
Chan 1998	No, retrospective.	Yes, ED diagnosis vs final diagnosis on same admission.	Yes, other patients with AMI.	Yes, not reported.	No, not adjusted.	No, cohort from 1995.
Chang 2019	No, retrospective.	No, patient could have gone to ED before for any reason.	Yes, other patients with ACS.	Yes, not reported.	Not applicable.	Yes, cohort from 2009 to 2015.
Jaffery 2007	No, retrospective.	No, patient could have seen healthcare professional before for any reason.	No, not defined clearly.	No, 76 patients had no documentation of encounters.	Not applicable.	No, cohort from 2004.
McCarthy 1993	No, retrospective and case-control.	Yes, ED visit with symptoms of ischemia before readmission for AMI.	Yes, no other AMI patients matched to site.	Yes, 11% initially missing follow up data and 2.6% could not be traced from original logbook or hospital records.	No, not adjusted.	No, cohort from 1979-1981.
Moy 2015	No, retrospective.	Yes, ED visit with chest pain or cardiac condition before readmission for AMI.	Yes, other patients with AMI.	Yes, 2.9% exclude because of missing data.	No, not adjusted.	No, cohort from 2007.
Pelberg 1989	No, retrospective.	No, missed AMI that resulted in legal action.	No, no control group.	No, unclear.	No, not adjusted.	No, cohort from 1977-1987.

Prattichizzo 1996	No, likely retrospective.	Unclear.	No, patients with cardiovascular disease.	No, unclear.	Not applicable.	No, cohort from 1992-1994.
Rusnak 1989	No, retrospective case-control.	No, malpractice claims for missed AMI.	No, not clearly defined.	No, unclear.	No, not adjusted.	No, cohort from 1981-1985.
Scheuermeyer 2012	Yes, prospective.	Yes, ED visit for chest pain of potential cardiac origin.	Yes, other patients with chest pain triaged to monitored bed or waiting room chair.	Yes, 24 loss to follow up.	Not applicable.	No, cohort from 2006.
Schull 2006	No, retrospective.	Yes, ED visit with symptoms from list and presented again with AMI.	Yes, other patients with AMI.	Yes, not reported.	Yes, adjusted.	No, cohort from 2002-2003.
Sequist 2005	No, retrospective case-control.	No, malpractice claims for missed AMI.	No, controls were chest pain encounters matched on month and day of encounter.	No, data missing for at least 8 cases and 25 controls.	Not applicable.	No, cohort from 1986-2002.
Sharp 2020	No, retrospective.	Yes, diagnostic error given a non-AMI treat-and-release discharge diagnosis and return with AMI.	Yes, other patients with AMI.	Yes, missing data for income 0.3-0.5% and for smoking 2.1-5.7%.	Not applicable.	Yes, cohort from 2009-2017.
Singer 2017	Yes, prospective.	No, low risk classification which turned out to be AMI.	Yes, other patients with AMI.	Yes, not reported.	Not applicable.	Yes, likely contemporary cohort.
Williams 2019	No, retrospective.	No, STEMI that failed to received	No, control is based on low risk by	Yes, not reported.	No, not adjusted.	Yes, cohort from 2011-2016.

		reperfusion within 4 hours.	different prediction rules.			
Wilson 2014	No, retrospective.	Yes, hospitalized with symptoms of ischemia before readmission for AMI.	Yes, other patients with AMI.	Yes, missing 1.55% or unreliable data 0.07%.	Yes, adjusted.	No, cohort from 2004-2005.

Supplementary Table 2: Factors associated with missed acute myocardial infarction

Study ID	Factors associated with missed AMI
Chan 1998	Missed vs identified AMI: Mean age: 68.1 vs 66.9, p>0.05 Male: 34/43 vs 78/116, p>0.05 Q wave: 40/43 vs 108/116, p>0.05 Typical angina: 29/43 vs 102/116, p<0.01 Absence of chest pain: 11/43 vs 12/116, p<0.05 Other symptoms: 3/43 vs 2/116, p>0.05 Spring: 12/43 vs 36/116, p>0.05 Summer 11/43 vs 26/116, p>0.05 Autumn 14/43 vs 23/116, p>0.05 Winter 6/43 vs 31/116, p>0.05 Time of presentation: 0900-2100: 24/43 vs 64/116, p>0.05 2100-0900: 19/43 vs 52/116, p>0.05 Diabetes mellitus: 7/43 vs 21/116, p>0.05 ECG ST elevation: 16/43 vs 95/116, p<0.001 ST depression: 3/43 vs 4/116, p>0.05 Non-specific ST changes: 10/43 vs 4/116, p<0.001 Normal 33/43 vs 13/116, p<0.01 Coronary care unit: 11/43 vs 78/116, p<0.01 Time of confirmed diagnosis mean 1.8 vs 0 days Thrombolytic therapy 13/43 vs 88/116, p<0.01 Not given due to delay: 15/43 vs 7/116, p<0.01
Chang 2019	Missed vs identified ACS at 7 days: Mean age: 59.7 vs 64.1 Male: 473/766 vs 14,511/24,148 White: 538/766 vs 17,333/24,148 Black: 127/766 vs 3,686/24,148 Asian: 15/766 vs 403/24,148 Other: 86/766 vs 2,726/24,148 Latino: 89/766 vs 2,256/24,148 Hypertension: 426/766 vs 11,489/24,148 Diabetes mellitus: 213/766 vs 6,804/24,148 Tobacco: 162/766 vs 5,435/24,148 Heart failure: 143/766 vs 5,216/24,148 Coronary artery disease: 74/766 vs 2,557/24,148 Family history of CAD: 55/766 vs 1,303/24,148 Obesity: 41/766 vs 1,029/24,148 Insured: 305/766 vs 9,001/24,148 Medicaid: 50/766 vs 1,194/24,148 Medicare: 246/766 vs 9,649/24,148 Uninsured: 165/766 vs 4,303/24,148 Day of the week: Sunday 112/766, Monday 125/766, Tuesday 88/766, Wednesday 96/766, Thursday 143/766, Friday 102/766, Saturday 101/766. Missed vs identified ACS at 30 days: Mean age: 60.8 vs 64.3 Male: 1319/2117 vs 13,665/22,797

	White: 1414/2117 vs 16,457/22,797 Black: 399/2117 vs 3,414/22,797 Asian: 38/2117 vs 380/22,797 Other: 266/2117 vs 2,546/22,797 Latino: 262/2117 vs 2,083/22,797 Hypertension: 1177/2117 vs 10,738/22,797 Diabetes mellitus: 657/2117 vs 6,360/22,797 Tobacco: 445/2117 vs 5152/22797 Heart failure: 518/2117 vs 4841/22797 Coronary artery disease: 254/2117 vs 2377/22797 Family history of CAD: 147/2117 vs 1211/22797 Obesity: 118/2117 vs 952/22797 Insured: 797/2117 vs 8,510/22797 Medicaid: 158/2117 vs 1,086/22797 Medicare: 696/2117 vs 9,199/22797 Uninsured: 466/2117 vs 4,002/22797 Day of the week: Sunday 305/2117, Monday 329/2117, Tuesday 284/2117, Wednesday 284/2117, Thursday 352/2117, Friday 287/2117, Saturday 276/2117.
Jaffery 2007	Missed vs identified AMI at 30 days: Mean age: 67.4±13.1 vs 66.6±14.4, p=0.694 Male: 38/68 vs 141/235, p=0.518 White: 43/68 vs 161/235, p=0.177 Black: 21/68 vs 65/235 Other: 3/68 vs 3/235 Prior MI: 22/68 vs 83/235, p=0.651 Prior CABG: 9/68 vs 16/235, p=0.090 Prior PCI: 7/68 vs 26/235, p=0.858 Hypertension: 59/68 vs 157/235, p=0.001 Diabetes mellitus: 26/68 vs 74/235, p=0.298 Current smoking: 20/68 vs 71/235, p=0.899 Family history of CAD: 30/68 vs 68/235, p=0.018 Mean LDL cholesterol: 96.6±39.1 vs 101.5±45.8, p=0.490
McCarthy 1993	Missed AMI patients University hospital 1.9% vs non-university hospital 1.9% Missed vs admitted AMI: Mean age: 60 years vs 66 years Male: 70% vs 54% History of AMI: 20% vs 37% History of nitroglycerin use: 15% vs 32% ST-elevation in 25% of missed AMI while 0% of discharged non-AMI had ST-elevation. For the 20 missed AMI, 12 had correct ECG interpretation while 3 had ST changes that were read as normal or nonspecific while 5 has ST-elevation.
Moy 2015	Missed diagnosis vs correct diagnosis: Mean age: 62.82±15.34 vs 68.06±14.76 years, p<0.001 Male: 60.5% vs 60.1%, p=0.67 Race White: 75.5% vs 76.9%, p=0.16 Black: 10.9% vs 8.3%, p<0.001

	Hispanic: 4.3% vs 6.5%, p<0.001 Other: 9.3% vs 8.4%, p=0.16 Primary expected payer Private insurance 33.1% vs 27.4%, p<0.001 Medicare: 46.0% 58.5%, p<0.001 Medicaid: 8.4% vs 5.2%, p<0.001 Uninsured: 9.5% 6.3%, p<0.001 Other: 3.0% vs 2.7%, p=0.36 Median household income: Highest: 12.7% vs 39.3%, p<0.001 Moderate: 18.6% vs 22.0%, p<0.001 Low: 25.2% vs 26.0%, p=0.41 Lowest: 43.5% vs 33.0%, p<0.001 Paralysis: 1.0% vs 1.6%, p=0.013 Other neurological disorder: 4.8% vs 6.0%, p=0.016 Diabetes: 28.5% vs 32.0% Hypothyroidism: 7.6% vs 9.0%, p=0.013 Renal failure: 12.4% vs 16.1%, p<0.001 Liver failure: 1.3% vs 1.1%, p=0.29 AIDS: 0.1% vs 0.1%, p=0.96 Lymphoma: 0.50% vs 0.51%, p=0.99 Metastatic cancer: 0.6% vs 1.0%, p=0.022 Solid tumor: 1.3% vs 1.5%, p=0.47 Rheumatoid arthritis: 1.9% vs 2.1%, p=0.63 Coagulopathy: 3.1% vs 4.0%, p=0.022 Obesity: 11.1% vs 8.9%, p=0.002 Weight loss: 0.9% vs 1.5%, p=0.002 Fluid and electrolyte disorder: 12.8% vs 18.3%, p<0.001 Chronic blood loss anemia: 0.8% vs 1.4%, p=0.005 Alcohol disorder: 2.4% vs 2.8%, p=0.33 Deficiency anemia: 10.2% vs 14.6%, p<0.001 Drug abuse: 2.9% vs 1.8%, p=0.001 Psychoses: 1.3% vs 1.9%, p=0.028 Depression: 5.2% vs 5.9%, =0.18 Hospital region: Northeast: 27.0% vs 34.0%, p<0.001 Midwest: 16.8% vs 9.9%, p<0.001 South: 49.9% vs 49.9%, p=0.017 West: 6.3% vs 8.9%, p<0.001 Population size: Large metropolitan area: 33.8% vs 56.1%, p<0.001 Small micropolitan area: 31.3% vs 36.3%, p<0.001 Micropolitan area: 20.2% vs 6.3%, p<0.001 Non core-based area: 14.6% vs 1.3%, p<0.001 Hospital ownership: Private, not-for-profit: 62.0% vs 69.2%, p<0.001 Government: 18.9% vs 13.2%, p<0.001 Private, for profit: 19.0% vs 17.6%, p=0.099 Available catheterization laboratory: 35.1% vs 71.2%, p<0.001 Teaching hospital: 22.0% vs 46.7%, p<0.001 Emergency department volume:

	Low: 60.0% vs 32.7%, p<0.001 Medium: 22.4% vs 34.6%, p<0.001 High: 17.6% vs 32.7%, p<0.001 Proportion of admission from emergency department: Low: 71.6% vs 32.5%, p<0.001 Medium: 19.5% vs 34.0%, p<0.001 High: 8.9% vs 33.5%, p<0.001 Hospital occupancy rate: Low: 19.9% vs 3.4%, p<0.001 Medium: 53.0% vs 53.0%, p=0.97 High: 27.1% vs 43.6%, p<0.001 ED crowding on day of visit: Low: 19.9% vs 3.4%, p<0.001 Medium: 53.0% vs 53.0%, p<0.001 High: 21.3% vs 33.2%, p<0.001 Weekend visit: 27.7% vs 24.7%, p=0.047 January to June visit: 48.2% vs 43.1%, p<0.001
Pelberg 1989	Half of patients were under 50 years old. Male: 45/75. Symptoms: Chest pain: 42/75 Epigastric pain: 6/75 Back pain: 4/75 Head, neck, shoulder or jaw pain: 4/75 Vertigo, nausea or vomiting: 4/75 Heart pounding: 2/75 Shortness of breath: 1/75 Most common risk factors: smoking, diabetes mellitus, hypertension, obesity and family history of atherosclerotic vascular disease Presented to ED within 24 hours of symptom onset: 43/75 Presented within 1 week: 12/75 Presented after 1 week: 9/75 Reason for missed AMI: Failure to admit: 25/75 Failure to order tests: 14/75 Failure to interpret diagnostic test: 14/75 Misdiagnosis: 11/75 Improper management: 11/75 Physician judgment factor: 9/75 Patient noncompliance: 3/75 Other: 14/75
Prattichizzo 1996	Characteristics of patients with missed AMI: Typical chest pain in 8/16 Acute pulmonary edema 4/16 Atypical clinical presentation in 4/16 ECG not performed in 1/16 Unrecognized AMI in 15/16 Most unrecognized ECG change was STEMI in V2-V3
Rusnak 1989	Missed AMI vs controls with AMI: Average age: 49.7±14.6 vs 62.6±13.3, p<0.001 Atypical complaints: 23/65 vs 4/65, p<0.001

	ECG: 28/65 vs 65/65, p<0.001 Abnormal ECG: 11/65 vs 54/65, p<0.001 Cardiac enzymes (CPK): 13/65 vs 36/65, p<0.001 Chest pain recorded: 3.0% vs 3.6%, p=0.04 Cardiac risk factors recorded: 32/65 vs 46/65, p=0.02 Lung examination recorded: 48/65 vs 58/65, p=0.04 Cardiac examination recorded: 42/65 vs 56/65, p=0.02 Average years' ED experience: 2.6 vs 5.1 years, p<0.001 Factors associated with correct classification: ECG obtained, age of patient, CPK obtained, physician board certification, years' ED experience, cardiac examination documented and chest radiograph obtained
Schull 2006	Missed AMI vs not missed AMI: Mean age: 65.0 vs 68.4 years Male 284/419 vs 12191/19244 Income quartile: Q1: 105/419 vs 4203/19244 Q2: 94/419 vs 4142/19244 Q3: 64/419 vs 3606/19244 Q4: 69/419 vs 3306/19244 Q5: 59/419 vs 3165/19244 Triage acuity: Resuscitation: ≤5/419 vs 967/19244 Emergency: 132/419 vs 10022/19244 Urgent: 228/419 vs 7415/19244 Less urgent: 48/419 vs 696/19244 Time of registration: Daytime: 190/419 vs 8270/19244 Evening: 166/419 vs 7222/19244 Nighttime 63/419 vs 3752/19244 Day of registration: Weekend: 98/419 vs 5398/19244 Weekday: 321/419 vs 13846/19244 Visits to same ED in previous year: 1.13 vs 0.62 Hospital type: Community: 321/419 vs 15163/19244 Small center: 45/419 vs 1116/19244 Teaching center: 53/419 vs 2965/19244 History of AMI: 65/419 vs 2721/19244 Shock: 6/419 vs 406/19244 Diabetes mellitus: 8/419 vs 771/19244 Heart failure: 57/419 vs 4065/19244 Cancer: 9/419 vs 439/19244 Stroke: 6/419 vs 517/19244 Pulmonary edema: ≤5/419 vs 219/19244 Acute renal failure: 17/419 vs 760/19244 Chronic renal failure: 21/419 vs 1013/19244 Dysrhythmia: 45/419 vs 2775/19244 Mean delay between previous ED visit and AMI was 2.3±1.9 days Higher annual ED visits was associated with lower risk of missed AMI. Factors associated with missed AMI

	ED AMI volume group: Very low: OR 1.96 (1.39-2.76) Low: OR 1.57 (1.10-2.25) Medium: OR 1.33 (0.98-1.82) High: OR 1.20 (0.89-1.63) Very high: OR 1.00 (ref) Age group: 20-49: OR 1.00 (ref) 50-64: OR 0.65 (0.49-0.88) 65-74: OR 0.75 (0.57-1.00) 75+: OR 0.53 (0.37-0.75) Income quartile: Q1: OR 1.31 (0.89-1.91) Q2: OR 1.19 (0.84-1.68) Q3: OR 0.95 (0.66-1.36) Q4: OR 1.08 (0.74-1.57) Q5: OR 1.00 (ref) History of AMI: OR 1.23 (0.93-1.62) Visit to same ED in previous year: OR 1.05 (0.93-1.19) Weekday vs weekend: OR 1.26 (1.01-1.58) Time of the day Day: OR 1.00 (ref) Evening: OR 1.01 (0.79-1.30) Night: OR 0.76 (0.57-1.02) Teaching vs community hospital: OR 0.91 (0.59-1.40) Shock: OR 0.88 (0.42-1.83) Diabetes: OR 0.37 (0.19-0.76) Congestive heart failure: OR 0.67 (0.51-0.90) Cancer: OR 0.97 (0.46-2.05) Stroke: OR 0.67 (0.31-1.44) Pulmonary edema: OR 1.35 (0.60-3.04) Acute renal failure: OR 1.43 (0.90-2.29) Chronic renal failure: OR 1.25 (0.82-1.96) Dysrhythmias: OR 0.84 (0.62-1.13)
Sequist 2005	Missed AMI vs controls: Mean age: 50±12 vs 47±14, p=0.37 Male: 12/18 vs 14/54, p=0.001 Diabetes: 2/18 vs 3/54, p=0.48 Smoking: 15/18 vs 20/54, p<0.001 Family history of CHD: 7/18 vs 14/54, p=1.00 Total cholesterol: 249±68 vs 210±38, p=0.01 HDL: 40±10 vs 58±15, p=0.002 LDL: 157±37 vs 146±34, p=0.28 Systolic BP: 128±17 vs 124±15, p=0.31 Diastolic BP: 81±12 vs 78±9, p=0.22 Symptoms: Chest pain: 12/18 vs 54/54, p<0.001 Shoulder/arm/back pain: 9/18 vs 11/54, p=0.02 Shortness of breath: 5/18 vs 6/54, p=0.08 Nausea/vomiting: 2/18 vs 2/54, p=0.28 ECG done: 12/18 vs 32/54, p=0.57

	ECG misinterpreted: 5/18 vs 0/54, p<0.001
Sharp 2020	Missed AMI vs not missed: Mean age: 68.9 vs 67.9 Female: 249/574 vs 1607/899 Race: Asian/pacific islander: 42/573 vs 3940/43899 Black: 83/574 vs 5028/43899 Hispanic: 142/574 vs 10758/43899 Others: 15/574 vs 922/43899 White: 291/574 vs 23251/43899 Income: <45K: 159/574 vs 10697/43899 45-60K: 159/574 vs 10422/43899 60-80K: 137/574 vs 10989/43899 ≥80K: 117/574 vs 25013/43899 Education at least college: 57.2 vs 58.0 Smoking: Never: 238/574 vs 19805/43899 Active: 66/574 vs 5327/43899 Quit: 258/574 vs 17102/43899 Hypertension: 476/574 vs 34893/43899 Diabetes: 251/574 vs 18144/43899 Lipid disorder: 467/574 vs 34060/43899 Stroke: 30/574 vs 2692/43899 PVD: 242/574 vs 16185/43899 Comorbidity index: >3 399/574 vs 27973/43899 Women: OR 1.3 (1.2-1.5), p<0.001 Black vs white: OR 1.3 (1.1-1.6), p=0.007
Williams 2019	Missed AMI vs treated STEMI Age: 66.3±12.4 vs 63.9±12.9, p=0.30 Male: 70/100 vs 950/1292, p=0.47 Indigenous: 4/100 vs 47/1292, p=0.78 Hypertension: 42/100 vs 796/1292, p=0.076 Dyslipidemia: 38/100 vs 496/1292, p=1.00 Diabetes: 33/100 vs 314/1292, p=0.081 Prior smoking: 42/100 vs 693/1292, p=0.039 Prior MI: 26/100 vs 231/1292, p=0.072 Prior CABG: 9/100 vs 37/1292, p=0.008 Prior PCI: 14/100 vs 130/1292, p=0.29 Presentation to hospital 7am-3pm: 62/100 vs 707/1292, p=0.19 3pm-11pm: 21/100 vs 377/1292, p=0.12 11pm-7am: 17/100 vs 204/1292, p=0.77 Symptom onset to presentation: 155.6±131.4 vs 150.5±144.4, p=0.90 Anterior infarction: 67/100 vs 528/1292, p<0.001 Missed AMI associated with failure to identify STEMI on ECG 72%, diagnostic uncertain 65%, 57% had ECG performed on machine with the Glasgow algorithm which correctly identified 93% of STEMI
Wilson 2014	Majority of missed AMI (65%) were admitted within 3 days of the initial ED visit. Rural hospital: aOR 2.61 (1.84-3.70)

	Public hospital: aOR 1.33 (1.08-1.61) ABEM certification: aOR 0.60 (0.50-0.73) ED chest pain volume: aOR 0.65 (0.51-0.82) Large hospital bed size: aOR 0.46 (0.37-0.57) Academic status: aOR 0.74 (0.58-0.94) Most protective hospital characteristic was having above a minimum level of chest pain acuity measured as hospitals where greater than 1.5% of all chest pain had AMI: aOR 0.23 (0.19-0.27).