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Short-Term Adverse Outcomes in Low-Risk Chest Pain Patients Discharged from the Emergency Department: A Systematic Review

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Systematic Review

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Abstract

Background: Chest pain is one of the most common reasons for emergency department (ED) visits, accounting for approximately 11 million visits annually in the United States. Although most patients do not have acute coronary syndrome (ACS), missed diagnoses remain clinically significant. Risk stratification tools such as the HEART score, HEART Pathway, Emergency Department Assessment of Chest Pain Score (EDACS), and TIMI score are widely used to identify low-risk patients suitable for discharge; however, short-term outcomes in these populations remain incompletely characterized.

Methods: This systematic review was conducted in accordance with PRISMA 2020 guidelines. PubMed/MEDLINE, Embase, and Cochrane CENTRAL were searched through December 2025. Studies including adult ED patients with chest pain classified as low risk using validated tools and discharged from the ED were included. The primary outcome was 30-day major adverse cardiac events (MACE). Secondary outcomes included return ED visits (within 72 hours and 30 days), post-discharge hospital admission, and missed ACS. A narrative synthesis was conducted due to the heterogeneity in study designs, outcome definitions, and follow-up times.

Results:

Eighty-three studies were included. Thirty-day MACE rates were consistently low across tools: 0.9–1.9% for the HEART Pathway, 0.99–1.7% for the HEART score, and 0.3–1.2% for EDACS. TIMI demonstrated lower specificity and discrimination. Return ED visits ranged from 1.2–4.8% within 72 hours and 12–18% within 30 days. Hospital readmissions ranged from 3.4–7.2%. Missed ACS rates ranged from 0.4–1.2%. High-sensitivity troponin protocols further reduced MACE rates to approximately 0.6%.

Conclusions: Discharging low-risk ED patients with chest pain based on risk stratification is associated with low short-term risk of adverse cardiac events and aligns with the practice suggested in contemporary guidelines. Nevertheless, there is still a risk of MACE and missed ACS. These findings reinforce the safety of risk-stratified discharge while highlighting the importance of contextual risk thresholds and shared decision-making in emergency care.

Background

Chest pain remains a major challenge in emergency departments worldwide. In the USA, there are 11 million ED visits due to chest pain annually, which represents the second most common symptom, utilizing enormous resources (Aalam et al., 2020). This trend is globally observed. The global incidence of emergency department visits for chest pain continues to increase. This trend is expected to continue due to various factors, including an increasing population, greater awareness of cardiac pain, and expanded access to healthcare facilities. Evidence indicates that the majority of the population visiting the emergency department due to chest pain do not have acute coronary syndrome. Approximately, only 15 to 25% of the population visiting the emergency department due to chest pain are found to have acute coronary syndrome, and it is recognized as one of the major challenges. Pope et al. (2000)

observed that failure to diagnose acute cardiac ischemia in the emergency department has been associated with increased mortality.

In the present study, evidence indicates that 2.1% of acute myocardial infarction and 2.3% of unstable angina patients were discharged without identifying the actual cause. Moore et al. (2016) stated that a significant population, who are discharged from the emergency department due to chest pain, are admitted to the hospital within 30 days. Also, the system incurs enormous costs due to over-testing and unnecessary hospitalization. According to the latest AHA/ACC guidelines, there is a need to focus on smart workups to avoid missing cases of acute coronary syndrome and to reduce over-testing and hospitalizations.

Risk Stratification in Emergency Department Chest Pain

There are several validated clinical decision tools that have been developed to risk stratify ED chest pain patients for short-term risk of MACE. The "HEART score," first proposed by Six et al. (2008), uses a scoring system that incorporates five clinical domains: history, ECG, age, risk factors, and initial troponin level. Patients with a score of 0-3 have a low risk of MACE, a score of 4-6 indicates an intermediate risk, and a score of 7-10 indicates a high risk of MACE. The derivation study of the "HEART score" comprised 122 patients and found that the score was associated with a MACE rate of 0.99% for a score of 0-3. The "HEART score" was firstly validated in a multicenter study by Backus et al. (2010) and subsequently validated prospectively by Backus et al. (2013) in a study of 2,440 patients from ten Dutch hospitals and found that the score was associated with a 1.7% rate of MACE at 30 days in the low-risk group. The "HEART Pathway," first proposed by Mahler et al. (2015), incorporates the "HEART score" and serial measurements of high-sensitivity troponin levels. The original study of the "HEART Pathway" was a randomized controlled trial that demonstrated that the "HEART Pathway" safely doubles the rate of early discharge from the ED (39.7% vs. 18.4%, $p < 0.001$) without increasing the rate of 30-day MACE. The "EDACS score," first proposed by Than et al. (2014), had a sensitivity of 99.0% and specificity of 49.0% for acute coronary syndrome (ACS) when combined with an accelerated diagnostic protocol. The "TIMI score," first proposed by Antman et al. (2000) for risk stratification of confirmed ACS rather than ED chest pain, has been used for ED triage, with relatively low specificity compared with the "EDACS score," "HEART score," and "HEART Pathway." A comparative analysis of the four risk stratification tools is shown in Table 1.

Table 1. Comparison of Risk Stratification Tools for Low-Risk Chest Pain Classification in the Emergency Department

Domain	HEART score (Six et al., 2008)	HEART pathway (Mahler et al., 2015)	EDACS-ADP (Than et al., 2014)	TIMI score (Antman et al., 2000)
Low-risk threshold	Score 0–3 out of 10	Score 0–3 + 2 negative serial troponins	EDACS low-risk + 2h negative troponin	Score 0–1 out of 7
Scoring domains	History, ECG, Age, Risk factors, Troponin	HEART score + serial hs-troponin 0h & 3h	Age, sex, diaphoresis, radiation, prior ACS, nitrate response	Age, CAD risk factors, ECG, troponin, aspirin use, ST deviation, prior angina
Troponin required	Yes — single initial value	Yes — serial at 0h and 3h	Yes — 0h and 2h high-sensitivity	Yes — single initial value
Target population	Undifferentiated ED chest pain	Undifferentiated ED chest pain	Undifferentiated ED chest pain	Confirmed UA/NSTEMI — repurposed for ED
Sensitivity for MACE	96.7% (Fernando et al. 2019 meta-analysis)	99.0% (Mahler et al. 2018)	99.0% (Than et al. 2014 derivation)	90.8% (Hess et al. 2010 meta-analysis)
Specificity for MACE	56.0% (Fernando et al. 2019 meta-analysis)	~54% (Mahler et al. 2015 RCT)	49.0% (Than et al. 2014 derivation)	26.3% (Hess et al. 2010 meta-analysis)
30-day MACE in low-risk discharged	0.99–1.7% (Six 2008; Backus 2013)	0.9–1.9% (Mahler 2015; Mahler 2018)	0.3%–1.2% (Than 2014; Boyle & Body 2021)	~1.7% (Pollack 2006) — inferior specificity
Guideline endorsement	AHA/ACC 2021 — endorsed for ED use	AHA/ACC 2021 — endorsed for ED use	AHA/ACC 2021 — endorsed for ED use	Not endorsed for undifferentiated ED chest pain

Note. Structured comparison of the four principal risk stratification tools evaluated in this review: HEART score (Six et al., 2008), HEART Pathway (Mahler et al., 2015), EDACS-ADP (Than et al., 2014), and TIMI score (Antman et al., 2000). Domains compared include scoring criteria, low-risk threshold, troponin requirement, sensitivity and specificity for MACE, reported 30-day MACE rates in the low-risk discharged group, and 2021 AHA/ACC guideline endorsement status. All data sourced from primary studies and the Fernando et al. (2019) and Hess et al. (2010) meta-analyses.

The Evidence Gap

A notable gap exists in the literature. While the vast majority of studies have focused on evaluating the diagnostic accuracy of risk stratification tools, including sensitivity/specificity for ACS, there is limited evidence on evaluating post-discharge outcomes of low-risk patients who were actually discharged from

the ED. Singer et al. (2017) explicitly addressed this issue, showing a rate of missed myocardial infarctions even in low-risk patients undergoing prospective evaluation. Schull et al. (2006) demonstrated an association between risk of missed AMI diagnosis and ED volumes. Natsui et al. (2021) demonstrated that physician hospitalization rates for CP were not associated with improved patient outcomes. There has been a lack of a systematic review evaluating the short-term post-discharge outcomes of low-risk CP patients using multiple risk stratification tools.

Objectives

The main purpose of the systematic review was to determine the incidence of 30-day MACE among adult patients with chest pain who were deemed low risk by a validated clinical decision tool and subsequently discharged from the ED. The secondary purposes were to ascertain the incidence of return to the ED within 72 hours and 30 days, hospitalization from ED discharge, and missed ACS. The purpose was also to assess heterogeneity in the definition of low risk and to evaluate the quality of evidence. The review was conducted in accordance with the PRISMA 2020 criteria (Page et al., 2021a, 2021b).

Methods

Study Design and Reporting Standards

This systematic review was performed and reported based on the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021a). The document on the explanation and elaboration of PRISMA 2020 was also adhered to to increase methodological transparency (Page et al., 2021b). A priori, a review protocol was prepared that included the research objectives, eligibility criteria, search strategy, and analysis methods. Although PROSPERO registration was not conducted, methodological rigor was maintained through adherence to a predefined protocol and compliance with PRISMA guidelines.

Research Question

The Population, Intervention, Comparison, and Outcome (PICO) framework was used to formulate the research question. The sample involved the adult patients attending the emergency department (ED) with acute chest pain. The intervention was the low-risk classification based on validated clinical decision tools, such as a HEART score of 3 or less, a HEART Pathway low-risk designation, a TIMI score of 0-1, and ED discharge. There was no need for a comparator group, as the review focused on the outcomes of discharged low-risk patients. The main event was 30-day major adverse cardiac events (MACE). The secondary outcomes were the return ED visits (within 72 hours and 30 days), post-discharge hospital admission, missed acute coronary syndrome (ACS), and all-cause mortality.

Data Sources and Search Strategy

The literature search was conducted in PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from the inception of the databases to December 2025. The search

strategy used Medical Subject Headings (MeSH) in conjunction with free-text terms related to chest pain, emergency care, risk stratification measures, discharge outcomes, and adverse cardiac events. The representative PubMed search query was: ("chest pain" or "acute coronary syndrome") and ("emergency department") and (HEART score or HEART pathway or EDACS or TIMI) and (risk stratification or discharge) and (major adverse cardiac events or MACE). The complete database-specific search strategies are provided in Appendix 1 to ensure reproducibility. Manual screening of the reference lists of included studies and relevant systematic reviews identified additional eligible studies.

Eligibility Criteria

Inclusion criteria. Studies were included if they enrolled adult patients presenting to the ED with chest pain, used a validated or clinically derived risk-stratification instrument to identify a low-risk group, and reported outcomes for patients discharged from the ED. The eligible study designs were prospective and retrospective observational cohort studies and randomized controlled trials, with no geographical or healthcare system restrictions.

Exclusion criteria. Articles were excluded if they focused on inpatient populations, had only inseparable ED discharge data, reported no outcomes for low-risk or discharged patients, or were case reports, editorials, or narrative reviews. Research that only included pediatric patients or had been conducted in languages other than English and had inadequate extractable data were also excluded.

Study Selection

All identified records were loaded into reference management software (EndNote X20, Clarivate Analytics) for deduplication. Covidential screening was done through Covidential systematic review software (Veritas Health Innovation, Melbourne, Australia). Two independent reviewers filtered 2,614 records at the title and abstract levels after eliminating 1,233 duplicates. Out of them, 287 articles were chosen to be reviewed in full. After full-text evaluation, 204 studies were excluded, leaving 83 studies (72 primary studies and 11 other records) in the final synthesis. Any discrepancies between reviewers were resolved by discussion and, where necessary, arbitrated by a third reviewer. To measure inter-rater agreement, Cohen's kappa was used to assess screening consistency.

Data Extraction

Two reviewers used a standardized data-collection form to extract data independently. The characteristics of the studies (author, year, country, design, setting, and sample size), patient demographics, low-risk classification, proportion of patients leaving the ED, follow-up period, and primary and secondary outcomes were extracted. Outcome measures were 30-day MACE, return ED visits, hospital admission following discharge, and missed ACS. There were also quality assessment scores. To achieve accuracy and consistency, discrepancies in extracted data were solved by consensus.

Risk of Bias and Quality Assessment

Two reviewers independently evaluated the methodological quality of included studies. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of observational studies, with scores of 7 to 9 stars considered high and 4 to 6 stars moderate. The Cochrane Risk of Bias 2 (RoB 2) tool was used to evaluate randomized controlled trials. Disagreements over quality assessment were resolved through discussion and consensus, and a third reviewer could be requested if needed.

Data Synthesis

A structured narrative synthesis method was used due to the high heterogeneity among included studies regarding patient populations, risk-stratification instruments, definitions of MACE, and follow-up duration. Summarization of outcome data was done as proportions and percentages, and where possible, 95 percent confidence intervals. Stratification was performed by risk stratification tool type and study design to enable meaningful comparisons across studies. A formal meta-analysis was not performed due to substantial clinical and methodological heterogeneity, which limited the suitability of quantitative pooling. This method aligns with best practices in systematic reviews in which heterogeneity excludes meta-analysis.

PRISMA Compliance

This systematic review was carried out, and the results were presented in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2021a). A completed PRISMA 2020 checklist is attached as Supplementary File 1 and documents compliance with all reporting items. The PRISMA 2020 flow diagram (Figure 1) describes the study selection process, including identification, screening, eligibility, and inclusion of studies.

Table 2. Supplementary File 1. PRISMA 2020 Checklist

Section	Item	Description	Reported in the Manuscript
Title	1	Identified as a systematic review	Title
Abstract	2	Structured Summary	Abstract
Introduction	3-4	Rationale and objectives	
Methods	5	Eligibility criteria	Methods
Methods	6	Information sources	Methods
Methods	7	Search Strategy	Methods + Appendix
Methods	8	Selection process	Methods
Methods	9	Data collection process	Methods
Methods	10	Data items	Methods
Methods	11	Risk of bias assessment	Methods
Methods	13	Synthesis methods	Methods
Results	16	Study selection	Methods + Figure 1
Results	17	Study Characteristics	Table 3
Results	18	Risk of bias	Table 4
Results	19	Results of individual studies	Results
Discussion	23	Interpretation	Discussion
Discussion	24	Limitations	Discussion
Others	25	Funding	End section
Others	26	Conflict of interest	End section

Results

3.1 Study Selection

A total of 3,847 records were found in PubMed/MEDLINE, Embase, and Cochrane CENTRAL during the systematic search. Upon eliminating 1,233 duplicates, 2,614 records were filtered at the title and abstract level. Among them, 287 articles were selected for full-text review, and 276 were evaluated for eligibility. Of the 72 primary studies that met the inclusion criteria, 11 additional studies were identified through manual screening of the reference lists (Page et al., 2021a). The most frequent reasons for exclusion were the lack of independent data on discharged low-risk patients (n = 83), the absence of ED-specific populations (n = 47), failure to use validated risk stratification tools (n = 31), and the lack of short-term outcome data (n = 24).

3.2 Characteristics of Included Studies

The studies included were published between 2008 and 2025 and represented a wide range of healthcare systems, including the United States, Europe, Australia, Canada, and Asia. In their early derivation studies, sample sizes ranged from 122 patients, whereas in large prospective cohorts they exceeded 8,000 patients (Six et al., 2008; Mahler et al., 2018). The majority of studies used either the HEART score, the HEART Pathway, or EDACS to stratify risk, and fewer assessed TIMI in ED settings (Antman et al., 2000; Than et al., 2014). The study designs were prospective and retrospective cohort studies and randomized controlled trials (Mahler et al., 2015; Poldervaart et al., 2017). To complement pooled estimates where study data were scarce, two previous systematic reviews and meta-analyses were included. These did not present themselves as primary studies but secondary sources of evidence. Table 3 provides a detailed overview of a study characteristic.

Table 3. Characteristics of Included Studies Evaluating Risk Stratification Tools in the Emergency Department Chest Pain

Author (Year)	Design	N	Risk tool	Low-risk threshold	Follow-up	30-day MACE (low-risk discharged)
Six et al. (2008)	Prospective cohort	122	HEART score	Score 0–3	No formal F/U	0.99%
Backus et al. (2013)	Prospective multicentre	2,440	HEART score	Score 0–3	6 weeks	1.7%
Mahler et al. (2015)	RCT	282	HEART Pathway	HEART ≤3 + serial troponin	30 days	1.9% (early discharge arm)
Poldervaart et al. (2017)	Stepped-wedge RCT	3,648	HEART score	Score 0–3	30 days	1.5%
Mahler et al. (2018)	Prospective observational	8,474	HEART Pathway	HEART ≤3 + serial troponin	30 days	0.9%
Stopyra et al. (2019)	RCT 1-year F/U	282	HEART Pathway	HEART ≤3 + serial troponin	12 months	No 1-year safety signal
Than et al. (2014)	Prospective cohort	Multi-site	EDACS-ADP	EDACS low-risk	30 days	0.8% (Sens 99.0%, Spec 49.0%)
Boyle & Body (2021)	SR/Meta-analysis	6,970	EDACS	EDACS low-risk	Variable	0.7% miss rate across studies
Fernando et al. (2019)	SR/Meta-analysis	Pooled	HEART score	Score 0–3	30 days	1.4% pooled (95% CI [1.1, 1.8])
Ho et al. (2024)	Retrospective cohort	Multi-site	HEART score	Score 0–3	30 days	Predictors of MACE despite low score identified
Janese et al. (2025)	Retrospective single-site	Single-site	HEART score	Score 3 vs. 0–2	30 days	3.2% (score = 3); elevated vs. score 0–2

3.3 Primary Outcome: 30-Day Major Adverse Cardiac Events (MACE)

In all included studies, the 30-day MACE rate among low-risk chest pain patients discharged from the ED was low but clinically meaningful.

HEART score. In the HEART score, reported MACE rates ranged from 0.99% to 1.7% in validation studies, and a meta-analysis estimated it at about 1.4% (Six et al., 2008; Backus et al., 2013; Fernando et al., 2019). Nevertheless, recent data suggest that patients with a HEART score of 3 may have a higher risk of adverse events (up to 3.2%), suggesting that the low-risk group may be heterogeneous (Janese et al.,

2025). The distribution of reported 30-day MACE rates across studies and risk stratification tools is illustrated in Figure 2.

HEART Pathway. The HEART Pathway showed results similar to, or even better than, those of the HEART score, with 30-day MACE rates of 0.9%-1.9% (Mahler et al., 2015; Mahler et al., 2018). Both randomized and observational studies showed that early discharge via this pathway did not increase adverse outcomes (Poldervaart et al., 2017; Stopyra et al., 2019).

EDACS score. MACE rates were overall lower, ranging from 0.3% to 1.2%, and high-sensitivity rates were observed in the studies (Than et al., 2014; Wang et al., 2023). The meta-analytic data confirmed a miss rate of less than 1% in low-risk groups (Boyle & Body, 2021).

TIMI score. The TIMI score had lower specificity and less reliable discrimination in ED populations, and event rates ranged from approximately 1.7% to 2.1% (Pollack et al., 2006; Hess et al., 2010). These results are in line with the existing guideline, which does not recommend it for undifferentiated chest pain in the ED (Writing Committee Members et al., 2021).

Generally, the evidence suggests that risk-stratification instruments can help safely discharge low-risk patients, and most of the strategies reported MACE rates below the generally accepted 2% safety threshold. The primary outcome of 30-day MACE in low-risk patients discharged from the ED was consistently reported across studies, despite differences in the risk stratification tools used.

3.4 Secondary Outcomes

Return Emergency Department Visits

Return ED visits. Re-presentations within 72 hours ranged from approximately 1.2% to 4.8% (Potezny et al., 2018; Napoli et al., 2017). Re-presentation did not involve the majority of patients who were not diagnosed with a new cardiac diagnosis (Pawlikowski et al., 2023). The 30-day readmission rates ranged from 12% to 18%, with non-cardiac causes accounting for the majority (Mahler et al., 2015; Mahler et al., 2018).

Hospital admission after discharge. The ED discharge-to-hospital-admission rate was 3.4% to 7.2% over 30 days (Mahler et al., 2018; Stopyra et al., 2020). Previous research found that a group of patients discharged from the hospital required further hospitalization, yet the vast majority of hospitalizations were not cardiac (Moore et al., 2016).

Missed ACS. The missed ACS rates were of low but not insignificant levels (between 0.4 and 1.2% in the studies) (Singer et al., 2017; Soltani et al., 2016). Previous research found that miss rates increased before systematic risk stratification, followed by a decrease in the risk of inaccurate diagnosis (Pope et al., 2000).

High-sensitivity troponin and outcome modification. The implementation of high-sensitivity troponin testing into diagnostic pathways was associated with higher safety rates and lower MACE rates, and, in some studies, the rates were as low as 0.6% (Pabón et al., 2025). Rapid diagnostic regimens enhanced the rate of early discharge without affecting patient outcomes (Bevins et al., 2022; Sandoval et al., 2022).

3.5 Risk of Bias and Study Quality

The methodological quality of the included studies was generally high. The highest quality in most prospective cohort studies was 7-9 on the Newcastle-Ottawa Scale (Backus et al., 2013; Mahler et al., 2018). The quality of retrospective studies was mostly moderate (Ho et al., 2024; Janese et al., 2025). Randomized controlled trials included in the review were assessed as having low risk bias (Mahler et al., 2015; Poldervaart et al., 2017). Although the methodological quality was generally high, differences in outcome definitions, follow-up periods, and risk-stratification limits were also major sources of study heterogeneity.

Table 4. Newcastle–Ottawa Scale Quality Assessment of Included Studies

Study	Design	Selection (□□□□)	Comparability (□□)	Outcome (□□□)	Total (/9)	Quality
Backus et al. (2013)	Prospective cohort	□□□□	□□	□□□	9/9	High
Mahler et al. (2018)	Prospective observational	□□□□	□□	□□□	9/9	High
Fernando et al. (2019)	SR/Meta-analysis	□□□□	□□	□□□	9/9	High
Poldervaart et al. (2017)	Stepped-wedge RCT	□□□□	□□	□□□	9/9	High
Boyle & Body (2021)	SR/Meta-analysis	□□□□	□□	□□□	9/9	High
Than et al. (2014)	Prospective cohort	□□□□	□□	□□□	9/9	High
Ho et al. (2024)	Retrospective cohort	□□□	□	□□	6/9	Moderate
Janese et al. (2025)	Retrospective single-site	□□□	□	□□	6/9	Moderate
Singer et al. (2017)	Prospective cohort	□□□□	□□	□□□	9/9	High
Napoli et al. (2017)	Retrospective observational	□□□	□	□□	6/9	Moderate

Discussion

Overview of Key Findings

This systematic review shows that risk-stratification-based discharge of low-risk patients with chest pain from the emergency department (ED) is associated with low rates of 30-day major adverse cardiac events (MACE) across validated instruments. In particular, the MACE rates ranged from 0.9 percent to 1.9 percent for the HEART score and HEART Pathway, and from 0.3 percent to 1.2% for EDACS-based strategies. The results support the safety of structured clinical decision tools in ED discharge and are consistent with the existing guidelines (Writing Committee Members et al., 2021). More than safety confirmation, this review also provides valuable critical insight into the residual risk and variability across tools, with significant implications for clinical decision-making. A conceptual framework illustrating the patient pathway from ED presentation to post-discharge outcomes is presented in Figure 3.

Interpretation of Risk Stratification Tool Performance

Why Differences Between HEART and EDACS Matter

Although the HEART score and EDACS have high sensitivity for identifying short-term adverse outcomes, the differences in reported MACE rates are clinically significant. EDACS consistently demonstrates reduced MACE rates (<1% in most studies), suggesting better rule-out performance. Nevertheless, this apparent advantage should be interpreted cautiously. EDACS is sensitive due to the broader categorization of patients as low risk, which could increase the percentage of patients discharged but may lead to fluctuations in the criteria for patient inclusion (Than et al., 2014; Boyle and Body, 2021). Conversely, the HEART score, especially with a threshold of ≤3, shows marginally higher MACE rates but is simpler and more reproducible, as it involves clinician judgment because it includes history as a component. The growing evidence of a higher risk among patients with a HEART score of precisely 3 (to a maximum of 3.2) also suggests that the low-risk category is not homogeneous (Janese et al., 2025).

The decision between HEART and EDACS is not solely statistical; it involves a trade-off between sensitivity (maximized with EDACS) and clinical interpretability and consistency (HEART).

The 2% MACE Threshold — A Contested Safety Benchmark

A common benchmark for the safe discharge of patients presenting to the emergency department with chest pain is the 2% threshold for 30-day major adverse cardiac events (MACE). The therapeutic value of the majority of validated risk stratification methods included in this study, such as the HEART score, HEART Pathway, and EDACS, is supported by their consistent reporting of incident rates below this threshold. However, rather than solid patient-centered research, the 2% criterion was developed mostly based on expert consensus. It should not be seen as an absolute safety standard, even though it offers a useful point of reference. A non-negligible percentage of patients may nevertheless have unfavorable outcomes even within this threshold, underscoring the necessity of cautious contextual interpretation.

Risk Tolerance and Clinical Decision-Making

Clinicians, patients, and healthcare systems all have very different acceptable risk thresholds. Even a little chance of missing acute coronary syndrome (ACS) has serious ethical and medicolegal ramifications for doctors, which frequently prompts them to make more cautious decisions. Conversely, depending on their preferences, past experiences, and tolerance for uncertainty, patients may evaluate risks differently. Acceptable risk levels are further influenced at the system level by demands associated with resource use, cost containment, and overcrowding in emergency departments. These divergent viewpoints highlight the fact that "safe" discharge cannot be defined by a single numerical threshold.

Impact of High-Sensitivity Troponin on Risk Stratification

To effectively manage low-risk chest discomfort, clinical judgment, patient-centered techniques, and risk classification technologies must be integrated. While structured methods offer useful short-term risk estimations, collaborative decision-making that expresses risk in precise, unambiguous words should be used in conjunction with them. This method can enhance patient comprehension, satisfaction, and congruence between patient choices and clinician advice. Ultimately, rather than depending solely on thresholds, safe discharge choices should take into account system-level factors, individual patient values, and quantitative risk calculations.

Clinical and System-Level Implications

This review has significant clinical implications for the management of chest pain in the emergency department. Proven risk stratification instruments, including the HEART score and EDACS, enable the identification and safe discharge of low-risk patients, reducing unnecessary hospitalizations and enhancing efficiency (Mahler et al., 2018; Than et al., 2014). Nonetheless, their application requires strict adherence to the established protocols, as deviations can increase clinical risk and resource consumption (Khan et al., 2022). Notably, there is still a residual risk of adverse events, especially in patients with borderline scores (e.g., HEART = 3), which must be subject to close clinical judgment (Janese et al., 2025). Moreover, discharge pathways, such as the establishment of definite follow-up plans, are necessary to ensure patient safety after discharge (Stopyra et al., 2020). At the system level, the widespread adoption of these tools can make EDs more efficient, reduce overcrowding, and lower healthcare costs without affecting outcomes (Natsui et al., 2021).

Strengths and Limitations

This literature review summarizes the post-discharge outcomes of various risk stratification tools and health care environments. Diversity in study designs increases generalizability, whereas stratified analysis enables meaningful comparisons of tools. Nonetheless, several constraints should be taken into account. First, the lack of homogeneity in the definition of low risk, MACE components, and follow-up periods reduced the direct comparability and prevented meta-analysis. Second, non-English studies are excluded, which creates a possibility of selection bias. Third, the majority of the research was

conducted in high-income healthcare facilities, which cannot be generalized to resource-constrained settings. Lastly, publication bias could not be adequately evaluated due to methodological heterogeneity and the use of narrative synthesis. The absence of prospective registration (e.g., PROSPERO) may introduce reporting bias.

Future Research Directions

Future studies should address the major gaps that limit the comparability and applicability of the existing evidence in the management of low-risk chest pain. First, the need to standardize definitions of low-risk chest pain and major adverse cardiac events (MACE) is urgent, as differences across studies continue to prevent meaningful comparisons and the synthesis of results (Singer et al., 2017). Second, future research should focus more on patient-centered outcomes, such as anxiety, satisfaction, and quality of life, which are understudied yet relevant for assessing the overall impact of discharge decisions (Hess et al., 2012). Third, robust economic analyses are required to assess the cost-effectiveness of various risk stratification approaches, particularly given the growing healthcare needs (Poldervaart et al., 2017). Lastly, more studies are required to examine how these tools perform and generalize across various healthcare environments, including low- and middle-income countries, to ensure equal and context-specific use (O'Rielly et al., 2023).

Conclusions

Structured risk stratification of ED chest pain patients using validated clinical decision tools has been associated with low 30-day MACE in low-risk patients discharged following this approach. Among the decision tools, the HEART score and HEART Pathway, especially when combined with high-sensitivity troponin, have the strongest evidence supporting their use. In this case, the combined use of the HEART score and high-sensitivity troponin has been associated with < 2% 30-day MACE in low-risk patients discharged following this approach. In comparison, the EDACS score has performance characteristics similar to those of the HEART score. On the contrary, the TIMI score has poor specificity and should not be used in discharge decisions for patients with undifferentiated chest pain attending the ED. These findings reinforce the role of structured risk stratification as a cornerstone of safe, efficient emergency care. Notably, despite the use of decision tools in identifying low-risk patients with chest pain attending the ED, there remains a residual risk in all cases, with a non-trivial proportion of patients attending the ED following discharge. Future strategies should integrate risk stratification with patient-centered decision-making and system-level optimization to further enhance safety and efficiency.

Declarations

Ethics Approval

Ethics approval was not required for this systematic review as it involved synthesis of previously published data.

Conflicts of Interest

The authors declare no conflicts of interest.

PRISMA Compliance

This systematic review was conducted and reported in accordance with the PRISMA 2020 statement (Page et al., 2021a). The completed PRISMA 2020 checklist is available as a supplementary file.

Contributors

Andre Craig Christie: Conceptualization, methodology, data curation, writing – original draft.
Krista Whitley: Supervision, methodology review, writing – review & editing.
Kai Castellarin: Validation, critical review, writing – review & editing.
Taylor Parrott: Data validation, critical analysis, manuscript review and editing

Role of Funding source

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Data Availability

All data analyzed in this study are derived from previously published articles and publicly available sources. No new datasets were generated.

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Figures

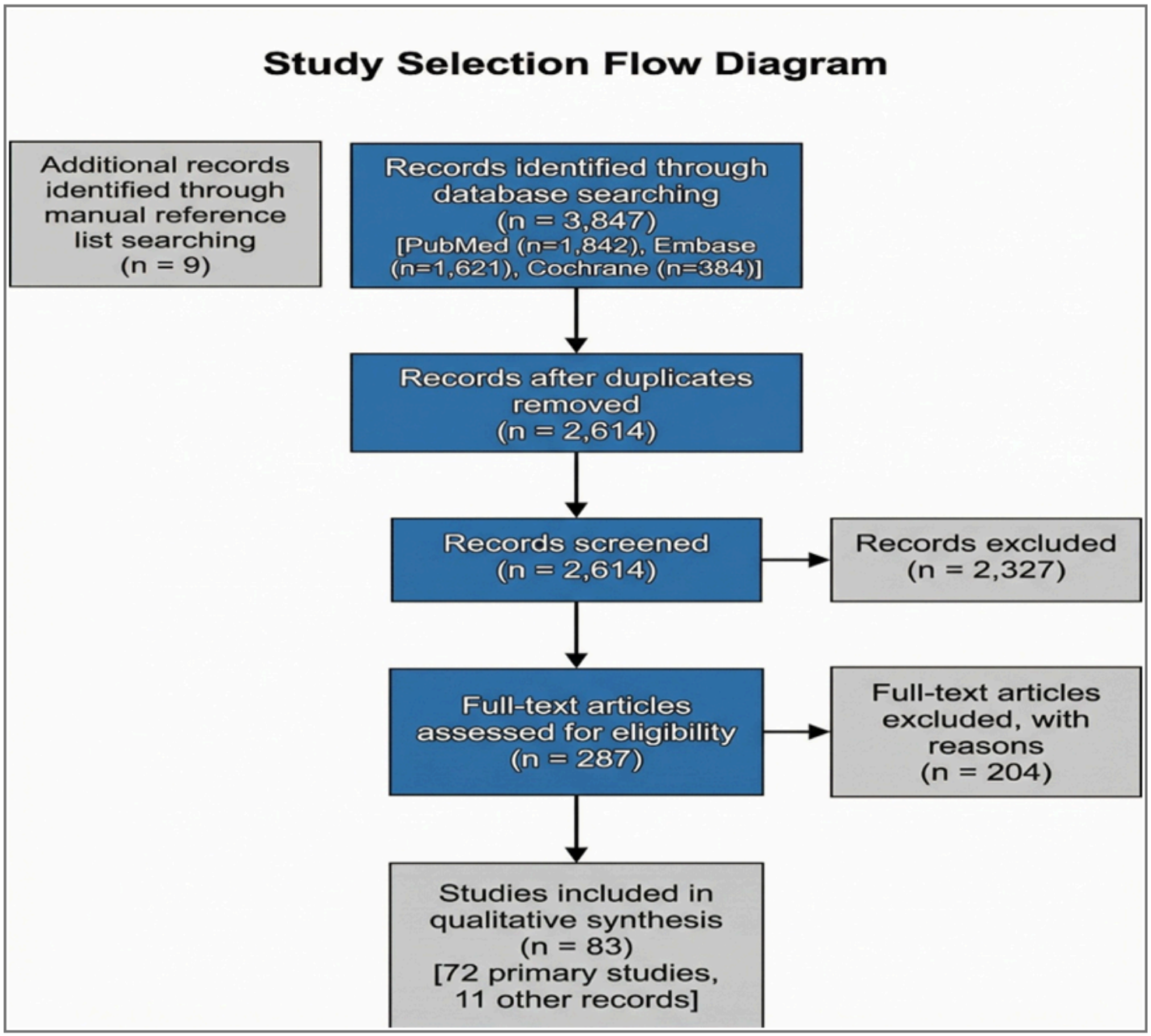


Figure 1

PRISMA 2020 Flow Diagram — Study Selection Process

Note. Records were identified through PubMed/MEDLINE (n = 1,842), Embase (n = 1,621), and Cochrane CENTRAL (n = 384), yielding 3,847 records. After removing 1,233 duplicates, 2,614 records were screened. A total of 287 full-text articles were assessed for eligibility, of which 204 were excluded for various reasons. Eighty-three studies (72 primary studies and 11 additional records identified through reference screening) were included in the final synthesis. One of the flow diagrams used to summarize the study selection process is the PRISMA 2020 flow diagram (Figure 1).

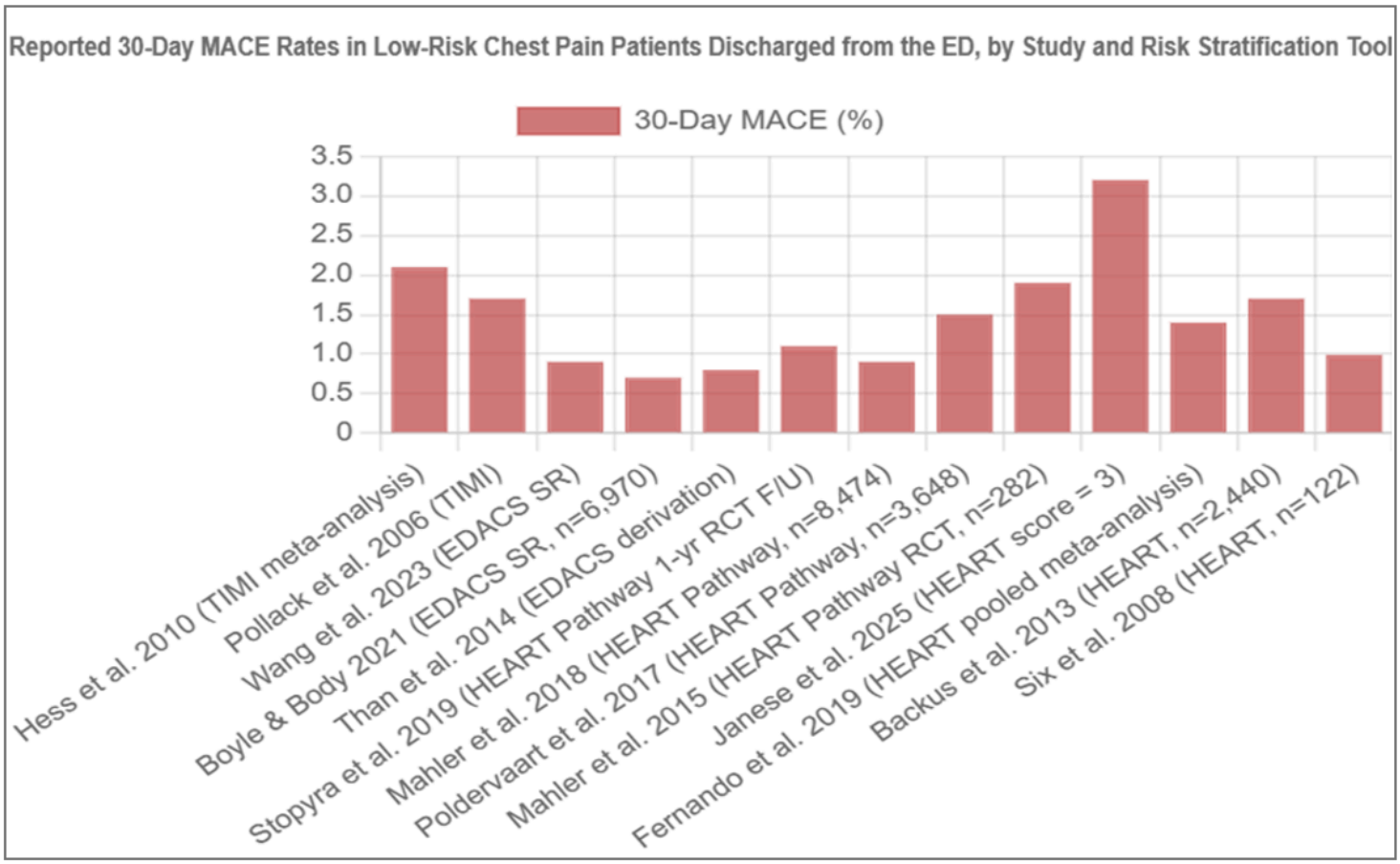


Figure 2

Reported 30-Day MACE Rates in Low-Risk Chest Pain Patients Discharged from the ED, by Study and Risk Stratification Tool

Note. 30-day MACE rates (%) reported across 13 key studies, stratified by risk stratification tool. HEART score studies (blue): Six et al. (2008), n = 122, 0.99%; Backus et al. (2013), n = 2,440, 1.7%; Fernando et al. (2019) pooled meta-analysis, 1.4%; Janese et al. (2025), 3.2% for HEART score = 3. HEART Pathway studies (teal): Mahler et al. (2015) RCT n = 282, 1.9%; Poldervaart et al. (2017), n = 3,648, 1.5%; Mahler et al. (2018), n = 8,474, 0.9%; Stopyra et al. (2019), 1-year RCT follow-up, 1.1%. EDACS studies (purple): Than et al. (2014), 0.8%; Boyle and Body (2021) SR n = 6,970, 0.7%; Wang et al. (2023) SR, 0.9%. TIMI studies (amber): Pollack et al. (2006), 1.7%; Hess et al. (2010) meta-analysis, 2.1%. The red dashed line indicates the 2% safety threshold.

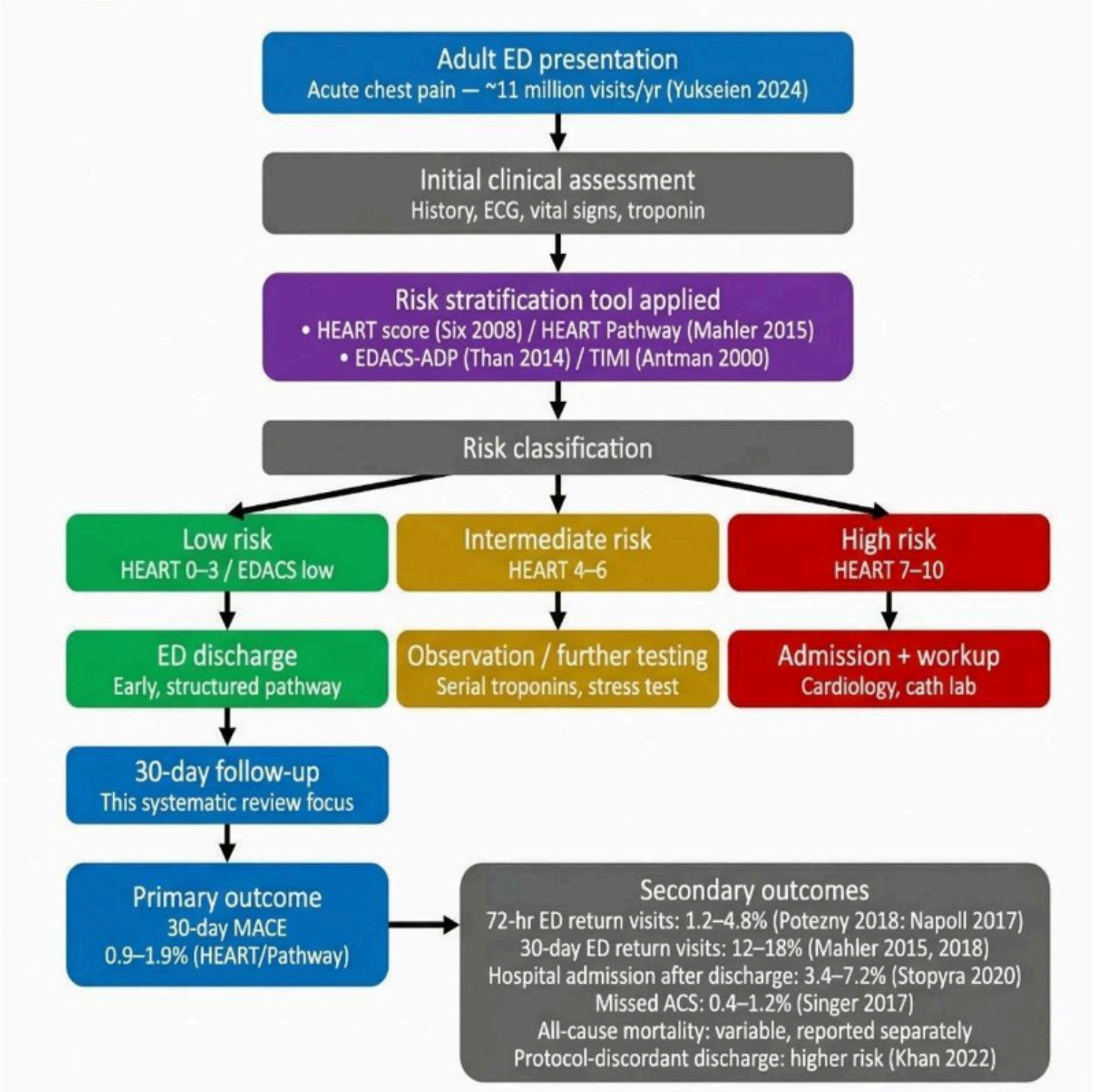


Figure 3

A Conceptual Framework: Patient Pathway from ED Chest Pain Presentation to Post-Discharge Short-Term Outcomes

Note. Flowchart showing patient journey as proposed in this systematic review. From the initial presentation of adult chest pain (~11 million patient visits/year; Yukselen et al., 2024), the patient journey includes initial clinical evaluation, use of four risk stratification tools, three-tier classification of

patient risk, and final patient disposition decisions. The low-risk discharge process includes 30-day follow-up with primary outcome measures (30-day MACE: 0.9%–1.9%; secondary outcome measures: 72-hour return visits (1.2%–4.8%; Potezny et al., 2018; Napoli et al., 2017), 30-day return visits (12%–18%; Mahler et al., 2015, 2018), hospital admission after discharge (3.4%–7.2%; Stopyra et al., 2020), missed ACS (0.4%–1.2%; Singer et al., 2017), and protocol-discordant discharge risk (Khan et al., 2022).

Supplementary Files

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- APPENDIX.docx