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Development and validation of a comprehensive early risk prediction model for patients with undifferentiated acute chest pain

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ABSTRACT

Aims: Existing risk scores for undifferentiated chest pain focus on excluding coronary events and do not represent a comprehensive risk assessment if an alternate serious diagnosis is present. This study aimed to develop and validate an all-inclusive risk prediction model among patients with undifferentiated chest pain.

Methods: We developed and validated a multivariable logistic regression model for a composite measure of early all-inclusive risk (defined as hospital admission excluding a discharge diagnosis of non-specific pain, 30-day all-cause mortality, or 30-day myocardial infarction [MI]) among adults assessed by emergency medical services (EMS) for non-traumatic chest pain using a large population-based cohort (January 2015 to June 2019). The cohort was randomly divided into development (146,507 patients [70%]) and validation (62,788 patients [30%]) cohorts.

Results: The composite outcome occurred in 28.4%, comprising hospital admission in 27.7%, mortality within 30-days in 1.8%, and MI within 30-days in 0.4%. The Early Chest pain Admission, MI, and Mortality (ECAMM) risk model was developed, demonstrating good discrimination in the development (C-statistic 0.775, 95% CI 0.772–0.777) and validation cohorts (C-statistic 0.765, 95% CI 0.761–0.769) with excellent calibration. Discriminatory performance for the composite outcome and individual components was higher than existing scores commonly used in undifferentiated chest pain risk stratification.

Conclusions: The ECAMM risk score model can be used as an all-inclusive risk stratification assessment of patients with non-traumatic chest pain without the limitation of a single diagnostic outcome. This model could be clinically useful to help guide decisions surrounding the need for non-coronary investigations and safety of early discharge.

Abbreviations: VEMD, Victorian Emergency Minimum Dataset; VAED, Victorian Admitted Episodes Dataset; VDI, Victorian Death Index; MI, myocardial infarction; CI, confidence interval.

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1. Introduction

Acute chest pain is a common reason for engaging emergency medical services (EMS), accounting for approximately one in ten calls for assistance [1–3]. Causes of chest pain are most commonly benign with half of patients eventually diagnosed with non-specific pain [4]. However, life-threatening conditions can be present and therefore rapid investigation and management is the default strategy for all patients to quickly identify serious pathologies, resulting in a significant burden on healthcare systems [4]. Existing risk score tools for undifferentiated chest pain used in pre-hospital and emergency department settings are focused on determining a patient's risk of acute coronary syndromes (ACS), which account for approximately 10% of presentations [1–3]. These scores were largely developed prior to the availability of high sensitivity troponin assays, and with the development of rapid high-sensitivity troponin rule-out pathways, their incremental value in improving classification performance has lessened [5–8]. Importantly, existing risk tools provide no information on the presence of serious non-coronary conditions (e.g. acute infections, other cardiac and respiratory conditions, pulmonary emboli, and acute aortic pathologies), which can account for up to 45% of chest pain presentations and may still require hospital admission [2,3,9–11]. Therefore, although patients may be classified as low-risk of ACS by rapid troponin testing pathways, existing clinical risk scores cannot be used in the risk stratification of serious non-coronary conditions that might require hospital admission, in turn limiting their usefulness in facilitating early discharge.

In the present study, we aimed to develop and validate a clinical prediction model and risk score, using routinely collected EMS data, among patients with undifferentiated chest pain to provide a more comprehensive risk assessment capturing both coronary and non-coronary diagnoses. The goal of this score is to guide decisions surrounding early discharge and the need for further non-coronary investigations. We also aimed to compare this risk score against existing clinical risk scores that are validated in undifferentiated chest pain cohorts.

2. Methods

The reporting of this study followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) statement for the development and validation of a multivariable prediction model [12]. Ethics approval for the data linkage in addition to this analysis was gained from the Monash University Human Research Ethics Committee (approval number 11681).

2.1. Study design and participants

We used a population-based cohort of consecutive adult patients attended by EMS for chest pain between 1 January 2015 and 30 June 2019 in Victoria, Australia. Pre-hospital data from the EMS electronic patient care records were available for use in the predictive model, with linkage to hospital and death outcome data from the Victorian Emergency Minimum Dataset (VEMD), the Victorian Admitted Episodes Dataset (VAED), and the Victorian Death Index (VDI). These databases are state-wide administrative datasets detailing individual patient care in the emergency department (VEMD) and during hospital admission (VAED), with long-term mortality data available through the VDI. Full details regarding the cohort and linkage processes are included in the Supplemental Methods. The cohort was randomly divided into a model development cohort (70%) and internal validation cohort (30%).

Consecutive patients contacting EMS for chest pain were included in the study if paramedics recorded either of the following on the patient care record: (1) pain in the chest, or (2) a final or secondary EMS diagnosis of ischaemic chest pain, ACS, pleuritic pain or angina. Exclusion criteria were (1) attendances recorded as having a case nature of 'Trauma'; (2) EMS attendances for transfers between hospitals; (3) age $<$ 18 years; (4) out-of-hospital cardiac arrest prior to EMS arrival; and (5) paramedic diagnosed ST-elevation myocardial infarction (STEMI).

2.2. Outcomes

This study aimed to assess a measure of all-inclusive early risk among chest pain cohorts. Current literature assessing early risk among chest pain focuses on the risk of myocardial infarction (MI), generally at 30 days [9–11,13–15]. Therefore, the composite primary endpoint included 30-day MI, in addition to admission to hospital at the index presentation and 30-day all-cause mortality, with the following specific criteria: (1) admission to hospital (excluding admission to emergency short stay assessment areas for $<$ 24 h) with any discharge diagnosis except for non-specific pain (including serious diagnoses such as myocardial infarction, pulmonary emboli, heart failure, pneumothorax, pneumonia and acute aortic pathologies); (2) myocardial infarction, defined as either an ST-elevation or non-ST elevation myocardial infarction within 30 days of emergency or hospital discharge; (3) all-cause mortality within 30 days of EMS attendance. All diagnoses were defined according to ICD 10 criteria at discharge from hospital (if admitted) or at discharge from emergency (if not admitted) (see Supplemental Methods).

2.3. Statistical analysis

Pre-hospital candidate variables considered to be plausibly related to the composite outcome were selected for potential inclusion in the model (Table 1). Only variables collected by EMS (rather than during the emergency or hospital admission) were used in model development. Continuous variables were visually explored for non-linear associations using fractional polynomials. Non-linear associations were identified for age, systolic blood pressure, heart rate, pain severity (out of ten), respiratory rate and oxygen saturations. Because the overall aim was to develop a clinically useable risk score, continuous variables with non-linear associations were categorised based on clinical plausibility in the following manner: age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–89, $\geq$90 years), initial systolic blood pressure ($<$90, 90–99, 100–109, 110–189, $\geq$190 mmHg), initial heart rate ($<$45, 45–79, 80–99, 100–119, 120–149, $\geq$150 beats per minute), initial oxygen saturations (98–100, 95–97, 92–94, 90–91, $<$90%), initial temperature ($<$36, 36–37.4, 37.5–37.9, $\geq$38 °C), initial respiratory rate ($\leq$12, 13–16, 17–24, 25–34, $\geq$35 breaths per minute), and initial pain score (0, 1, 2–4, 5–7, 8–10).

To handle missing data, we used multiple imputation with chained equations assuming missingness at random. Twenty datasets were imputed separately using available explanatory variables (Table 1) for both the development and validation cohorts. The outcome variable was included as a predictor in the development cohort but not the validation cohort. Rubin's rules were used to pool results of logistic regression models [16]. Full models were fitted initially, and variables retained if they had an adjusted odds ratio of greater than 1.10 or $<$0.90, and were statistically significant at the 0.01 level. The final model was then used to generate a simplified scoring system according to the strategy proposed by Sullivan et al. [17] Two models were developed, including: (1) A full model with all variables meeting the above criteria for clinical use through an app-based system, and (2) a simplified model that could be calculated at the bedside/roadside without an app or calculator. Discrimination of the full and simplified risk scores in both the development and validation imputed datasets was assessed using the C-statistic (area under the receiver operating characteristic curve), with a value of 0.5 indicating no predictive value, 0.8 considered good, and 1.0 perfect. Goodness of fit was assessed with the Brier score [18], a measure ranging from 0 to 1 with lower values indicating superior model performance. Model calibration curves were plotted to examine agreement between predicted and observed risk across deciles of discharge safety

Table 1
Pre-hospital candidate variables considered for risk score development.

	Development (n = 141,801) **Composite outcome***		**Validation** (n = 60,772) **Composite outcome***	
Variable	**No** (n = 101,600)	**Yes** (n = 40,201)	**No** (n = 43,590)	**Yes** (n = 17,182)
Age	59.2 ± 18.6	69.8 ± 15.8	59.1 ± 18.6	69.7 ± 15.9
Sex	47,595	21,881	20,370	9,422
Male	(46.9%)53,970	(54.4%)18,310	(46.8%)23,206	(54.9%)7,755
Female	(53.1%)	(45.6%)	(53.3%)	(45.2%)
Morning (4-10am)	18,773 (18.5%)	9,727 (24.2%)	8,154 (18.7%)	4,160 (24.2%)
Hypertension	39,911 (41.5%)	20,211 (51.5%)	17,340 (42.0%)	8,574 (51.0%)
Hyperlipidaemia	29,432 (30.6%)	14,057 (35.8%)	12,768 (30.9%)	5,915 (35.2%)
Diabetes mellitus	17,731 (18.4%)	10,560 (26.9%)	7,576 (28.4%)	4,365 (26.0%)
Chronic kidney disease	1,998 (2.1%)	2,302 (5.9%)	886 (2.2%)	1,042 (6.2%)
Coronary artery disease	30,763 (32.0%)	16,551 (42.1%)	13,219 (32.0%)	7,144 (42.5%)
Prior stroke	6,040 (6.3%)	3,055 (7.8%)	2,631 (6.4%)	1,336 (8.0%)
PVD	881 (0.9%)	723 (1.8%)	381 (0.9%)	303 (1.8%)
COPD	6,751 (7.0%)	5,851 (14.9%)	2,889 (7.0%)	2,436 (14.5%)
Clinical statusHeart rate				
(bpm)Systolic BP	86.4 ± 21.7	92.5 ± 26.2	86.4 ± 21.8	92.6 ± 26.3
(mmHg)	142.6 ± 26.4	142.4 ± 30.6	142.7 ± 26.4	142.1 ± 30.5
Respiratory rateOxygen Sats	18.3 ± 4.5	21.0 ± 7.0	18.4 ± 4.6	21.0 ± 7.0
(%)	97.2 ± 3.1	94.9 ± 5.5	97.2 ± 3.1	95.0 ± 5.3
Temperature	36.7 ± 0.7	36.8 ± 0.9	36.7 ± 0.7	36.8 ± 0.9
GCS	14.9 ± 0.5	14.9 ± 0.6	14.9 ± 0.5	14.9 ± 0.5
Pain score	4.1 ± 3.0	4.2 ± 3.1	4.2 ± 3.0	4.2 ± 3.1
Pain radiation	13,143	4,698	5,710	2,070
Left arm/shoulder	(12.9%)3,414	(11.7%)1,801	(13.1%)1,538	(12.1%)805
Right arm/shoulder	(3.4%)8,588	(4.5%)2,885	(3.5%)3,654	(4.7%)1,231
Jaw/neck	(8.5%)9,363	(7.2%)3,230	(8.4%)4,035	(7.2%)1,397
Back	(9.2%)4,116	(8.0%)	(9.3%)	(8.1%)736
Abdomen	(4.1%)	1,852 (4.6%)	1,747 (4.0%)	(4.3%)
Pain character	22,212	8,275	9,630	3,559
Heavy/crushing/pressure	(21.9%)23,827	(20.6%)8,095	(22.1%)10,330	(20.7%)3,461
Sharp	(23.5%)3,845	(20.1%)1,325	(23.7%)1,667	(20.1%)575
Burning	(3.8%)34,005	(3.3%)14,262	(3.8%)14,405	(3.4%)6,095
Discomfort/tight	(33.5%)	(35.5%)	(33.1%)	(35.5%)
Pain aggravation	22,876	9,293	9,989	3,943
Coughing/breathing	(22.5%)2,662	(23.1%)1,529	(22.9%)1,167	(23.0%)662
Exertion	(2.6%)11,000	(3.8%)3,919	(2.7%)4,746	(3.9%)1,648
Movement	(10.8%	(9.8%)4,288	(10.9%)5,654	(9.6%)1,767
Palpation	13,028 (12.8%)5,471	(10.7%)1,937	(13.0%)2,330	(10.3%)863
Position	(5.4%)	(4.8%)	(5.4%)	(5.0%)
Other symptoms & signs	23,009	16,995	10,057	7,326
Dyspnoea	(22.7%)23,416	(42.3%)9,563	(23.1%)10,055	(42.6%)4,049
Nausea	(23.1%)7,127	(23.8%)3,962	(23.1%)3,091	(23.6%)1,724
Vomiting or diarrhoea	(7.0%)17,643	(9.9%)11,235	(7.1%)7,682	(10.0%)4,865
Cough or sputum	(17.4%)7,931	(28.0%)4,857	(17.6%)3,390	(28.3%)2,147
Drowsy or lethargy	(7.8%)9,512	(12.1%)5,355	(7.8%)4,089	(12.5%)2,236
Sweating	(9.4%)2,133	(13.3%)2,629	(9.4%)927	(13.0%)1,108
Oedema	(2.1%)	(6.5%)	(2.1%)	(6.5%)
Paramedic suspect serious pathology	27,881 (27.4%)	19,157 (47.7%)	11,998 (27.5%)	8,117 (47.2%)
Electrocardiogram	8,429	7,459	3,679	3,171
Not sinus rhythm	(8.3%)1,842	(18.6%)	(8.4%)	(18.5%)
LBBB	(1.8%)	1,480 (3.7%)1,524	789 (1.8%)1,171	631 (3.7%)619
RBBB	2,631 (2.6%)821	(3.8%)539	(2.0.7%)324	(3.6%)217
IVCD	(0.8%)3,249	(1.4%)1,726	(0.8%)1,476	(1.3%)707
T wave changes	(5.2%)3,074	(7.3%)3,315	(5.5%)1,381	(7.0%)1,356
ST changes	(4.9%)	(13.9%)	(5.1%)	(13.5%)

*Composite outcome defined as index admission to hospital (excluding non-specific pain), 30-day myocardial infarction, or 30-day mortality.
Continuous variables presented as mean ± SD for age, and median (IQR) for clinical status. PVD = peripheral vascular disease, COPD = chronic obstructive pulmonary disease. Region defined according to Accessibility and Remoteness Index of Australia. Paramedic suspicion defined according to whether the final paramedic diagnosis would generally require admission to hospital vs. could be managed as an outpatient (see Supplemental Material).

and calibration slope and intercept were calculated, with a slope of 1 and an intercept of 0 indicating perfect calibration. Given that ECG data are sometimes not available, we also assessed the performance of the full and simplified ECAMM score models without inclusion of ECG data.

For comparison, the 'History, Electrocardiography, Age, Risk factors' (HEAR) risk score and the Emergency Department Assessment of Chest Pain (EDACS) risk score were also calculated in our cohort [9,11]. Both are existing clinical risk scores used in chest pain risk stratification for patients with suspected ACS. The C-statistic was calculated for each risk score individually for prediction of the composite outcome and each of its individual components. Statistical analysis was conducted using StataMP version 17.0 for Mac (College Station, Texas, USA).

3. Results

A total of 202,573 participants were included in the analysis (Supplemental Figure I), 141,801 in the development cohort and 60,772 in the internal validation cohort. In both cohorts, mean (standard deviation, SD) age was 62 (19) years and 51% were women. The criteria for the composite outcome were met in 57,383 patients (28.4%),

comprising admission to hospital with a final diagnosis other than non-specific pain (excluding emergency short stay admissions) among 56,025 patients (27.7%), 30-day mortality in 3,598 patients (1.8%), and 30-day MI post-discharge among 710 patients (0.4%). Discharge diagnoses for patients admitted to hospital included myocardial infarction (11,070 patients, 5.5%), heart failure (4,877 patients, 2.4%), arrhythmia (597 patients, 0.3%), other cardiovascular conditions (19,441 patients, 9.6%), pneumonia (6,512 patients, 3.2%), exacerbations of chronic obstructive pulmonary disease (COPD) (4,287 patients, 2.1%), other respiratory conditions (3,458 patients, 1.7%), gastrointestinal disorders (6,834 patients, 3.4%), and other medical conditions (14,754 patients, 7.3%) (Supplemental Table II). Pre-hospital candidate variables used in the risk score development and rates of missing data for both cohorts are presented in Table 1 and Supplemental Table I.

3.1. Model development and performance

Forty-six candidate predictor variables measured by paramedics in the pre-hospital setting were identified for model creation (Table 1). The final multivariable model included 25 variables (Supplemental Table II), with regression coefficients used to develop the Early Chest pain Admission MI and Mortality (ECAMM) full model risk score (Fig. 1). Discrimination in the validation cohort was similar to that of the development cohort (C-statistic 0.775 vs 0.765; Supplemental Table V). Calibration was excellent in the validation cohort across the full range of risk (equal observed [28.3%] vs. predicted [28.3%] discharge safety; calibration in the large 0.000; slope 1.037; Brier score 0.1631; Supplemental Table V and Supplemental Figure II). Discrimination across various subgroups is shown in Supplemental Table V.

To derive the simplified ECAMM risk model, variables included in the full model were combined into new ordinal variables. The final

A **Full Model Risk Score Calculator**

Risk factors		Pts	Clinical status		Pts	Clinical status		Pts	Other features		Pts
Age	18-29	0	SBP	<90	+12	Sats	98-100	0	Suspect serious diagnosis		+12
	30-39	+4		90-99	+10		95-97	+4	Morning presentation		+5
	40-49	+17		100-109	+8		92-94	+13	ECG	Not sinus	+6
	50-59	+28		110-189	0		90-91	25		LBBB	+8
	60-69	+39		≥190	+5		<90	+42		T wave inv.	+13
	70-79	+47	HR	<45	+18	Temp	<36	+4		ST changes	+27
	80-89	+53		45-79	0		36-37.4	0	Other	Dyspnoea	+9
	≥90	+60		80-99	+4		37.5-37.9	+10		Vomiting	+12
Sex	Male	+10		100-119	+12		≥38	+30		Coughing	+6
	Female	0		120-149	+18	Pain score	0	0		Drowsy	+6
PHx	DM	+6		≥150	+14		1	+2		Oedema	+13
	PVD	+7	RR	<16	0		2-4	+1	Pain features	R arm pain	+10
	CKD	+19		16-24	+4		5-7	+4		Abdo pain	+7
				25-34	+10		8-10	+8		On exertion	+11
				>34	+30						

B **Simplified Model Risk Score Calculator for Bedside / Roadside Use**

Variable	Pts
Age	<50y: 0
	50-69y: +3
	≥70y: +5
Male	+1
Observations out of range *SBP<110mmHg, HR >100bpm, Sats<95%, T>37.5C, RR>24*	+2 (per item, max 10)
Risk factors and features *Diabetes, CKD, PVD, pain radiates to right, abdominal pain, ≥8/10 pain severity, dyspnoea, vomiting, cough, drowsy, oedema*	+1 (per item, max 6)
Suspect serious pathology	+2
High risk ECG *ST changes (2pts), LBBB, not sinus rhythm, T wave changes*	+1 (per item, max 3)

Score	ECAMM risk	30-day mortality	Admission with diagnosis: MI	CCF	LRTI & Resp.	Other	Non-specific pain	% of patients
0	4.6%	0.0%	0.5%	0.0%	0.2%	3.9%	61.1%	1.9%
1	4.5%	0.1%	1.1%	0.1%	0.7%	2.4%	66.4%	5.5%
2	8.1%	0.1%	1.6%	0.1%	0.5%	5.7%	60.7%	9.8%
3	8.5%	0.2%	1.6%	0.1%	1.0%	5.7%	63.9%	15.9%
4	11.6%	0.2%	3.5%	0.2%	0.8%	6.9%	63.6%	23.6%
5	15.8%	0.3%	4.1%	0.3%	1.2%	10.1%	62.6%	33.3%
6	20.4%	0.4%	6.0%	0.5%	1.6%	12.1%	57.4%	44.1%
7	22.5%	0.7%	6.2%	0.8%	1.8%	13.1%	54.3%	55.7%
8	28.5%	1.1%	7.0%	1.3%	3.0%	16.2%	50.0%	65.8%
9	33.6%	2.1%	7.4%	1.4%	4.8%	18.8%	45.2%	74.5%
10	40.5%	2.4%	8.4%	2.8%	6.1%	22.4%	37.4%	81.3%
11	45.8%	3.1%	7.4%	4.2%	9,5%	23.4%	33.9%	86.6%
12	53.5%	5.1%	9.8%	6.0%	13.4%	22.5%	28.6%	90.5%
13	60.9%	6.6%	10.3%	6.7%	17.1%	24.7%	21.8%	93.5%
14	68.2%	6.8%	11.0%	9.1%	21.9%	25.2%	16.6%	95.7%
≥15	78.5%	9.2%	10.2%	11.2%	33.3%	22.0%	10.9%	100.0%

SBP = systolic blood pressure, HR = heart rate, RR = respiratory rate, T = temperature, CKD = chronic kidney disease, PVD = peripheral vascular disease, LBBB = left bundle branch block, ECAMM = early chest pain admission, major adverse cardiac events, and mortality, MI = myocardial infarction, CCF = congestive cardiac failure, LRTI = lower respiratory tract infection, Resp. = respiratory diagnosis
Other diagnoses include other cardiovascular conditions, gastroenterological conditions, and other medical conditions requiring admission to hospital

Fig. 1. Full and simplified ECAMM risk score calculators for composite risk of admission, mortality and major cardiac events. (A) Full model ECAMM risk score calculator for the composite outcome designed for use in an app-based setting. (B) Simplified model ECAMM risk score calculator designed for bedside / roadside use. PHx = past medical history, DM = diabetes mellitus, PVD = peripheral vascular disease, CKD = chronic kidney disease, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, SBP = systolic blood pressure, HR = heart rate, Sats = oxygen saturations, RR = respiratory rate, Temp = temperature.

multivariable model for the simplified model risk score used six variables (Fig. 1, Supplemental Table IV). Discrimination in the validation cohort was similar to the development cohort (C-statistic 0.759 vs 0.751, Supplemental Table V) with excellent calibration (calibration in the large 0.000, slope 1.005, Supplemental Figure III). Both the full and simplified ECAMM models had marginally worse discrimination with exclusion of ECG data (C-statistics 0.759 for the full model and 0.744 for the simplified model, Supplemental Figure V).

3.2. Outcome rates

Rates of the composite outcome and individual components according to various risk categories using the full model score are shown in Fig. 2, Panel A. In the validation sample, the composite discharge risk endpoint occurred in 5.5% of patients with a score <30 points and in 69.9% of patients with a score greater than or equal to 110 points. Rates of admissions for specific final diagnoses according to risk categories in the validation cohort are shown in Fig. 2, Panel B. Among patients with <40 points, admission rates for myocardial infarction were 0.5%, congestive heart failure were 0.1%, and lower respiratory tract infections were 0.1%. Among patients with greater than or equal to 110 points, admission rates for myocardial infarction were 9.9%, congestive heart failure were 9.0%, and lower respiratory tract infections were 11.9%. Rates of composite outcome, individual components and specific diagnoses across the full range of scores for the full ECAMM model are shown in Supplemental Table V.

3.3. Comparison with existing risk scores

A literature search for clinical risk scores (that is, without measurement of troponin or other biomarkers) was performed to identify existing risk scores that could be derived using these data. In the validation sample, the full and simplified ECAMM risk models performed better than existing scores for prediction of the composite outcome (C-statistic 0.765 [full model] vs. 0.751 [simplified model] vs. 0.618 [HEAR] vs. 0.647 [EDACS]), in addition to all individual components, including 30-day MI (Table 2).

4. Discussion

In the present study, we developed and validated a clinical prediction model and the ECAMM risk score to predict index hospital admission for any specific diagnosis and 30-day outcomes, including MI and mortality, in a population-based cohort study of 202,573 patients attended by EMS for undifferentiated chest pain. The ECAMM risk models use demographic, comorbidity, clinical observation, and electrocardiography data routinely collected by paramedics in the pre-hospital setting and are readily applicable using a smart-phone or web-based app (or at the roadside or bedside for the simplified model) in conjunction with electronic pre-hospital medical record. The model is intended for use in the pre-hospital or early emergency setting and provides a probability output of the composite outcome and individual components including the chance of hospital admission for multiple specific diagnoses. We suggest the score could be useful in: (1) stratifying of all-cause risk in the pre-hospital or early emergency setting prior to blood sampling and other investigations; (2) guiding clinical decisions regarding the need to further investigate non-coronary causes of chest pain; and (3) guiding clinical decisions regarding early discharge among patients that are categorised as low-risk of ACS by rapid high-sensitivity troponin testing pathways.

Chest pain accounts for one in ten EMS attendances, and reflects a broad spectrum of potential diagnoses [2,3]. Of EMS attendances for chest pain, approximately half of affected patients are diagnosed with non-specific pain and 25% are diagnosed with non-cardiac conditions, such as pneumonia, pulmonary emboli, acute aortic pathologies, and gastrointestinal pathologies, as well as a gamut of other less common diseases [3]. Cardiac conditions are responsible for 25% of presentations, with 10% being related to ACS [2,3]. Mortality varies by condition, and high rates are observed across several conditions not limited to those related to the heart (e.g. pneumonia and acute aortic pathologies have similarly high mortality) [2]. Rapid assessment and management is prioritised due to the serious, time-critical nature of some of these diagnoses, meaning that almost all patients with chest pain engaging EMS are urgently transferred to emergency departments regardless of eventual diagnosis. This approach certainly has benefits in identifying patients at high risk, but potentially does so at the expense of over-triaging the 50% of patients with non-specific pain to often long, expensive emergency or hospital admissions. This impacts the ability of health systems to respond to other emergencies, in addition to the impost and stress placed on the patient with frequently prolonged ED assessment times. Chest pain decision pathways, which frequently incorporate risk scores for MI, have been shown to reduce rates of admission and unnecessary investigations [4,19], and the ECAMM score might be useful to incorporate into future decision pathways.

Due to the heterogenous nature of the causes of chest pain, stratifying patients into those who do and do not require urgent treatment and hospital admission is challenging. Predictive models that prioritise identification of specific conditions (such as ACS) may do so at the expense of missing alternative diagnosis that also have high mortality (such as aortic pathologies, pneumonia and heart failure). While such models are useful in some circumstances, they may be less useful at a patient level, where exclusion of a single condition does not provide a diagnosis or estimation of overall patient risk. The HEART, EDACS and TIMI risk scores stratify chest pain patients according to risk of ACS or subsequent MI, and the discriminatory metrics of these scores may relate to differentiating ACS from other serious conditions that require treatment [5,9–11]. Moreover, these scores were developed in the conventional troponin era and while each have been validated with high-sensitivity troponin assays, they may offer more limited benefits in the setting of newer rapid rule-out pathways [5,6]. Existing scores and rapid troponin pathways do not provide information regarding the risk of a non-coronary diagnosis being present, which partially limits their utility in facilitating early discharge. Several pre-hospital scores (such as NEWS, MEWS, PMEWS) are aimed at determining critically unwell patients for transport to hospital, but the focus of these has been to identify patients at risk of imminent deterioration rather than patients that need further investigation or are safe for early discharge [20–23]. To our knowledge, the ECAMM risk score model is the first clinical risk score addressing this need, and discriminatory performance for the composite outcome, and its individual components, was substantially higher in comparison to the HEAR and EDACS scores. In terms of how the ECAMM score may be used in clinical practice, a patient could present via ambulance to ED with chest pain, arriving with the ECAMM score calculated by paramedics, which could then be used to assist in triage decisions and in guiding patients towards a low risk pathway or more clinical investigations. This might be especially advantageous in ensuring adequate ED workup for patients with normal troponins but a high ECAMM risk score. However, the clinical use of the ECAMM score requires further prospective assessment prior to implementation into clinical practice.

The ECAMM model was developed from a large dataset of undifferentiated chest pain with 46 pre-hospital candidate variables considered for inclusion, which is a substantial strength in comparison to existing scores that relied on expert opinion or smaller datasets to select included variables [9–11]. An advantage of developing predictive models from large datasets is that candidate variables with poor discrimination are not included in the final model, even if conventional teaching suggests these increase the likelihood of the outcome being present. In this setting, some variables included in existing scores (e.g. pain radiation to the jaw or left side, pressure-like pain, sweating, and a past history of hypertension, hypercholesterolemia or coronary artery disease) were poor discriminators for the composite outcome in our cohort and

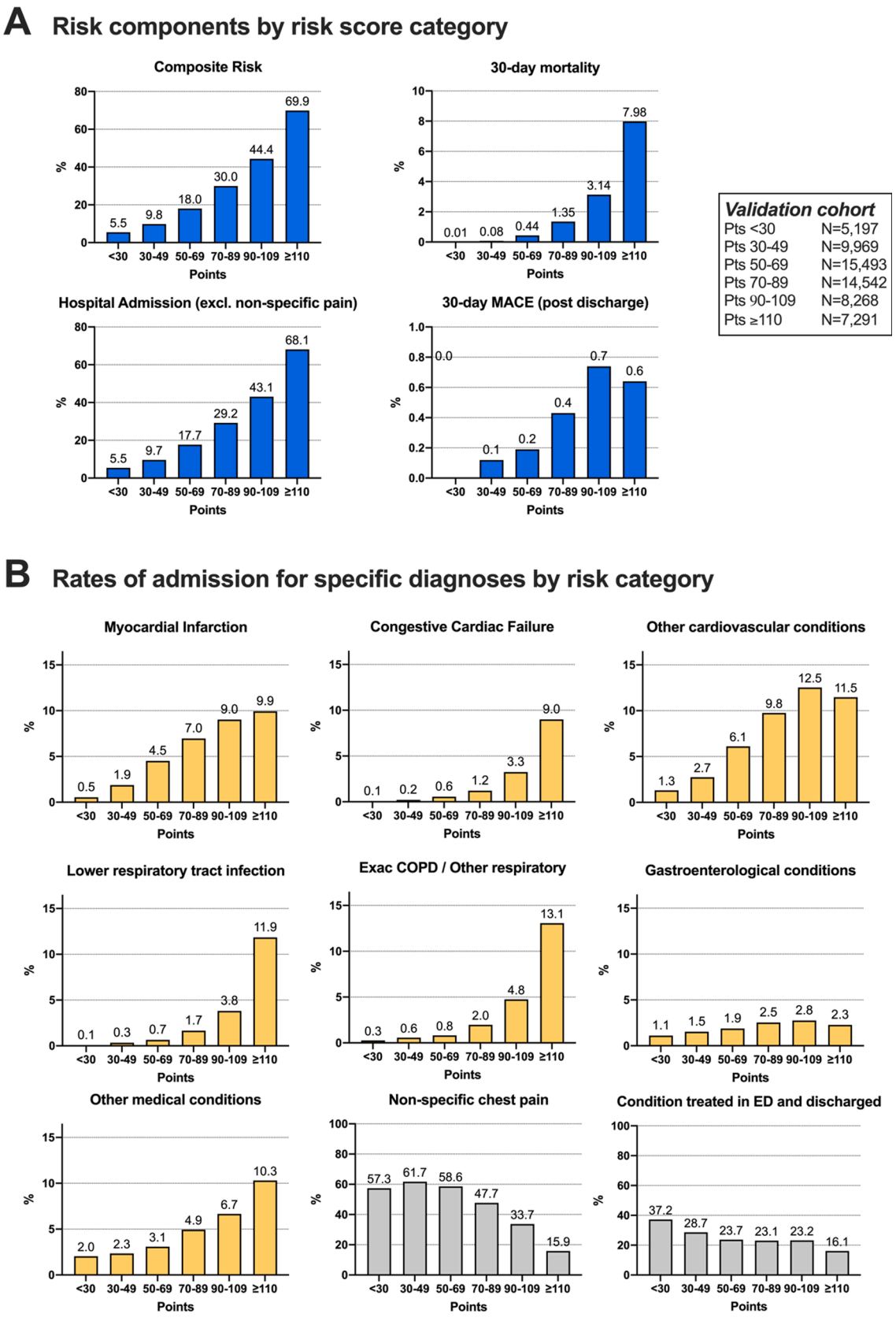

Fig. 2. Rate of composite discharge risk, individual endpoint components, and hospital admission discharge diagnoses across risk score categories. (A) Rates of composite discharge risk and individual components according to risk score categories in the validation sample. (B) Rates of hospital admissions resulting in a final diagnosis of myocardial infarction, congestive cardiac failure, other cardiovascular conditions, lower respiratory tract infection, exacerbations of COPD / other respiratory conditions, gastroenterological conditions, and other medical conditions in the validation sample according to risk score categories are shown in yellow. Rates of a final diagnosis of non-specific chest pain and conditions able to be treated by the emergency department and discharged are shown in grey.

Table 2
Comparison between the ECAMM models and existing clinical risk scores for chest pain in the validation sample (C-statistic and 95% CI).

Endpoint	ECAMM Full model	ECAMM Simplified model	HEAR score	EDACS score
Admission, MI, mortality	0.765 (0.761 – 0.769)	0.751 (0.746 – 0.755)	0.618 (0.613 – 0.622)	0.647 (0.642 – 0.651)
Admission to hospital*	0.761 (0.757 – 0.765)	0.747 (0.743 – 0.751)	0.618 (0.613 – 0.622)	0.643 (0.638 – 0.648)
30-day mortality	0.833 (0.822 – 0.843)	0.822 (0.811 – 0.833)	0.598 (0.582 – 0.613)	0.739 (0.710 – 0.769)
30-day MI (post discharge)	0.692 (0.663 – 0.722)	0.680 (0.650 – 0.710)	0.678 (0.644 – 0.711)	0.682 (0.667 – 0.697)

Data shown indicate area under the receiver operator curve with 95% confidence intervals shown in brackets.
*Admission includes admissions to hospital with any discharge diagnosis other than non-specific pain (excluding short stay admissions).
Note the HEAR and EDACS scores are validated for risk of 30-day major adverse cardiac events rather than admission or mortality. MI = myocardial infarction, CI = confidence interval.

therefore were not included in the final models. Moreover, the use of routinely collected data from clinical records and administrative datasets allows these models to be instituted without altering current clinical care pathways.

5. Limitations

Our study has several limitations. First, the score was derived in a single geographic region with a predominantly Caucasian population and its generalisability to other regions and populations requires external validation. The composite outcome used ICD-10 coding for final diagnoses, which can be susceptible to inaccuracies in comparison to independently adjudicated diagnoses [24]. Similarly, hospital admission as an outcome may vary with differing clinical practices in other jurisdictions outside Victoria. Pre-hospital 12-lead ECGs were incorporated into all ambulances by early 2017 in Victoria, and therefore prior to 2017 many patients had missing 12-lead ECG data. However, this was handled with multiple imputation, and the subgroup analysis for 2015 and 2016 demonstrated similar discrimination compared to 2017 onwards. Similarly, some clinically relevant features were not available in the ambulance dataset, such as duration of chest pain prior to ambulance attendance. Finally, patients with EMS records that could not be linked to hospital emergency or admission records (18% of the total cohort) were excluded, which may have introduced selection bias, although the magnitude and direction of any bias was not clear. Similarly, 30-day MI was derived from linked hospital records and therefore the same limitations apply to this outcome measure.

6. Conclusions

The ECAMM prediction score has been developed and internally validated using routinely collected pre-hospital clinical data to predict risk of hospital admission for any diagnosis, 30-day MI, and 30-day mortality among patients with undifferentiated chest pain, and is readily applicable using a smart-phone or web-based app. This tool provides a numerical risk assessment not limited to coronary diagnoses alone and is intended for use in the pre-hospital or early emergency department setting to assist in decisions regarding early discharge and the need to investigate for non-coronary conditions. This study paves the way for further prospective validation studies of this model including incorporating pre-hospital point-of-care troponin assays to improve risk stratification of patients with chest pain and potentially select patients appropriate for earlier discharge.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2022.101043.

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