

BMJ Open Long-term cardiovascular risk prediction in the emergency department: a mixed-methods study protocol

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ABSTRACT

Introduction Cardiovascular disease (CVD) remains one of the leading causes of preventable death in Europe, therefore any opportunity to intervene and improve care should be maximised. Known CVD risk factors are routinely collected in the emergency department (ED), yet they are often not acted on. If the risk factors have prognostic value and a pathway can be created, then this would provide more holistic care for patients and reduce health system inefficiency.

Methods and analysis In this mixed-methods study, we will use quantitative methods to investigate the prognostic characteristics of routinely collected data for long-term CVD outcomes, and qualitative methods to investigate how to use and implement this knowledge. The quantitative arm will use a database of approximately 21 000 chest pain patient episodes with a mean follow-up of 7.3 years. We will use Cox regression to evaluate the prognostic characteristics of routinely collected ED data for long-term CVD outcomes. We will also use a series of semi-structured interviews to co-design a prototype care pathway with stakeholders via thematic analysis. To enable the development of prototypes, themes will be structured into a logic model consisting of situation, inputs, outputs and mechanism.

Ethics and dissemination This work has been approved by Research Ethics Committee (Wales REC7) and the Human Research Authority under reference 19/WA/0312 and 19/WA/0311. It has also been approved by the Confidentiality Advisory Group reference 19/CAG/0209. Dissent recorded in the NHS' opt-out scheme will be applied to the dataset by NHS Digital. This work will be disseminated through peer-review publication, conference presentation and a public dissemination strategy.

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INTRODUCTION

The opportunity for long-term cardiovascular risk prediction in the emergency department

Cardiovascular disease (CVD) remains the leading cause of premature death in Europe.¹ It is estimated that if population-based primary prevention reduced mean blood pressure and cholesterol by 10%, it would reduce the incidence of major CVD by 45%.² There is an enormous human and economic

Strengths and limitations of this study

- A pathway to quantify and address long-term cardiovascular risk is potentially valuable in acute care settings as it would promote holistic patient care and improve long-term health outcomes.
- The quantitative arm of the study will examine the prognostic value of routinely collected data in the emergency department for long-term cardiovascular outcomes.
- The qualitative arm of the study aims to co-design a care pathway to use the information from the quantitative arm in a way that is acceptable to all stakeholders and is therefore easily implemented.
- A retrospective cohort study can suffer from more bias than a prospective study, including selection, information and confusion bias; however, it enables a timely answer and can highlight key areas to be followed up by prospective work.

cost associated with CVD. There are approximately 7 million people living with CVD in the UK, and it is responsible for one-quarter of all UK deaths and costs the UK £19 billion per year.^{3,4}

While in the emergency department (ED), all patients with suspected acute coronary syndrome (ACS) will have vital signs recorded as a standard of care. However, these data are not currently used to identify patients at risk of CVD, which represents an important missed opportunity. Previous research has demonstrated that patients with high blood pressure in the ED have over 90% probability of having persistently elevated blood pressure in the community setting.⁵ Recent studies have shown that hypertension measured in the ED is predictive of 10-year major adverse cardiovascular outcomes.⁶

There were 23.4 million patients presentations to the UK's ED in 2016, and this has been increasing by 10% each year.⁷ This increase in ED attendance represents a paradigm shift in the way patients are accessing healthcare, and while it has caused many previously noted



problems, it also presents opportunities. Patients who do not see their GP frequently are more likely to attend the ED, whose staff are therefore interacting with a portion of society underserved by primary care.⁸ Furthermore, in the drive for National Health Service (NHS) system-wide efficiency, we must maximise the use of each patient interaction with the health service. Considering the large amount of data already collected and stored routinely from the ED around the UK, this presents an ideal opportunity to predict and intervene in cardiovascular risk. Preventative medicine is not a new concept to emergency medicine (EM), and it has been researched and implemented successfully before.⁹ Furthermore, patients expect clinical staff in the acute care setting to have tools to inform them of their long-term CVD risk.¹⁰ It has also been demonstrated that such encounters represent teachable moments, where patients are more likely to accept advice about modifiable risk factors.^{11 12}

In a pilot trial comparing a clinical prediction model (CPM) with standard care for diagnosing acute myocardial infarction (AMI), we evaluated patient satisfaction regarding using the CPM as a rule-in/rule-out decision aid.¹⁰ While overall satisfaction was high (mean overall score 3.78/5), patients gave lower ratings (mean 2.78/5) for “advice you got about ways to avoid illness and stay healthy”. Patients are dissatisfied with an approach that simply informs them that they ‘do not have ACS’ but that does not address future cardiovascular risk.¹⁰ This sentiment was echoed by two patient groups and became an unexpected theme in a recent qualitative study of ED patients.¹³ While such tasks may previously have fallen to inpatient teams, the widespread use of early rule-out strategies means that emergency physicians must increasingly bear responsibility for informing patients of their future risk.

Furthermore, there is evidence that algorithms used to risk stratify patients with suspected ACS can also be predictive of long-term CVD.¹⁴ Farkouh *et al* demonstrated that patients with acute chest pain who were deemed to be at high risk of in-hospital complications had an HR of 2.45 (95% CI 1.67 to 3.58) for cardiovascular and cerebrovascular events at a medium follow-up of 7.3 years.

In primary care, the QRISK-2 (or QRISK-3) tool is routinely used to predict patients’ 10-year risk of CVD.¹⁵ If the 10-year risk exceeds 10%, the National Institute for Health and Care Excellence recommends that statin therapy should be considered. A range of other measures (advice on smoking cessation, weight loss, diet, exercise and review of comorbidities) should also be undertaken.¹⁶

This tool could potentially be used in the ED because most of the data required to calculate QRISK-2/QRISK-3 are already routinely collected. This could identify patients at high risk of CVD who would otherwise have been unidentified.

We aim to assess the prognostic value of routinely collected ED data for long-term cardiovascular outcomes. We will also examine the optimal method for deploying this knowledge with a co-designed clinical pathway created

through qualitative methods. Due to the potential to take advantage of the teachable moment among patients with suspected AMI, we will focus our investigations on this population. The care of patients with suspected AMI has evolved from a plethora of biomarkers assays to high-sensitivity troponins, and then to include CPMs.^{17–19} Each of these brought incremental improvements in the clinical diagnosis of AMI, and may have different long-term prognostic characteristics.¹⁷ We will focus our investigation on each of these diagnostic innovations.

METHODS

We will use quantitative methods to ascertain the prognostic value of routinely collected data for long-term CVD outcomes. The outcome data will be retrieved from NHS Digital’s data repository. Given the age of the data being linked, this will primarily be a limited scale feasibility study with exploratory analysis of the prognostic characteristics of the data. We will also use qualitative methods (via semi-structured interviews) to co-design a care pathway to be deployed in future to intervene and modify risk if individuals are noted to be at high risk of long-term CVD.

QUANTITATIVE ARM

Study arm design and study setting

We will use routinely collected data from patients attending the ED at Manchester Royal Infirmary (MRI) in the last 10 years. Patients with suspected AMI will be included. MRI has an annual ED attendance of 104 449, an inpatient capacity of 1721 beds and is a major trauma centre.

Study population

We will include patients who presented to the ED during three separate 12-month periods. Due to resource constraints only 3 years of data were accessible, so they were chosen to coincide with new diagnostic innovations (high-sensitivity troponin and a CPM) and a base line cohort to enable 10-year follow-up (box 1).

Sample size

We conducted a sample size calculation based on sample size methodology by Riley *et al*.^{20 21} We estimated that our Cox regression would have 10–20 candidate predictors, however this is dependent on the availability of data which is not yet known. We also estimated mean follow-up

Box 1 Cohorts that constitute the study population

- 1 January 2009 to 31 December 2009: selected to enable 10-year follow-up.
- 1 November 2011 to 31 October 2012: selected to coincide with the implementation of a high-sensitivity cardiac troponin assay.
- 1 July 2016 to 30 June 2017: selected to coincide with the implementation of a digital clinical prediction model (troponin-only Manchester acute coronary syndromes).

Table 1 Data variables to be collected

	Source
Outcome data	
Index event date time	Local EPR
Index event ICD-10 codes	Local EPR
Index event ICD-10-OPCS codes	Local EPR
Subsequent event date time	NHSD
Subsequent event ICD-10 codes	NHSD
Subsequent event ICD-10-OPCS codes	NHSD
Subsequent event treatment specialty	NHSD
Date of death	NHSD
Cause of death	NHSD
Predictor data	
Age	Local EPR
Gender	Local EPR
Ethnicity	Local EPR/NHSD
Physiological observations	Local EPR
Triage data	Local EPR
Time of departmental events	Local EPR
Laboratory investigations	Local EPR
T-MACS data	Local EPR
Rural/Urban indicator	NHSD
Indices of deprivation	NHSD

T-MACS diagnostic algorithm includes BP, sweating, crescendo angina, ECG ischaemia, troponin, pain radiating to the right arm or shoulder.

BP, blood pressure; EPR, electronic patient record; ICD, International Classification of Diseases; NHSD, NHS Digital; T-MACS, troponin-only Manchester acute coronary syndromes.

to be 7.3 years and the other sample size calculation inputs were calculated from the derivation of QRISK-3.¹⁵ The minimum sample size for 10 candidate predictors was calculated to be 3255, and for 20 candidate predictors 6509 participants. Given that we expect the cohort to consist of >20 000 participants, we believe that we will have sufficient data.

Data collection

We will include patients identified from the electronic patient record at MRI and collated with local biochemistry and coded diagnosis datasets. This will then be cross-referenced with NHS Digital's Hospital Episode Statistics database (table 1).

Outcome variables

We will examine the primary outcome of CVD defined as angina pectoris, myocardial infarction, coronary artery revascularisation, ischaemic heart disease, atraumatic stroke and transient ischaemic attack and cardiovascular mortality. International Classification of Diseases-10 outcomes include I20-24, I60-64 and G45.9, and Office

of Population Censuses and Surveys intervention version four codes include K40-50, K63 and K75.

Analysis

The incidence of cardiovascular outcomes and measures of data completeness (including the success of data linkage) will be summarised using descriptive statistics. We will use multiple imputation and also test the diagnostic plots of the algorithms to ensure convergence.

We will conduct a prognostic factor study for suspected CVD risk factors using a cox proportional hazard model to adjust for other co-variables. We will examine outcome data for CVD disease at 10-year (2009 data), 9-year (2011 data) or 4-year (2016 data) CVD onset. We will assess that the proportionality assumption holds and will apply time-varying interactions if not. In such an instance, we will consider flexible parametric survival models as alternatives. Although our sample is large enough to include all available covariates, we will consider various methods to reduce the number of parameters and make the tool easier to use (clinical judgement, collinearity, poor data quality or very high level of missingness).

We will quantify discrimination (ability to differentiate cases from controls) using C statistic. We will assess calibration (agreement between the observed and expected event rates) with flexible calibration plots, and calibration intercepts/slopes.

Using the 2011/2016 datasets, we will assess the prognostic value (in terms of calibration and discrimination) of high-sensitivity troponin T to predict cardiovascular events, using the aforementioned measurements. Then using the 2016 dataset we will assess the prognostic value of the troponin-only Manchester acute coronary syndromes acute chest pain algorithm to assess 4-year cardiovascular events.

We will also seek to externally validate other long-term cardiovascular risk prediction models that are available, such as the Framingham score and QRISK-3.^{15 22}

Qualitative arm

Study setting

The qualitative study will seek to co-design a care pathway for long-term CVD in the ED.²³ We will conduct two waves of semi-structured interviews to produce this. In the first wave of interviews, we aim to induct the design of potential solutions, this will be conducted according to the topic guide in the online supplemental material. The analysis will be mapped to a logic map, which in turn will be used to develop prototype care pathways. In the second wave of interviews, we will present prototype care pathways developed from the ideas of the first wave. We will invite feedback on prototype solutions developed from the first wave, seeking to illicit the participants' perspectives on the benefits or challenges of the different approaches. Specific feedback will be invited against the implementation outcome variables highlighted by Peters *et al* (acceptability, adoption, appropriateness and feasibility).²⁴

**Table 2** Inclusion and exclusion criteria for semi-structured interviews

Inclusion criteria	▶ Participant belongs to an identified stakeholder group. Patient with suspected cardiac chest pain deemed low risk by local care pathway.
Exclusion criteria	▶ Patient with suspected cardiac chest pain deemed moderate or high risk by local care pathway. ▶ Participant not fluent in English language. ▶ Participant unwilling to take part.

Stakeholders include emergency medicine consultants, general practitioners, acute care nurses and patients with chest pain.

Study population

Eligible participants will include ED doctors, general practitioners and nurses who will be recruited from local NHS centres. Also, patients will be recruited from local EDs within Manchester University NHS Foundation Trust. We will endeavour to conduct at least 4 interviews per stakeholder group, giving a total of 20 interviews per wave.

Patients will be eligible if they have presented to the ED with chest pain that their treating clinician suspected may be caused by an ACS (see table 2 for inclusion and exclusion criteria). We will approach potential participants while they are awaiting investigations, in the midst of what we anticipate is the ‘teachable moment’,¹² when the intervention will be applied in practice, is most likely to yield findings that can be generalised. The interview will be conducted in a separate ED clinic room to ensure privacy.

We will aim to recruit new participants for the second wave of the interviews. This will allow us to test our findings on a wider population and counter, to a degree, selection bias. We will use purposive sampling to ensure that we recruit participants with demographic characteristics that are representative.

We will record the background and reflexivity of the interviewers to ensure context and transferability of the findings. The interviews will be predominantly conducted by a junior doctor. It seems unlikely that this will influence the willingness of participants to respond freely, but the potential impact of positionality of the interviewer will be considered when analysing and interpreting the data.

Data collection

Analysis

The semi-structure interviews will be digitally recorded, transcribed and analysed according to multigrounded theory described by Goldkuhl and Cronholm.²⁵ This enables a mixture of deductive and inductive reasoning, using ‘pure’ grounded method to deduct and existing theory to induct creating a more robust analysis as a whole. The transcribed audio will be analysed using thematic analysis,²⁶ while also mapping against a logic model. This

model will follow the situation, inputs, outputs and mechanism format.²⁷ After this inductive process, we will deduct further iterations to the logic model by inviting feedback in the second wave of interviews, as demonstrated by Smith *et al.*²⁸ In this second wave of interviews, we will also invite feedback on prototype care pathways drawn from the initial logic model by trial steering committee.

It is also intended to use an evidenced based co-design approach to develop the care pathway.²⁹ This encompasses four stages: capture, understand, improve and measure. The ‘capture’ phase is where ideas are generated and prominent issues for resolution are condensed, then in the ‘understand’ phase the selected issues are extensively mapped. In the ‘improve’ phase, solutions are conceived to the issues in the first phases then in the ‘measure’ phase the implementation of the proposed solution is checked for improvement. This research will encompass the capture, understand and improve phase. The measure phase is a focus for future research.

We will construct a logic model of potential care pathways from our initial interviews using the situation-inputs-outputs-mechanism-outcome definition.

Coding and thematic analysis sensitivity analysis

Two separate clinical academic EM researchers will code a sample of the transcripts independently to ensure that no themes are misinterpreted or omitted. Each researcher will be blinded to the process and if conflicting codes are identified then a third researcher will adjudicate. This will ensure the transferability of the findings.

Sample size calculation

The interviews will continue until data saturation is achieved. Data saturation will be defined as a no new emerging themes and will be adjudicated by the researchers coding the transcripts. We anticipate that this is likely to occur by the end of the work packages but will continue if deemed necessary.

Ethics and dissemination

This study has received approval from the National Research Ethics Service and the confidentiality advisory group (references 19/WA/0312, 19/WA/0311 and 19/CAG/0209).

We will publish the results of our study in peer-reviewed journals. This mixed-methods co-design approach is in keeping with the Medical Research Council’s complex intervention guidelines, we believe that this will increase the implementation of our findings.³⁰

We will present the findings of our research at international conferences and develop a public engagement strategy in collaboration with our patient groups.

DISCUSSION

Risk prediction is not a new concept to the ED. In the short-term, we already use tools to identify those patients who are at high risk of complications (eg, 30-day major

adverse cardiac events in patients with acute coronary syndromes³¹; CURB-65 and community-acquired pneumonia³² and ABCD-2 score³³). However, we are becoming increasingly responsible for identifying long-term complications, for example, using CHA2DS2-VASc in new-onset atrial fibrillation.³⁴

EM physicians act on red flags for other conditions as part of routine care, such as a shadow on a chest radiograph that may be a small cell carcinoma and therefore lead to the patient's death in 6 months. So why ignore cardiovascular risk factors that could do the same? Previously, this may have been due to ED-measured hypertension being negated as 'white coat' hypertension, however more recent studies have suggested that 50% of patients who are found to be hypertensive in the ED have persistent hypertension at follow-up.^{35 36} Our quantitative analysis will add to the evidence base for the prognostic value of cardiovascular risk factors that are identified in the ED.

There is increasing concern for EM as it is perceived by some to be a service in crisis due to ever-increasing demand.³⁷ A conceivable consequence of the pathway we proposed is that it could exacerbate this issue by propagating the idea that EM is a solution for all conditions and their presentations. However, across our patient and public involvement group there was broad support for this proposal primarily due to the efficiency and its ability to reach otherwise inaccessible patients. Furthermore, the opportunity for preventative medicine in the ED has been highlighted previously.³⁸ We expect this topic to be explored in qualitative arm of this work, and a potential middle ground to be found where the hard-to-reach patients can be helped but the perception of EM is not adversely affected.

This multifaceted research project seeks to improve CVD care in the acute setting by answering two questions: (1) can routinely collected ED data predict long-term CVD and (2) how should long-term CVD advice be given in the acute care setting? If successful, this study would present a method for an efficiency in the health-care system, where each patient interaction is seized on to provide the greatest value to the individual and to the NHS.

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Competing interests RB has consulted for Siemens, Roche, Beckman, Singulex, LumiraDx and Abbott.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the 'Methods' section for further details.

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