CCU046: Severe mental illness and receipt of acute cardiac care and mortality following myocardial infarction

Output 1: Severe mental illness and receipt of acute cardiac care following myocardial infarction

Protocol

Version 1.0

Version control

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0.1	17 October 2022	Kelly Fleetwood Caroline Jackson	Initial draft
1.0	23 November 2022	Kelly Fleetwood Caroline Jackson	Approved version. Incorporated feedback from reviewers.

Summary

Severe mental illness (SMI), which includes schizophrenia, bipolar disorder and major depression, affects roughly one in ten adults every year in the United Kingdom (1). People with SMI die 10-20 years earlier than people without SMI (2, 3). This is mainly due to poorer physical health, in particular a higher risk of cardiovascular disease (CVD), including myocardial infarction (MI) (2, 4).

After an MI, people with SMI are more likely to die than those without SMI (5). The reasons for this are not well understood, but they are likely to be multifactorial, with systemic disparities in diagnosis, clinical investigation and treatment in primary and secondary care settings thought to be an important contributory factor (6). With respect to management of MI in the early post-event period, receipt of coronary revascularisation has been most studied, with lower rates observed in those with SMI (7-9). However, detailed understanding of how and why acute care for MI differs by SMI status and the contribution of this to short-term post-MI mortality is lacking. Furthermore, we do not know whether any differences in delivery of care and risk of dying after an MI have been affected by the COVID-19 pandemic. It is important to investigate this, to inform responses to this now and in future situations where disruptions of care occur.

This protocol describes the methods we will use to examine SMI and receipt of acute cardiac care following myocardial infarction. A second protocol will describe our methods for examining severe mental illness and mortality following MI.

Objectives

(1) Among people with an MI:
    a) how does receipt of guideline recommended acute cardiac process-of-care standards differ by comorbid SMI status?
    b) how has the COVID-19 pandemic affected any SMI differences in receipt of cardiac process-of-care standards?

Background

Myocardial infarction

MI can be classified as ST segment elevation (STEMI) or non-ST segment elevation (NSTEMI). A STEMI is caused by a complete blockage of the coronary artery and is more severe than an NSTEMI which is caused by a partial blockage of the coronary artery. The term 'acute coronary syndrome' (ACS) includes STEMI and NSTEMI, as well as unstable angina.

Acute cardiac process-of-care standards

Receipt of guideline recommended acute process-of-care standards is associated with improved survival (10, 11).

The UK National Institute for Health and Care Excellence (NICE) publishes guidelines for the care of ACS. NICE also publishes quality standards for ACS. The quality standards are a smaller set of prioritised process-of-care standards, including targets for the receipt and timeliness of percutaneous coronary intervention (PCI). The National Institute for Cardiovascular Outcomes Research (NICOR) publishes an annual report on acute cardiac process-of-care standards, based on data collected by the Myocardial Ischaemia National Audit Project.

In this study, we will evaluate process-of-care standards using data from 2017 to the present. The key guidelines, quality standards and reports are as follows:

NICE guidelines

- The most recent NICE guideline for acute coronary syndromes (NG185) was published on the 18th of November 2020 (12). It gives recommendations for people diagnosed with an ACS. A summary of this guideline was published by Corbett et al. (13)
- NG185 replaced several earlier guidelines:
    - CG172: Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease. Published 13 November 2013.
    - CG167: Myocardial infarction with ST-segment elevation: acute management. Published July 2013.
    - CG94: Unstable angina and NSTEMI: early management. Published March 2010.
    - TA230: Bivalirudin for the treatment of ST-segment-elevation myocardial infarction. Published July 2011.
    - CG130: Hyperglycaemia in acute coronary syndromes: management. Published October 2011.
    - MTG1: SeQuent Please balloon catheter for in-stent coronary restenosis. Published 1 December 2010.
- It also partially replaced:
    - TA152: Drug-eluting stents for the treatment of coronary artery disease (published July 2008, last updated November 2020)
    - TA71: Guidance on the use of coronary artery stents (published October 2003, last updated November 2020).
- The recommendations in NG185 were largely similar to those in previous guidelines, however there were some updates, especially to the advice on drug therapy.
- NICE guideline CG95 (Recent-onset chest pain of suspected cardiac origin: assessment and diagnosis) is also relevant because it provides recommendations for diagnosis of ACS.

NICE quality standards

- [QS68] Acute coronary syndromes in adults. Published 5 September 2014. (14)
- [QS99] Secondary prevention after a myocardial infarction. Published 4 September 2015. (15)

MINAP annual reports

- The MINAP 2022 Summary Report (16) evaluated 11 process-of-care standards for MI. The same 11 standards were also evaluated in the MINAP 2020 and 2021 summary reports.

Data

Data for this project will come from the CVD-COVID-UK/COVID-IMPACT consortium (17). The data includes individual health records from England from multiple healthcare settings, including GP data (for people alive on 1 November 2019), hospital data, CVD clinical audit data and COVID-19 test results.

Specifically, we will use the following datasets from NHS Digital's Trusted Research Environment (TRE) for England for the CVD-COVID-UK/COVID-IMPACT consortium:

1. GDPPR: GPES Data for Pandemic Planning and Research
2. HES: Hospital Episode Statistics
3. COVID-19 SGSS: Second Generation Surveillance System
4. Civil Registration – Deaths
5. ICNARC: Intensive Care National Audit and Research Centre
6. Medicines Dispensed in Primary Care (NHS BSA)
7. Myocardial Ischaemia National Audit Project (MINAP)
8. NICOR – PCI: Percutaneous Coronary Interventions
9. NICOR – NACSA: National Adult Cardiac Surgery Audit

A description of each of these datasets and the data that we will require is included below.

Myocardial Ischaemia National Audit Project (MINAP)

MINAP is an audit of patients admitted to hospital in England, Wales and Northern Ireland with MI (data from England is available in the TRE for England). It is administered by NICOR. MINAP seeks to include all hospitalised STEMI or NSTEMI events, with participating centres submitting information from across the patient journey, from the point of call to ambulance service or self-presentation at hospital, through diagnosis and treatment, to medication prescribed at discharge (18). Case ascertainment in MINAP is considered to be very good, with the most recent median case ascertainment in England reported as 99%. The MINAP collects a substantial breadth and depth of information on 130 data items, including patient characteristics and medical history, smoking status, various physiological and biological measures, diagnostic tests, investigations and interventions received (including reasons for non-receipt), and medications on admission and discharge. Information on time intervals/delays are also collected (i.e. time from patients' call for help to receipt of PCI [call-to-balloon] and arrival at hospital [call-to-door] and from arrival at hospital to receipt of PCI [door-to-balloon]).

The CVD-COVID-UK/COVID-IMPACT resource includes MINAP data for admissions from January 2017. Currently, records appear to be complete up to March 2022. We will use MINAP to ascertain data on cardiac care.

NICOR – NAPCI

NICOR also conducts the National Audit of Percutaneous Coronary Intervention (NAPCI). This audit collects data on PCIs including patient characteristics (e.g. demographic characteristics, medical history) and procedure characteristics (e.g. date of PCI, arterial access, type of stent, complications).

The CVD-COVID-UK/COVID-IMPACT resource includes NAPCI data from January 2017. Currently, records appear to be complete up to March 2022. We will use the NAPCI data as a supplement to the MINAP data, to ascertain additional information on receipt of PCI post-MI.

NICOR – NACSA

NICOR also administers the National Adult Cardiac Surgery Audit. This audit collects data on heart operations including coronary artery bypass grafts (CABG) and valve surgery, but not data on procedures that are performed with catheters such as PCI.

We will use the cardiac surgery audit to ascertain receipt of cardiac surgery following a heart attack.

Medicines Dispensed in Primary Care (NHS BSA)

The Medicines Dispensed in Primary Care dataset includes data on prescriptions dispensed in England, and prescriptions written in England but dispensed elsewhere in the UK. It includes prescriptions issued by general practice, community and hospital clinics, dentists and community nurses (https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/medicines-dispensed-in-primary-care-nhsbsa-data).

The CVD-COVID-UK/COVID-IMPACT resource includes NHS BSA data from April 2018. Currently, records appear to be complete up to June 2022. We will use the NHS BSA data to identify psychotropic medication use.

GDPPR: General Practice Extraction Service (GPES) Data for Pandemic Planning and Research

The GDPPR dataset (https://digital.nhs.uk/coronavirus/gpes-data-for-pandemic-planning-and-research/guide-for-analysts-and-users-of-the-data) includes GP records from individuals with active, current registrations at participating practices and deceased patients with a date of death on or after 1 November 2019. Individuals who opted out of secondary use of their GP data via the National Data Opt-out scheme are excluded from the dataset.

Clinical records are coded using SNOMED-CT codes. The GDPPR dataset does not include all codes recorded in primary care. It includes a selection related to specific diagnoses, prescriptions and lifestyle factors. Some codes are available from the start of each individual's records, however a subset are only available for clinical records within the last two years. Codes for MI, schizophrenia, bipolar disorder and depression are available from the start of each individual's records.

We will use primary care data to ascertain history of severe mental illness in some analyses, as well as comorbidities and other factors to be adjusted for in analyses (e.g. BMI, smoking). We will also identify MI from primary care records for some analyses. Currently, records appear to be complete up to July 2022.

HES APC: Hospital Episode Statistics Admitted Patient Care

The HES APC dataset includes records of all regular NHS hospital treatment in England. It excludes records from accident and emergency departments and from outpatient appointments. The dataset includes information about the date of admission, the primary diagnosis, up to 19 secondary diagnoses and operations, amongst other variables. Diagnoses are coded using the International Classification of Diseases 10th revision (ICD-10).

We will use HES data to identify severe mental illness, myocardial infarction and other comorbidities.

The CVD-COVID-UK/COVID-IMPACT resource includes HES data for all completed episodes of care from 1997. Currently, records appear to be complete up to March 2022.

COVID-19 SGSS: Second Generation Surveillance System

The COVID-19 SGSS dataset includes data on individuals who tested positive for COVID-19. We will use this data to identify COVID-19 status immediately prior to and after MI.

The CVD-COVID-UK/COVID-IMPACT resource includes SGSS data for admissions from the start of records in 2020. Currently, records are available up to August 2022.

Civil Registration – Deaths

The death records include all deaths registered in England or Wales. The data includes information on the date of death, the primary cause of death and up to 15 secondary causes of death. Causes of death are coded using ICD-10 codes.

We will use death records to identify deaths following myocardial infarction.

The CVD-COVID-UK/COVID-IMPACT resource includes death records from January 1993. Currently, records appear to be complete up to June 2022.

ICNARC: Intensive Care National Audit and Research Centre

The ICNARC dataset collects information on admissions to adult intensive care units (ICUs) and high dependency units (HDUs).

We will use this dataset to identify admission to ICUs and HDUs, including admission related to COVID-19 infection.

The CVD-COVID-UK/COVID-IMPACT resource includes ICNARC data for admissions from October 2019. Currently, records appear to be complete up to July 2022.

Methods

Cohorts

Primary cohort: Adults with a STEMI or NSTEMI recorded in MINAP from 1 November 2019 to latest date of complete MINAP records

Our primary cohort will include adults (≥ 18 years of age) with a final diagnosis of STEMI or NSTEMI recorded in MINAP from 1 November 2019 to latest date of complete MINAP records. For each individual we will include the first record of an MI within the study period.

Individuals in this dataset were, by definition, alive on the 1 November 2019. Thus we expect to have GP records for the majority of these individuals from their earliest GP record up to their most recent GP record. For these individuals we will be able to identify history of SMI based on a combination of both their GP records and their hospital records.

We will perform the following data checks (and we may adjust the final specification of the cohort based on these data checks):

- Percentage of cohort, with at least one GP record available in the GDPPR data (in order to identify if there are individuals with MINAP data, but without GDPPR data, e.g. individuals who live outside of England, but had an MI whilst visiting England),
- Length of GP lookback period for individuals with at least one GP record in the GDPPR data
- Cross-check of MIs identified from the MINAP data versus MIs identified from the GDPPR data, overall and stratified by history of a severe mental illness, and
- Cross-check of MIs identified from the MINAP data versus MIs identified from HES data, overall and stratified by history of a severe mental illness.

Secondary cohort: Adults with a STEMI or NSTEMI recorded in MINAP from 1 January 2017 to latest date of complete MINAP records

Our secondary cohort will include adults (≥ 18 years of age) with a final diagnosis of STEMI or NSTEMI recorded in MINAP from 1 January 2017 to latest date of complete MINAP records. For each individual we will include the first record of an MI within the study period.

This cohort provides us with a longer period of pre-pandemic MI data. It will give us more data to evaluate whether the COVID-19 pandemic affected any SMI differences in receipt of cardiac process-of-care standards. However, GP records are not available for people who died prior to 1 November 2019, hence for this cohort history of SMI will be based only on hospital data. We will therefore under-ascertain the proportion of people in the dataset with a history of SMI.

We will perform the following data checks (and we may adjust the final specification of the cohort based on these data checks):

- Cross-check of MIs identified from the MINAP data versus MIs identified from HES data, overall and stratified by history of a severe mental illness.

Exposure: severe mental illness

We will ascertain schizophrenia, bipolar disorder and major depression from primary care and hospital data.

For the primary care data, SMI will be identified using systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) codes.

For the hospital data, SMI will be identified using ICD-10 codes. We will identify SMI based on both primary and secondary diagnoses.

For analysis, we will define mutually exclusive groups of people with schizophrenia, bipolar disorder or depression. We will categorise people with a history of more than one SMI according to their most severe illness, with schizophrenia considered the most severe, followed by bipolar disorder and depression. Our analyses will compare people in each of these three groups to a control group. The precise definition of our control group will be discussed in our first collaborator meeting in December 2022, but will likely be either a) people without a prior diagnosis of SMI, or b) people without a prior diagnosis of any mental illness.

Outcomes: acute cardiac process-of-care standards

Initially, we plan to evaluate the process-of-care standards described below. However, we may modify the process-of-care standards that we plan to evaluate based on feedback from our first collaborator meeting in December 2022 and our first advisory board meeting in early 2023. We may also add additional standards of care based on findings from the qualitative element of this study (the qualitative element will include interviews with healthcare providers involved in the care of people with MI and patients with a history of both MI and SMI).

Standards of care relevant to STEMI include

- receipt and timeliness of PCI
    - call-to-balloon time (i.e. time from call for help to receipt of PCI) analysed both continuously and dichotomously using the standard 120 and 150 minute targets
    - door-to-balloon time (i.e. time from arrival at hospital to receipt of PCI) analysed both continuously and dichotomously using the standard 60 and 90 minute targets
- receipt of thrombolysis [where PCI is inappropriate]
- reason for no reperfusion; and
- receipt of echocardiography (for evaluation of left ventricular function).

Those relevant to NSTEMI include:

- admission to a cardiac ward;
- eligibility for and receipt of angiogram; and
- angiogram within 72 hours.

Care standards relevant to all MIs include

- suitable secondary prevention medication prescribed at discharge
- referral for cardiac rehabilitation
- smoking cessation advice

Covariates

In our analyses, we will adjust for covariates that may affect receipt of acute cardiac process-of-care standards. The covariates we plan to adjust for are listed below, however, we may modify this list based on feedback from our first collaborator meeting in December 2022 and our first advisory board meeting in early 2023. We may also modify this list based on findings from the qualitative element of this study.

Patient characteristics

- Age
- Sex
- Socioeconomic status
- Ethnicity
- Medical history, including previous MI, previous chronic cardiac failure, previous angina, diabetes, chronic renal failure, previous PCI and cerebrovascular disease

MI characteristics

- Baseline risk (GRACE risk score)
- Cardiogenic shock
- ST-segment changes
- Cardiac arrest
- Troponin elevation
- COVID-19 status

Care characteristics

- Hospital where treatment took place (this field isn't directly available from the MINAP dataset however we will explore linking the MINAP dataset to the HES APC dataset in order to derive hospital)
- Month and year of admission
- Timing of admission (e.g. weekday or weekend, daytime or overnight)

Statistical analysis

This section describes our initial plan for the statistical analyses. However, we may modify this plan based on feedback from our first collaborator meeting in December 2022 and our first advisory board meeting in early 2023. We may also modify this plan based on findings from the qualitative element of this study.

Data quality assessment

We will review the completeness of all variables that we plan to use in analyses and also cross-check variables against each other where possible. We will also examine how COVID-19 testing changed over time, as community testing was introduced, which will inform how we will account for COVID-19 infection in the analyses. We will also explore the appropriateness of adjusting for hospital stay and/or admission to an intensive care unit.

Descriptive analyses

We will compare patient, event and care characteristics among people with versus without SMI. We will examine whether volume of MI admissions by SMI status, characteristics of patients, and receipt of care changed during the COVID-19 pandemic.

Objective 1: Do people with an SMI experience any differences in acute cardiac care?

In order to address objective 1, we will use our primary cohort, as defined above. We will analyse patients with STEMI and NSTEMI separately, given the guideline-recommended standards of care differ by MI type.

We will analyse receipt of acute cardiac process-of-care standards in those with versus without SMI using logistic regression analyses or Cox proportional hazards regression depending on whether we are analysing occurrence of event or time to event. We will use a competing risks model where appropriate (e.g. accounting for competing risk of death for when analysing time to coronary revascularisation). Models will be adjusted for covariates including patient, MI event and care characteristics. We will use multiple imputation by chained equations to handle missing data in covariates.

Objective 2: How have any differences in acute cardiac care been affected by the COVID-19 pandemic?

In order to address objective 2, we will use our secondary cohort, as defined above. To examine the effect of the COVID-19 pandemic on associations between SMI and outcomes, we will include continuous calendar time in the models and evaluate interactions between continuous calendar time and SMI. This will allow us to determine the effect of the pandemic on MI outcomes and care without imposing a somewhat artificial cut-point for “pre” versus “post” pandemic.

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