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

Output 3: Severe mental illness and incidence of heart attack, heart failure and stroke

Protocol

Version 1.0

Version control

Version	Date	Author(s)	Comment
0.1	13 October 2023	Kelly Fleetwood Caroline Jackson	Initial draft
1.0	9 November 2023	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) (2). The COVID-19 pandemic is thought to have worsened various pre-existing health inequalities (4), but the extent to which mental health inequalities have been exacerbated remains unclear.

Previous research, including analyses of the CVD-COVID-UK resource have shown that attendance at cardiology services (5) and hospital admission for multiple CVD conditions, including heart disease, heart failure and stroke, decreased during the early period of the pandemic (6). Although admission rates for some conditions returned to normal during 2021, admission rates for certain conditions, including heart failure and stroke increased. Moreover, analyses of cardioprotective drug prescribing suggest a decrease in cardiovascular medication prescribing in the first year of the pandemic (7). These findings may reflect delays in accessing health care, with more major CVD events occurring due to interrupted or delayed primary or secondary prevention treatment. This may have disproportionately affected vulnerable sub-groups of the population, including those with SMI.

This study will use English data from the CVD-COVID-UK resource to determine the impact of the COVID-19 pandemic on associations between mental illness and incidence of myocardial infarction, heart failure and stroke. This understanding will inform strategies to address these mental health inequalities and to mitigate the impact of future disruptions to health care provision.

Context

This protocol describes our plans for Output 3 of CCU046 'Severe mental illness and receipt of acute cardiac care and mortality following myocardial infarction'. There are three other outputs planned:

- Output 1 examines, amongst people with myocardial infarction, whether guideline recommended acute cardiac process-of-care standards differ by comorbid SMI status, and whether any differences have been impacted by the COVID-19 pandemic.
- Output 2 examines whether mortality following myocardial infarction differs by comorbid SMI status, and whether any differences have been impacted by the COVID-19 pandemic.
- Output 4 is very similar to Output 3, however it will compare incidence based on mental health service use profiles (based on data from the mental health services dataset) instead of SMI diagnoses.

Objectives

- To investigate the impact of the COVID-19 pandemic on **myocardial infarction** incidence, comparing people with schizophrenia, bipolar disorder or depression to people without any of these disorders.
- To investigate the impact of the COVID-19 pandemic on **heart failure** incidence, comparing people with schizophrenia, bipolar disorder or depression to people without any of these disorders.
- To investigate the impact of the COVID-19 pandemic on **stroke** incidence, comparing people with schizophrenia, bipolar disorder or depression to people without any of these disorders.

Data

Data for this project will come from the CVD-COVID-UK/COVID-IMPACT consortium (8). 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. Civil Registration – Deaths

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

We will use the GDPPR and HES datasets to identify SMI, and all datasets to identify myocardial infarction, heart failure and stroke. Further details of how we will identify the conditions is provided in the Methods section. We considered additionally using audit data to identify myocardial infarction, heart failure and stroke, via the Myocardial Ischaemia National Audit Project (MINAP), National Heart Failure Audit (NHFA) and Sentinel Stroke National Audit Programme (SSNAP) audits. As at November 2023, the English data from the TRE for England includes:

- MINAP records from January 2017 to March 2022,
- SSNAP records from April 2018 to June 2023, and
- NHFA records from January 2018 to September 2020.

However, we decided not to use the audit data in this project because the aim of this project is to provide a broad overview of the impact of the COVID-19 pandemic on myocardial infarction, heart failure and stroke incidence by SMI. Since the MINAP and the NHFA audits only had records up to March 2022 and September 2020 respectively, whereas the GDPPR, HES and death records all had data up to June 2023, inclusion of the audit data would lead to a shortening of the analysis periods for myocardial infarction and heart failure and variation in the analysis periods between conditions. Audit data would be useful for inclusion in more detailed individual evaluations of myocardial infarction, heart failure and stroke incidence by SMI status, however this is beyond the scope of the current project.

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 myocardial infarction, heart failure, stroke, schizophrenia, bipolar disorder and depression are available from the start of each individual's records.

We will use primary care data to ascertain myocardial infarction, heart failure, stroke, schizophrenia, bipolar disorder and depression in some analyses. Currently, records appear to be complete up to June 2023.

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 myocardial infarction, heart failure, stroke, schizophrenia, bipolar disorder and depression.

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 June 2023.

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, heart failure and stroke.

The CVD-COVID-UK/COVID-IMPACT resource includes death records from January 1993. Currently, records appear to be complete up to June 2023.

Methods

We will examine the association between diagnosed schizophrenia, bipolar disorder and depression and CVD incidence using two different approaches to address the differing limitations of the datasets available.

In the **primary analysis** we will define mental illness using GP records and HES data and incident CVD outcomes using these data plus mortality records. This analysis benefits from the inclusion of GP data which will improve ascertainment of mental illness exposures and CVD outcomes. However since GP records are not available for people who died prior to November 2019, this analysis will only evaluate CVD incidence from November 2019, which does not give us much data on pre-pandemic incidence.

In the **secondary analysis** we will define mental illness using HES data and incident CVD outcomes using these data plus mortality records. This analysis will allow us to evaluate CVD incidence from April 2007.

All analyses will be conducted in R (9).

Primary analysis

Cohort

We will base this cohort on adults (age ≥ 40 years) with a record in the GDPPR dataset.

Exposure

We will ascertain schizophrenia, bipolar disorder and major depression from the HES APC dataset, using records from 1997 onwards and from the GDPPR dataset, using all available data. For the HES APC dataset, we will identify SMI based on both primary and secondary diagnoses, using the following ICD-10 codes:

- Schizophrenia: F20, F25
- Bipolar disorder: F30, F31
- Depression: F32, F33

For the GDPPR dataset, we will identify SMI using SNOMED codelists that were developed as part of CVD-COVID-UK project CCU046_01.

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. Individuals will enter the exposed group from the date of first hospital admission for the most severe of the three disorders.

Outcomes

We will identify first myocardial infarction, heart failure and stroke events from the GDPPR dataset, the HES APC dataset and the death records from 1 November 2019 to the most recent date of complete data. We will define an event as incident if the person has no previous records for the event recorded during the preceding 10 years. We will identify outcome events based on GDPPR diagnoses, primary and secondary HES APC diagnoses and primary causes of death. For the GDPPR dataset we will identify outcome events using the following SNOMED code lists

- Myocardial infarction: codelist developed for project CCU046_01 (see https://app.box.com/file/1143067272238, SNOMED-CT codes tab). This code list was developed from existing codelists by excluding codes for history of myocardial infarction.
- Heart failure: https://phenotypes.healthdatagateway.org/phenotypes/PH968/version/2146/detail/
- Stroke: we have not previously used a SNOMED codelist for stroke. We searched the HDR UK phenotype library for stroke, but did not find an existing codelist. We will ask the CVD-COVID-UK data wrangling team if they are aware of any SNOMED codelists for stroke. If an appropriate codelist is not available we will develop one based on the STRK_COD cluster from the GDPPR dataset. We will search for additional relevant SNOMED codes by mapping stroke codelists available for other coding systems such as Read V2 and searching for appropriate terms amongst the GDPPR dataset codes.

For the HES APC dataset and the death records we will identify outcome events using the following ICD-10 codes:

- Myocardial infarction: I21, I22
- Heart failure: I50, I11.0, I13.0, I13.2
- Stroke: I60, I61, I63 and I64

Covariates

For each person in the cohort we will identify age, sex, deprivation (based on quintiles of the Index of Multiple Deprivation) and ethnicity.

Data preparation

For each of the three outcomes (myocardial infarction, heart failure and stroke) we will model monthly incidence by age, sex, deprivation quintile, ethnicity and SMI group. We will adopt a similar approach to that used in our previous analyses of mental illness and CVD incidence in Scotland, using a dynamic cohort design (with individuals able to move from the non-exposed to exposed group at point of mental illness recording).

For each outcome and month:

- We will identify people aged at least 40 years by the end of the month, excluding people who died before the start of the month, or have a previous record of the outcome.
- We will then calculate the person-months contributed by each person with
    - Start of follow-up defined as the latest of first day of the month, or date of 40th birthday
    - End of follow-up defined as the earliest of outcome event, death, or last day of the month
- We will then summarise the person years by age on the first day of the month, sex, deprivation ethnicity and SMI group. If a person has their first admission for their most severe SMI within the month, we will allocate the person years prior to this admission to the non-exposed group and the person-years from this admission to the appropriate SMI group.
- We will then count the number of outcome events in the month by age on the first day of the month, sex, deprivation, ethnicity and SMI group. As above, we will take care to appropriately allocate any events which occur in the same month a person has their first admission for their most severe SMI.

Statistical analysis

We will conduct separate analyses for each outcome (myocardial infarction, heart failure and stroke).

For each outcome, we will summarise the sociodemographic characteristics of the people with the outcome by severe mental illness.

For each outcome, we will calculate calculated age-standardised incidence rates, per 1000 person-years, using the 2013 European Standard Population (http://www.isdscotland.org/Products-and-Services/GPD-Support/Population/Standard-Populations/).

For each outcome, we will model incidence with Poisson or quasi-Poisson models, as appropriate. We will model incidence (number of people with the outcome by number of person years) by severe mental illness, age, sex, calendar month, deprivation and ethnicity. We will evaluate interactions between continuous and categorical calendar month and mental illness in order to examine the effect of the COVID-19 pandemic.

We will estimate relative risks of each outcome for people with each severe mental illness versus people without a severe mental illness.

Secondary analysis

In the secondary analysis we will define mental illness using HES data and incident CVD outcomes using these data plus mortality records. This analysis will allow us to evaluate CVD incidence from April 2007.

Cohort

We will base this cohort on England's adult (age ≥ 40 years) population. We will use mid-year population estimates for England to define the full cohort.

Exposure

We will ascertain schizophrenia, bipolar disorder and major depression from the HES APC dataset, using records from 1997 onwards. We will identify SMI based on both primary and secondary diagnoses, using the following ICD-10 codes:

- Schizophrenia: F20, F25
- Bipolar disorder: F30, F31
- Depression: F32, F33

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. Individuals will enter the exposed group from the date of first hospital admission for the most severe of the three disorders.

Outcomes

We will identify first myocardial infarction, heart failure and stroke events from the HES APC dataset and the death records from 1 April 2007 to the most recent date of complete data. We will define an event as incident if the person has no previous admissions to hospital for the event recorded during the preceding 10 years. We will identify outcome events based on both primary and secondary HES APC diagnoses and primary causes of death, using the following ICD-10 codes:

- Myocardial infarction: I21, I22
- Heart failure: I50, I11.0, I13.0, I13.2
- Stroke: I60, I61, I63 and I64

Covariates

In this analysis, we would have ideally adjusted for age, sex, deprivation based on the IMD and ethnicity. In order to adjust for all of these variables we would need yearly population estimates for England by age, sex, deprivation quintile and ethnicity. However, such estimates are not publicly available (we confirmed this by contacting the ONS). Hence, we will adjust for age, sex and deprivation.

Population estimates by age, sex and deprivation are available from the ONS website:

1. Yearly data for 2001-2019: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/adhocs/12386populationbyindexofmultipledeprivationimdengland2001to2019
2. Monthly data from January 2019 to August 2022: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationprojections/adhocs/15363monthlypopulationsbyindexofmultipledeprivationimddecileenglandjanuary2019toaugust2022

Data preparation

For each of the three outcomes (myocardial infarction, heart failure and stroke) we will model monthly incidence by age, sex, deprivation quintile, and ethnicity and SMI group. We will adopt a similar approach to that used in our previous analyses of mental illness and CVD incidence in Scotland, using a dynamic cohort design (with individuals able to move from the non-exposed to exposed group at point of mental illness recording).

For each outcome, SMI and month:

- We will identify the population of people aged at least 40 years with the SMI, including people who were diagnosed with the SMI on or before the end of the month, and excluding people who died before the start of the month, or have a previous record of the outcome.
- We will then calculate the person-months contributed by each person with
    - Start of follow-up defined as the latest of first day of the month, or date of SMI diagnosis
    - End of follow-up defined as the earliest of outcome event, death, or last day of the month
- We will then summarise the person years by age on the first day of the month, sex, deprivation and ethnicity
- We will then count the number of outcome events in the month by age on the first day of the month, sex, deprivation and ethnicity

To get the data for people without an SMI, we will derive monthly population estimates for England by interpolating the mid-year population estimates, as required. For each outcome and month:

- We will then estimate the number of person months for people without an SMI by subtracting the number of person months for people with an SMI from the total number of person months for people in England.
- Likewise, we will estimate the number of outcome events in people without an SMI by subtracting the number of outcome events for people with an SMI from the total number of outcome events for people in England

Statistical analysis

We will use the same approach as used for the primary analysis.

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