CCU068

The impact of vaccination on the excess clinical risks of COVID-19 in patients with congenital heart disease

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Project members

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Background

Our group has investigated the clinical risk associated with COVID-19 infection in patients with congenital heart disease (CHD) in the UK health system using the Clinical Practice Research Datalink (CPRD), containing primary care medical information from >20 million people in England. We identified 86,896 CHD patients among whom there were 3,654 COVID diagnoses. Comparing these with 340,000 matched controls, we used information on positive PCR COVID-19 test surveillance, hospital episode data and death registration to examine the relationship between CHD complexity and COVID-19 infection severity in the context of age, sex,

ethnicity and associated pulmonary vascular disease. We found that CHD patients were at nearly twice the risk of COVID hospitalisation (N=823) and of death (N=223, an order of magnitude higher than previous studies) compared to controls without CHD, a much more striking finding in the UK healthcare context than has been provided from previous US studies.

All previous studies in this area, including our own, have used data which pre-dated large-scale vaccination programmes and, as such, were unable to determine the impact of vaccination in COVID-19 risk in CHD patients. The proposed study will aim to confirm and refine our estimates of the magnitude of the risks we have already identified in UK CHD patients with COVID using a much larger dataset than previously available. Larger numbers will also enable more accurate determination of the influence of comorbidities in COVID-19 risk. Finally, the more up-to-date data held by the BHF DSC for CVD-COVID-UK will allow us to assess the impact of vaccination as a strategy for mitigating these risks.

Research questions

1. Firstly, to confirm our previous work demonstrating that unvaccinated patients with CHD are at greater risk of hospitalisation and death than matched unvaccinated controls due to COVID-19 infection, and to increase the precision of our estimates of that risk through additional data.
2. What is the impact of vaccination on CHD patients in terms of infection severity, and requirement for any additional mitigation strategies?

Protocol

Data sources

TRE England

- GDPPR: GPES data for pandemic planning and research
- HES: hospital episode statistics
- COVID-19 SGSS: Second generation surveillance system
- Vaccination status
- Civil registration – Deaths
- COVID-19 SARI-Watch

SAIL Wales

- WLGP: Welsh longitudinal general practice
- OPDW: Outpatient dataset for Wales
- PEDW: Patient episode dataset for Wales
- PATD: COVID-19 test results
- CVVD: Covid vaccination dataset
- ADDE: Annual district death extract (ONS deaths)

Study windows

Two study windows will be used to assess COVID-19 outcomes in pre- and post-widespread vaccination.

- The pre-vaccination window is defined as the period from 1st March 2020 to 8th December 2020, the date of the first UK COVID-19 vaccination.
- The post-vaccination window encompasses the time between 1st March 2021 and 1st April 2022. The second assessment window was chosen based on the period from the successful completion of vaccination of the top four priority groups to the end of the NHS contact tracing service and scale-down of testing capacity.

Cohort selection

Case cohort

The electronic health records (EHRs) from eligible patients (registered to a practice in the country and alive at the beginning of the respective study windows) will be filtered for clinical codes indicating a CHD diagnosis or procedure (ICD-10, SNOMED, Read, or OPCS-4). Patients with CHD-specific codes (appendix 1A) will be classified as cases. Patients with codes relating to aortic valve disease (appendix 1B) - which could result from a congenitally defective bicuspid aortic valve (BAV), or from age-related degeneration of a normal aortic valve - undergo additional filtering. Specifically, patients whose first record of aortic valve disease occurred after age 65 were excluded. Subsequently, patients whose earliest record of aortic valve disease occurred after a condition which could damage the aortic valve (appendix 1C) are also excluded.

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Control cohort

Within each assessment window, eligible CHD patients will be matched to up to four controls – patients who had had documented Sars-CoV2 infection within the window and had not been identified as a CHD case based on the protocol above. For the pre-vaccination window, cases were matched to controls with the same GP practice, year of birth, ethnicity, and sex. For the post-vaccination window, having the same vaccination status was also required. To enable matching, information for patients with conflicting records for sex, ethnicity, or GP practice need to be resolved. Therefore, the person's most frequently recorded response is chosen in cases where conflicting records are present, and in the event of a tie, the most recent of the tied responses is chosen. Cases for which controls cannot be identified undergo a second round of matching, with the date of birth criterion relaxed; cases can be matched to controls with a date of birth within four years of their own.

Identification of COVID-19 infections

Infections will be identified in English EHRs by the presence of specific SNOMED codes in the GDPPR dataset (840539006, 1119302008, or 1240581000000104), positive COVID-19 PCR test results in the SGSS dataset, hospital admissions recorded in COVID-19 Hospitalisations in England Surveillance System (CHESS), or ICD-10 codes in Hospital Episode Statistics - Admitted Patient Care (HES APC) denoting COVID-19 disease (U07.1 or U07.2). In the Welsh data, infections will be identified in a corresponding manner. Specific Read codes relating to COVID-19 in WLGP (Y20fa, Y20fb, Y211c, Y228e, A7951, and 4J3R1), the COVID-19 Test Results (PATD) database identify positive COVID-19 PCR tests, and COVID-19 ICD-10 codes identified from PEDW. From these records of SARS-CoV-2 infection, the earliest for each patient can be determined. Patients who had not contracted

SARS-CoV-2 for the first time during the study window are excluded from the cohorts.

Identification of COVID-19 vaccinations

For the post-vaccination time window only, the vaccination status of each person upon their first SARS-CoV-2 infection will be identified. Records of vaccination will be identified from the English Vaccination Status database and the Welsh COVID Vaccination Dataset (CVVD), as well as from SNOMED (1156257001, 1324681000000101 or 1324691000000104) codes found in the primary care datasets.

Identification of associated conditions

To assess the incidence of medical complications - ischaemic stroke, ischaemic heart disease (new myocardial infarction and onset of angina), venous thrombotic disease (deep vein thrombosis, venous thromboembolism, pulmonary embolism), myocarditis and pericarditis - associated with either COVID-19 infection or vaccination, we will identify these conditions using specific codes. The baseline rate of these will be calculated in individuals prior to COVID-19 infection and pre-vaccination, as CHD cases will have a greater incidence than controls at baseline.

Statistical analysis

The odds ratios for severe COVID-19 outcomes between cases and controls will be estimated using conditional logistic regression. The variables used for case/control matching (age, sex, ethnicity, general practice) will be included as strata in the model. Smoking status will be included as a covariate in the regression.

To assess the influence of age, sex, ethnicity, CHD severity and the presence of pulmonary vascular disease/cyanosis on COVID-19 outcomes in CHD patients following vaccination we will conduct a case-only analysis. Multivariable logistic regression will be used to estimate the effect of each variable on the probability of hospitalisation or death with a patient's first SARS-CoV-2 infection.

To assess the incidence of medical complications, such as inflammatory or thrombotic events, associated with either COVID-19 infection or vaccination we will identify these conditions using specific codes (appendix 1D). The baseline rate of these will be calculated in individuals prior to COVID-19 infection and pre-vaccination, as CHD cases will have a greater incidence than controls at baseline. Then, identifying these diagnoses post-vaccination, we will calculate incidence rate ratios (IRRs) compared to baseline using Poisson regression, adjusting for age and sex.

Outcomes

- We will report demographics of the case and control cohorts to demonstrate their suitability in this study.
- We will also report a breakdown of the numbers of different CHD phenotypes included in the case cohort.
- Confirming our previous work, we will assess the difference in severe COVID-19 outcomes (hospitalisation and death) between CHD patients and controls in the pre-vaccination window.

- We will assess these differences again in the post-vaccination window to determine the impact of vaccination in this cohort with excessive risk.
- We will assess the incidence of events associated with COVID-19 infection and vaccination such as cardiac inflammation and thrombotic events, to determine if CHD patients are at greater risk of these complications.
- Phenotype codes and code used during the project will be deposited in the BHF DSC github repository.

Output

Manuscript on planned output: “COVID vaccination impact on CHD patients”