

## Leveraging the NIHR Health Informatics Collaborative (HIC) for Clinical Research in COVID-19 Infection

### Background

As part of the NIHR Health Informatics Collaborative (HIC), NHS trusts with BRCs have been collating and sharing routinely-collected data to support research. The HIC trusts have now started to collate and share data to support research into COVID-19. Participation is open to any trust that has signed (or is willing to sign) the NIHR HIC data sharing framework agreement.

### Approach

Each trust collates data from clinical systems into a local secondary database. The data is collated 'as is': no manual collection or curation is required. Extracts from this secondary database are used to support local and national research projects. This avoids duplication of effort in the extraction of raw data.

The data transformations needed to address the requirements of any particular project can be co-developed and shared – by the research project, or by the participating trusts (via the HIC). This avoids duplication of effort in the design of transformations.

For trusts that do not already have a secondary database or data warehouse for COVID-relevant data, or would like to take the opportunity to map their data to a new schema, an example schema is available at <http://nihr-hic.org/covid>.

### Dataset

The NIHR HIC COVID-19 dataset is also described at <http://nihr-hic.org/covid>. It includes routinely-collected data on: admissions; blood tests; virology; microbiology; prescribing; medicines administration; orders; vital signs; and critical care. The data should be collated for every patient with a COVID test.

The secondary database should contain data corresponding to the dataset specification. Trusts may wish to use their own names for data points and values (for tests, in particular) and then share information as to how these correspond to the names used in the specification.

The HIC coordinating centre will provide support for the sharing of this information and for the design of data transformations. The centre is working closely with NHS Digital and HDR UK on data standards and interoperability.

### Alignment

The design of the dataset has been informed by data sharing activity in the NIHR HIC cardiovascular, infection, and critical care themes. In each theme, trusts with BRCs have already worked together to collate and standardise routinely-collected data.

The secondary databases should provide data to support collaborative, translational research in these areas: in particular, in the area of cardiovascular medicine (see below). They should also provide data to support other key initiatives, including the CAPACITY-COVID registry and the DeCOVID project.

Part of the dataset corresponds to data already supplied in commissioning or reporting datasets. These data points should be populated automatically from the submissions made by the trust, or from the same systems used to generate these submissions.

The dataset specification may be updated and extended periodically to reflect additional, shared insights and opportunities, as well as changes to national reporting requirements.

### **Example: Leveraging the HIC Cardiovascular Theme**

The NIHR HIC Cardiovascular Theme is led by ICHT, with support from the coordinating team at Oxford. UCLH, GSTT, Imperial, and Oxford have shared data, and several other trusts are preparing to do so. The work has been prioritised by the NIHR/BHF Cardiovascular Partnership, connecting the cross-BRC collaboration to the network of BHF Centres and Accelerators. The value of the collaboration has been demonstrated by the recent publication of age-stratified risk profiles for troponin testing in more than a quarter of a million people <sup>1,2</sup>.

Adverse outcomes in COVID-19 infection are strongly influenced by co-existent cardiovascular risk. Myocardial ischemia, infarction, and myocarditis are all clinically important features of acute COVID-19 infection and are likely to be major factors in prognosis and stratification. The requirement for ITU treatment, the need for ventilation, and subsequent mortality are all strongly associated with a background of cardiovascular disease, including coronary artery disease.

COVID-19 infection can cause acute myocarditis, and both ischemia/infarction and myocarditis may co-exist in the same patient. Furthermore, many acutely unwell patients with COVID-19 infection and hypoxia will have a background of bystander coronary artery disease, which may or may not be a direct contributor to the acute deterioration. Understanding the contribution of these different mechanisms of myocardial injury will be important in establishing appropriate patient pathways <sup>3</sup>.

Troponin is known to be a prognostic biomarker in acute COVID-19 infection.<sup>4,5</sup> However, the nature and implications of the relationship between troponin level and risk – well-established in acute coronary syndromes – is unclear in acute COVID-19 infection, particularly if ischemia/infarction and myocarditis both contribute troponin elevation. Elevation of troponin, if not correctly interpreted, could lead to inappropriate coronary angiography and/or PCI, which has major adverse consequences for the patient, and for the delivery of health care, in the context of a COVID-19 epidemic.

Other relevant plasma biomarkers include lymphocyte count, ferritin, creatinine, NT-proBNP, and D-dimer, but it remains unclear how these are related to myocardial injury, and their potential relevance to the interpretation of troponin levels <sup>6,7</sup>. There is an urgent clinical need to characterise the nature of acute myocardial injury in the context of COVID-19 infection, and to understand the utility of existing blood biomarkers, so that they can be applied appropriately and rapidly <sup>3</sup>.

### **Next steps**

Trusts are asked to collate data corresponding to the HIC COVID-19 dataset, following the secondary database approach set out above; many trusts have already started to do this. The HIC coordinating centre will work with all trusts to help share insights and, where necessary, assist with the production and submission of data extracts for cross-centre or national research activities.

Trusts are asked also to submit de-identified extracts of the dataset to ICHT. The HIC cardiovascular theme will then facilitate collaborative cross-centre research in the area of cardiovascular medicine, providing researchers from all sites with secure access to a research-ready version of the data – one that has been subject to additional anonymisation procedures.

With the explicit, subsequent agreement of the contributing trusts, the cardiovascular theme will be able to supply a copy or an extract of the integrated data to other trusts, to other HIC themes – in particular, the critical care and infection themes – and to other national research activities. The code produced for data integration will be shared to assist trusts in providing data directly to these activities.

This activity is already underway. The HIC coordinating centre is working with trusts who are collating data and preparing to supply de-identified extracts to ICHT. The centre will provide example DPIAs and – for any partner trust that has yet to sign the framework agreement – a copy of the agreement for signature.

## References

1. Kaura A, Panoulas V, Glampson B, Davies J, Mulla A, Woods K, Omigie J, Shah AD, Channon KM, Weber JN, Thursz MR, Elliott P, Hemingway H, Williams B, Asselbergs F, O'Sullivan M, Kharbanda R, Lord GM, Melikian N, Patel RS, Perera D, Shah AM, Francis DP and Mayet J. Association of troponin level and age with mortality in 250 000 patients: cohort study across five UK acute care centres. *BMJ*. 2019;367:l6055.
2. Kaura A, Arnold AD, Panoulas V, Glampson B, Davies J, Mulla A, Woods K, Omigie J, Shah AD, Channon KM, Weber JN, Thursz MR, Elliott P, Hemingway H, Williams B, Asselbergs FW, O'Sullivan M, Lord GM, Melikian N, Lefroy DC, Francis DP, Shah AM, Kharbanda R, Perera D, Patel RS and Mayet J. Prognostic significance of troponin level in 3121 patients presenting with atrial fibrillation (The NIHR Health Informatics Collaborative TROP-AF study). *J Am Heart Assoc*. 2020;9:e013684.
3. Mattiuzzi C and Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak? *Ann Transl Med*. 2020;8:48.
4. Lippi G, Lavie CJ and Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. *Prog Cardiovasc Dis*. 2020.
5. Ruan Q, Yang K, Wang W, Jiang L and Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020.
6. Lippi G and Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med*. 2020.
7. Xie J, Tong Z, Guan X, Du B, Qiu H and Slutsky AS. Critical care crisis and some recommendations during the COVID-19 epidemic in China. *Intensive Care Med*. 2020.

## Governance

The data will be used for service improvement, clinical audit, and research. It will be supplied in de-identified form, with a unique subject number in place of NHS number (or other local patient identifier). The contributing trusts will maintain the mappings between subject numbers and NHS numbers (or other local patient identifier) so that:

- information pertaining to the same patient may be correctly linked across multiple extracts from a the same trust
- issues of data quality, including any errors in data de-identification, can be quickly and reliably addressed
- trusts can take advantage of any subsequent opportunity, under appropriate governance, to make the data available for linkage to/federation with other, approved studies

All data will be held and processed under NHS control, according to the SOPs and framework data sharing agreement already in place.

The data transferred to ICHT for the HIC cardiovascular theme will be de-identified, and the mappings will not be shared. Each of the participating trusts will complete a DPIA; any privacy risks identified will be reviewed and mitigating actions agreed with the local Caldicott Guardian and/or Data Protection Officer.