Geriatric Medicine Research Collaborative

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CovidCollab

A panspecialty international project to determine point of care predictors from routinely collected data

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Contents

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Background

On 11th March 2020 the World Health Organization declared the international spread of the Covid-19 virus to represent a global pandemic. Since initial identification, researchers have been working tirelessly to understand how to best manage this virus, whilst front line workers have worked to save those infected by the virus. The likelihood of adverse outcomes from the virus in those infected is known to increase with age, and in those with multiple comorbidities. However, more information is still needed on factors that can help prevent adverse outcomes, particularly in these most vulnerable of patients.

A number of laboratory studies have been shown to increase risk of adverse outcomes in patients suffering with Covid-19. There has also been some suggestion of increased risk in those taking angiotensin converting enzyme inhibitors and anti-inflammatory drugs, although there has been no proven association between these factors.

We consider that adverse outcomes in frail older adults are not just mortality. The increased likelihood of delirium in these patients has already been considered by experts in the field, especially considering that these patients may be isolated in an unfamiliar environment, with reduced contact with their relatives/ carers. Delirium is known to be highly distressing to those who are suffering from it, and increases likelihood of cognitive impairment in the long-term. In addition, frail older adults may have longer lengths of stay, and increased levels of dependency on discharge.

Aim

This project will utilise routinely collected data in order to understand how to best treat and care for those infected with Covid-19 of all ages.

Objectives

This project aims to assess the following:

- Predictive data modelling using routine laboratory data and patient factors
- Medication utilisation and discontinuation
- Antibiotic prescribing processes
- Specific management of Covid-19 in frail older adults

Patient identification

Ideally patients should be identified prospectively at the time of COVID-19 diagnosis. However, given the rapid progression of the global pandemic, there may be no further new cases of COVID-19 infection in some hospitals that treated large numbers of COVID-19 earlier in the pandemic. It is important to capture the experience of these centres; therefore, retrospective patient identification and data entry is permitted. No one should be putting themselves at additional risk in this study. This means that no one should be entering clinical areas purely for data collection who would not otherwise be in these clinical areas. Therefore, data should either be collected "point of care" by the clinicians directly responsible for the patient, via remote electronic systems, or retrospectively from patient notes after the patient has been discharged or died. Please see our "local information governance section" for examples of how this might work in practice at individual sites.

Prospective patient identification

Please ensure that as many staff at your site as possible are aware that your site is participating in "CovidCollab". Any clinician who identifies a patient with suspected Covid-19 should ensure that necessary data is collected. This means that they themselves should assess the Clinical Frailty Scale and delirium status at the point of patient contact (this is part of routine care and should be done for all patients with suspected Covid-19). See information governance section on examples of how this might work practically.

Retrospective patient identification

Sites should contact their local clinical audit/ coding team for all patients who were coded as having Covid-19 infection during the pandemic, who fit our inclusion/ exclusion criteria. Where it is necessary to access data from patient notes, please access this consecutively in the order that patients were admitted.

Inclusion criteria

- Aged 18 years and over
- Unscheduled admission to hospital
- Suspected or confirmed Covid-19 infection

Exclusion criteria

- Patient has specifically expressed a wish to dissent from use of their anonymised data for this purpose (informed consent for use of anonymised data will not normally be obtaining but please respect the wishes of anyone who has specifically dissented).
- Patient discharged from the emergency department for community management (i.e. not admitted)

Data collection

We will ask you to declare if your data was collected prospectively or retrospectively, as this will affect how data is recorded. There is an importance to balance burden of data collection on clinical staff against collecting data that we consider to be helpful towards improving care of vulnerable hospitalised patients. **We are prepared that the data collection may need to evolve over time** as more aspects are identified. At present, we are asking sites to collect all of the following information for hospitalised patients who are suspected to have Covid-19 infection on presentation to hospital:

- Country
- Hospital
- Age
- Biological sex
    - If female and under 60, pregnant Y/N
- Presenting symptoms
- Confirmed diagnosis – Y/N, Method used (PCR/Antibody test)
    - If negative, - is there a strong clinical suspicion that this patient may still have Covid-19 infection Y/N
- Heart rate, blood pressure, oxygen levels, respiratory rate, temperature on admission, height, weight (to assess impact of obesity, under-nutrition, and calculate e.g. Glomerular Filtration Weight in a standardised manner), Glasgow Coma Scale
- Arterial/ venous blood gas results
- Chest X-ray changes: none/ pneumonia/ acute respiratory distress syndrome (ARDS) changes/ not performed
- Prevalent delirium on admission? Y/N – Screen with 4AT (see appendix)
- Incident delirium (delirium that develops at any point during admission)? Y/N
- Clinical Frailty Scale – derived based on function TWO WEEKs prior to admission (see appendix)
- Previous residence (home without formal care support/ home with formal package of care/ 24-hour long-term care facility)
    - Were there other known/ suspected cases at this residence?
- Co-morbidities (Diabetes Mellitus, Cardiovascular Disease, Respiratory Disease/ Cancer/ Anxiety or Depression)
- Regular medications – Y/N to each of Angiotensin Converting Enzyme Inhibitors (ACE-i)/ Angiotensin Receptor Blockers (ARBs); Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); Steroids; Immunosuppressants; Chemotherapy
- If on any of the above – were these stopped on admission Y/N?
- Antibiotics – none/oral/IV, time administered after presentation to hospital
- IV fluids commenced, volume within first 24 hours
- Evidence of other concomitant infection e.g. blood culture, sputum culture results?
- Steroids newly commenced during admission for any indication?
- NSAIDs newly commenced during admission for any indication?
- Routine laboratory results at point first measured during admission (only if measured as part of routine care) – urea, creatinine, haemoglobin, lymphocytes, neutrophils, C-Reactive protein (CRP), Alanine Aminotransferease (ALT), ferritin, D-Dimers, troponin

- Was a Do Not Attempt Cardio-Pulmonary Resuscitation (DNACPR) decision made during admission? Were there other treatment and escalation limitation decisions in place?
    - If yes, was this already in place prior to admission?
- Death during admission and days to death
    - If death during admission, was end of life care instituted prior to this?
    - Were family members present?
    - Preferred place of care?
- Intensive Care Unit (ICU) admission at any point? Y/N
    - Length of ICU stay (Other details of this are beyond the scope of this project)
      NB: We are happy to link in our dataset with ICU datasets so please contact us if you wish to link our REDCap IDs for this purpose covidcollab2020@gmail.com
- Emergency surgery at any point? Y/N (Details of this are beyond the scope of this project but please consider if details can be included in separate CovidSurg project and include CovidSurg REDCap ID for patient)
- Length of stay
- Discharge destination/ care required on discharge
- Delayed discharge due to concerns about community spread e.g. to nursing homes?

Sites may also consider signing up for the ISARIC global Covid-19 data collection platform. Please email ncov@isaric.org to obtain access. https://isaric.tghn.org/covid-19-clinical-research-resources/

Information governance

Local information governance

No patient identifiable information should leave the hospital site; this should all be maintained on site. Only anonymised data will be uploaded to REDCap. Local sites will be able to maintain and use the data that they collect locally for local purposes. This includes linking this data with other studies where the patient has given informed consent for use of their data and biological specimens (e.g. through a UK Biobank), or ISARIC. A designated collaborator at each site will be provided with REDCap project server login details, allowing them to securely submit anonymised data directly to the REDCap at point of care using case report forms. We recommend that an electronic database is maintained on local site encrypted computers (e.g. in the UK, a local NHS server) with records of each REDCap ID cross-referenced against patient identifiers. Pending additional approvals, this may enable data linkage to GP or other records (e.g. ECLIPSE).

However, we recognise that in some sites that may be a paucity of available computers, and time may not allow real time upload to REDCap. Therefore, an alternative approach will be to use the paper templates provided to record, as a minimum, key information that is best collected at the point of care (e.g. Clinical Frailty Scale, presence of delirium), and can not be extracted from electronic records. These paper templates can be kept securely on site in a designated folder, so that records can be uploaded to REDCap at least weekly. We realise that this will be an extremely busy time for everyone clinically. Once data has been collected, data upload to REDCap can be completed by anyone who has local site approval (e.g. administrative staff who are part of the direct care team, clinical staff who are seconded away from clinical work due to health/ personal reasons, medical students).

Central information governance

Data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application. REDCap allows collaborators to enter and store data in a secure system. A designated collaborator at each participating site will be provided with REDCap project server login details, allowing them to securely submit data on to the REDCap system. REDCap has previously been successfully used for a range of other international cohort studies led by the central unit, including the GlobalSurg and ESCP Cohort studies. The REDCap server is managed by the University of Birmingham, UK. Only anonymised data will be uploaded to the database. No patient identifiable data will be collected.

Local approvals

The lead investigator at each participating site is responsible for obtaining necessary local approvals in line with their hospitals' regulations (this can be any clinician). Collaborators will be required to confirm that a local approval is in place at the time of uploading each patient record to the study database. Lead investigators at each site should discuss with their head of department whether it is possible to expedite the approvals process in view of the urgency of global pandemic. Whatever approvals pathway is followed, it should be highlighted that this is an **investigator-led, non-commercial, observational (no changes to normal patient care) study which is extremely low risk, as only routinely available non-identifiable data will be collected.**

Within the UK, we consider that this project should be considered as audit or service evaluation. Guidelines have been released by the World Health Organization for the management of patients with suspected Covid-19 and may serve as audit standards. In the UK, the National Institute for Health and Care Excellence (NICE) has produced guidelines on the management of patients with suspected Covid-19 infection and assessment of CFS is recommended as part of standard care for all hospitalised patients (https://www.nice.org.uk/guidance/ng159/resources/critical-care-admission-algorithm-pdf-8708948893). **Therefore, approvals can be obtained via standard approvals for service evaluation and clinical audit. If there is any uncertainty, please discuss with your local information governance team.**

As more information becomes available about approvals processes necessary in other countries we will continue to update this document. Please email covidcollab2020@gmail.com

Analysis

Analyses will be overseen by the data monitoring committee (DMC). **If we find that certain datapoints are frequently missing, and these are non-essential, we will look to revise our protocol to remove these.** Multivariable modelling will be undertaken to identify risk factors for 30-day mortality and ICU

admission. We will also specifically assess treatment and care of frail older adults, and those at the end of life. Interim analyses will be performed as guided by the DMC. Hospital-level data will not be released or published. Country-level analyses will only be conducted with permission of lead investigators from each participating country. Local investigators may access their local data at any time directly from the REDCap database. Investigators may choose to pool data across their country to perform country-level analyses (all participating hospitals should consent to their data being used in this way).

Authorship

Collaborators from each site who contribute patients will be recognised on any resulting publications as PubMed-citable co-authors. A corporate authorship model will be used (example: https://pubmed.ncbi.nlm.nih.gov/29452941). Specific collaboratives who have significantly contributed should email covidcollab2020@gmail.com so that the input of their collaborative can be acknowledged alongside individual collaboration.

Appendix

Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging. Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Figure I. 4AT assessment sticker