A protocol for a rapid network study on extracorporeal membrane oxygenation (ECMO) to inform its use in the management of COVID-19: characterising adults with ARDS who underwent ECMO between 2014 to 2019 and those with COVID-19 who underwent ECMO in 2020

# Background

## Rationale

Critical care is a key component in the response to the ongoing coronavirus disease 2019 (COVID-19) pandemic. Many patients who have severe COVID-19 develop acute respiratory distress syndrome (ARDS), which is characterised by the acute onset of hypoxemic respiratory failure.[1] Evidence-based treatment guidelines support the use of a range of interventions for such patients,[2] however one area of uncertainty relates to the use extracorporeal membrane oxygenation (ECMO). ECMO is an extracorporeal support that can be used in the treatment of respiratory and/or cardiac failure.[3] Evidence from a couple of randomised control trials has suggested that ECMO can lead to improved survival for patients with ARDS.[4,5] Moreover, its use for patients with influenza A(H1N1)-associated ARDS has been associated with reduced hospital mortality during that pandemic.[6]

The role of ECMO in the response to COVID-19 is relatively undefined, but it is likely to be an important treatment option in a subset of patients under conditions where the high-intensity therapy can still be offered.[7] Given the ever-increasing number of patients requiring critical care, further evidence is required so as to best guide its use. A better understanding of the patients with ARDS undergoing the procedure and their prognosis will help to inform decision-making.

## Research objective

To inform the ongoing response to the COVID-19 pandemic, our aims are:

1. To characterise patients with ARDS who underwent ECMO between 2014 to 2019
2. To characterise patients with COVID-19 who underwent ECMO in 2020

# Methods

## Study design

The study will be a cohort study based on routine-collected health care data which has been mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).

## Study participants

## Study participants in the *ECMO for ARDS 2014-2019* will

* Have had an ECMO (index event), with only the first ECMO during an individual's history considered, between 1st January 2014 and 1st December 2019,
* Have a record of acute respiratory failure over 30 days prior to day of index event,
* Be aged at or over 18 at their index event,
* Have at least 30 days of observation time prior to their index event
* Not have a record of heart or lung transplantation, or a record of one being planned, between 30 days prior to day of index event
* Not have a record of primary lung disease (cystic fibrosis, hemorrhagic autoimmune diseases. Idiopathic fibrosis, sickle cell crisis, primary pulmonary hypertension) between 30 days prior to day of index event
* Not have a record of chest trauma between 30 days prior to day of index event
* Not have a record of pneumonectomy between 30 days prior to day of index event
* Not have a record of pulmonary embolism between 30 days prior to 1 day prior to index event
* Not have had a cardiac procedure between 30 days prior to day of index event

Study participants in the *ECMO for COVID-19* will

* Have had an ECMO (index event), with only the first ECMO during an individual's history considered, after January 1st 2020,
* Have a record of COVID-19 over 30 days prior to day of index event,
* Be aged at or over 18 at their index event,
* Have at least 30 days of observation time prior to their index event
* Not have a record of heart or lung transplantation, or a record of one being planned, between 30 days prior to day of index event
* Not have a record of primary lung disease (cystic fibrosis, hemorrhagic autoimmune diseases. Idiopathic fibrosis, sickle cell crisis, primary pulmonary hypertension) between 30 days prior to day of index event
* Not have a record of chest trauma between 30 days prior to day of index event
* Not have a record of pneumonectomy between 30 days prior to day of index event
* Not have a record of pulmonary embolism between 30 days prior to 1 day prior to index event
* Not have had a cardiac procedure between 30 days prior to day of index event

### Exposure of interest

ECMO will be identified on the basis of records in the procedure occurrence table in the OMOP CDM. ARDS will be identified on the basis of SNOMED codes in the condition occurrence table. COVID-19 will be identified based on the presence of a diagnosis code indicating the presence or suspicion of COVID-19 or a positive test result for the disease. Other eligibility criteria will be assessed using the condition and procedure occurrence tables, with OMOP CDM ‘standard codes’ specified (with conditions identified using SNOMED codes and procedures mapped to a number of different codes, including SNOMED, ICD10PCS, ICD9Proc, and CPT4).

Characterising cohorts of time of ECMO

We will identify the following characteristics of the study participants: sex, age, observation time prior to their index date, and their index year and month. Individuals’ prior medical conditions observed up to the year prior to their index date will be summarized. Medications will be summarised over the 30 days before index date. Continuous variables will be summarized using median and interquartile ranges, while binary covariates will be described in terms of the proportion of the cohort having the covariate. Standardized mean differences (SMD) will be calculated when comparing characteristics of study cohorts, with plots showing comparing the mean values of characteristics for each of the characteristics (with the colour indicating the absolute value of the standardized difference of the mean).

# References

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