Protocol for collection of convalescent samples by RCGP RSC

1. Background

Severity assessment of COVID-19 requires the detection of asymptomatic and mild infections and the determination of the true number of infections within the general population. The number of true infections can be determined if the prevalence of immunity of the population prior to, during and after the epidemic are known.

Public Health England (PHE) are conducting a number population-based surveys in England to inform our understanding of the extent of transmission of SARS-CoV-2. This requires the collection of representative serum samples across England. As part of this, convalescent sera – serum from patients who have had and are recovering from a confirmed COVID-19 infection – are required to understand the antibody response following infection and to validate the assays used to detect antibodies.

The RCGP RSC can coordinate the collection of convalescent samples through their network of GP practices across England. This protocol describes the number and type of convalescent samples that will be sought through this network, and the minimum data set that is required from patients providing these samples.

2. Study Objectives

- To obtain serial convalescent samples from 4 weeks to 20 weeks after symptom onset, from PCR confirmed individuals across all age groups, to determine the duration of the COVID-19 antibody response.
- To obtain convalescent samples from patients with a) mild disease and b) moderate or severe disease (as defined by requiring hospital admission) to understand the antibody response relative to disease severity.
- To use convalescent samples to evaluate the sensitivity of assays used to detect antibodies to SARS CoV-2.

3. Study design

The seroprevalence study will use serial convalescent samples from patients who have recently been diagnosed with COVID-19 by PCR testing to understand the antibody response following infection and to assist with assay validation. Convalescent serum will be obtained from two main sources:

1. A study conducted by Mary Ramsay et al. which obtained convalescent samples from "FF100" patients (i.e. the first 100 patients to be diagnosed in England)
2. The RCGP RSC network.

Adult patients (≥ 16 years old) or the parent / legal guardian of children (< 16 years old) will be asked to consent to:

1. Answer a short questionnaire regarding their symptom onset and disease severity;
2. Submit sequential blood samples for antibody testing.

3.1. Participants

Potential participants will be categorised according to age and disease severity.

Patients will be categorised according to one of 3 age groups:

- Children aged < 16
- Adults aged 16 – 64
- Adults aged ≥ 65 years.

Patients will be categorised as having either "mild" disease or "moderate / severe" disease using the following classification:

- Mild: COVID-19 symptoms were managed in the community and did not require an overnight hospital stay.
- Moderate or severe: COVID-19 symptoms required a hospital stay of at least one night.

The **numbers of patients** sought via the RCGP RSC network in each category are summarised below:

	Disease Severity	
Age	Mild	Moderate / Severe
< 16	50	0
16 – 64	0	25
≥ 65 years.	16 patients have already provided 1 sample. These patients should be contacted to provide 2 further samples. 34 new patients will need to be recruited to provide 3 samples.	25

3.2. Serum Samples

Patients will be asked to provide serum samples at the following 3 time points after symptom onset:

- 3 weeks to 6 weeks (i.e. day 21 to day 42)
- 12 weeks +/- 3 days (i.e. day 84 +/- 3 days)
- 20 weeks +/- 3 days (i.e. day 140 +/- 3 days)

It is anticipated that not all patients will be able to submit all 3 samples. However, patients will be required to submit a convalescent sample at the first time point and at least one other time point.

3.3. Inclusion Criteria

Adults (≥16 years old) or children (< 16 years old), who:

- Have been diagnosed with COVID-19 by PCR
- Can give informed verbal consent for participation in the study (adults), or in the case of children aged < 16, whose parent or legal guardian can give informed verbal consent for participation in the study.
- Are able to submit a minimum of one convalescent sample at the first time point and at least one other time point.

3.4. Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- Adults unable to understand the study information and give consent to take part in the study.
- Eligible children with parents or legal guardians who are unable to understand the study information and give consent.
- Patients who have not previously received a diagnosis of COVID-19 by PCR testing.
- Patients for whom information on date of symptom onset, date of PCR swab, or whether they were admitted to hospital is not available.
- Adults who are resident in a care home.

4. Study Procedures

4.1. Informed Consent

A patient information leaflet will be prepared by PHE and shared with the RCGP RSC. This can be provided to the patient by the GP in either a physical or in electronic format. Only verbal consent is required from the patient, parent or guardian including adults for any minors for whom they are parents/guardians. This is in line with NHS Health Research Authority guidelines.[1]

Consent is obtained verbally and can be withdrawn subsequently if the patient does not wish the blood sample to be taken. Participants are not required to give a reason for withdrawal. Withdrawn participants should be sought to be replaced with a patient from the same age and disease severity category.

4.2. Minimum data set

The following data should be collected at the time of each sample and should be entered on the sample request form (which will be prepared by PHE):

- Patient name
- DOB
- NHS No.
- GP Details
- Date sample collected
- Date of symptom onset

[1] NHS Health Research Authority. Consent and Participant Information Guidance. Principles of Consent: General principles and role of Participant Information Sheets. Accessed from www.hra-decisiontools.org.uk/consent/principles-general.html on 17 June 2020.

- Date PCR test conducted
- Whether the patient has been admitted to hospital overnight for treatment of COVID-19, the date that they were admitted, and length of hospital stay
- Ethnicity

4.3. Collection of samples

Samples will be collected at the GP practice following standard infection control / PPE procedures that are in place at that practice. No further precautions are required.