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Long-term mental and brain health effects of COVID among adult patients

Submission date	Recruitment status	[_] Prospectively registered
30/08/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/09/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
01/09/2022	Nervous System Diseases	[_] Record updated in last year

Plain English summary of protocol
Background and study aims
This study explores the long-term neurological and psychiatric impact of COVID-19 in adults infected by the SARS-CoV-2 virus.

Who can participate?
We are recruiting two groups of participants: a COVID group who are aged 18 to 65 years with confirmed SARS-CoV-2 (a.k.a. novel coronavirus) infection that happened more than one year ago, and a matched control group.

What does the study involve?
Participants will complete mobile app-based questionnaires about their health and social conditions, and their recent mental health. They will also complete a few simple cognitive tasks on the mobile app. We will also ask for consent to check the COVID group participants' electronic health records for analysis. Selected COVID subjects will be invited to receive MRI brain imaging. The study is done online.

What are the possible benefits and risks of participating?
None

Where is the study run from?
Department of Psychiatry, The Chinese University of Hong Kong

When is the study starting and how long is it expected to run for?
January 2022 to May 2024

Who is funding the study?
Research Grant Council, Hong Kong

Who is the main contact?
Dr Steven Chau, stevenwaihochau@cuhk.edu.hk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Neuropsychiatric 'long-COVID' in adult patients (Phase 1)

Acronym
NPLOC-HK(Phase 1)

Study objectives
1. Patients infected with COVID over a year ago have a higher frequency of neuropsychiatric symptoms compared to controls who have never been infected.
2. Patients infected with COVID over a year ago have lower HRQoL compared to controls who have never been infected.
3. Neuropsychiatric symptoms in patients infected with COVID over a year ago are clustered
4. The risk of neuropsychiatric symptoms in patients infected with COVID over a year ago is correlated with clinical characteristics of their acute COVID episode e.g severity.
5. The risk of neuropsychiatric symptoms in patients infected with COVID over a year ago is correlated with their vaccination status before they got infected.
6. The risk of neuropsychiatric symptoms in patients infected with COVID over a year ago is correlated with their socioeconomic status e.g. level of social deprivation.
7. There is significant difference in grey matter volume between COVID patients one year after initial infection who suffers from neuropsychiatric symptom cluster(s) and those who do not as

measured by MRI imaging, particularly in the olfactory cortex, limbic cortex, frontal cortex, and the brainstem.
8. There is significant difference in white matter integrity between COVID patients one year after initial infection who suffer from neuropsychiatric symptom cluster(s) and those who do not as measured by diffusion MRI, particularly in the olfactory cortex, limbic cortex, frontal cortex, and the brainstem.
9. There is significant differences in diffusivity and the index along the perivascular space (ALPS index) between COVID patients one year after initial infection who suffers from neuropsychiatric symptom cluster(s) and those who do not as measured by diffusion MRI.
10. There is significant difference in perfusion between COVID patients one year after initial infection who suffers from neuropsychiatric symptom cluster(s) and those who do not as measured by MRI

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 04/07/2022, Hospital Authority Central Institutional Review Board (A503, 5/F, Block A, Centre for Health Protection, 147B Argyle Street, Kowloon, Hong Kong; +852 23007054; no email provided), ref: CIRB-2002-006-1
2. Approved 23/06/2022, Joint CUHK-New Territories East Cluster Clinical Research Ethics Committee (8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong; +852 25053935; no email provided), ref: 2022.139

Study design
Cross-sectional case-controlled observational study with a nested case-control MRI sub-study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Long term neuropsychiatric symptoms of COVID

Interventions
The method of assessment will be an online survey, supplemented by subject's electronic health record. The following data will be collected via the online survey: (i) demographic data; (ii) pre-COVID physical and mental health status; (iii) socioeconomic profile and social impact of COVID-19, including level of social deprivation and health behaviour (iv) clinical parameters of acute COVID-19 episode; (v) self reported symptoms checklist for 'long-COVID', which include items of neuropsychiatric dimensions e.g. cognitive complaint, fatigue, depression, anxiety, insomnia; (iv) neuropsychiatric symptoms scales of mood, anxiety, post-traumatic stress, sleep and fatigue symptoms (vii) brief online cognitive tests with focuses on attention and memory(a. One-back memory test: subjects will be presented with sequence of letters, and they are asked to decide whether the letter they see is the same as the last letter presented; b. Psychomotor vigilance test: the subjects are asked to press the button as quickly as possible when they see the display turn red; c. Digit symbol substitution test : subjects will be presented with symbols, and they are asked to search for the correct symbol-digit pairing from a list, and respond by choosing the paired digit); d. finger tap test.

Separately, we will ask for COVID group's subjects' consent to access their clinical data in relation to their clinical characteristics and treatment of COVID in the premises run by the Hospital Authority via the electronic Clinical Management System (CMS), or CDARS and the Hospital Authority Data Sharing Portal. Specifically, we will ask for permission to access the following details of consented subjects:
1. The dates of admissions and discharges; 2. The progress of the subject during the admission period(s), including any intensive care unit admission record; 3. All of the investigation results and reports, including but not limited to haematological, biochemical, microbiological and radiological investigations, during the admission period(s); 4. The treatment record, including medication and other therapeutic intervention e.g. oxygen therapy, during the admission periods. 5. All medical diagnoses the subject were given at all-time until the end of the research project. No control group's subjects' medical record will be retrieved.
The MRI brain imaging sub-study is a nested case control study of under the main study. We will recruit 2 groups of subjects – a COVID patients group suffering from core neuropsychiatric symptoms cluster and a matched COVID patients control group which do not have core neuropsychiatric symptom. The sample of the MRI subpart will be recruited from the subject pool of the main study.
MRI brain examinations will be performed using a 3.0 Tesla scanner (MAGNETOM Prisma; Siemens AG, Munich, Germany) equipped with high-performance gradients. A standard 64-channel head coil with parallel imaging capability will be used for signal reception. The scanning sequences will include 1. T1W Multi-echo MPRAGE; 2.T2W ; 3. Multi shell DWI: 2shells (b=1500 /3000s/mm2) 92-93 directions per shell, MB = 4, TR = 3.23s, 1.5mm voxels, and 4. Arterial spin labelling.

Intervention Type
Other

Primary outcome(s)
Core neuropsychiatric symptom cluster(s) among COVID patients measured using self-reported questionnaires one year after initial infection.

Key secondary outcome(s))
1. Grey matter volume differences between COVID patients who suffer from core neuropsychiatric symptom cluster(s) and those who do not as measured by MRI, particularly in the olfactory cortex, limbic cortex, frontal cortex, and the brainstem one year after initial infection.
2. Differences in white matter integrity between COVID patients who suffers from core neuropsychiatric symptom cluster(s) and those who do not as measured by MRI, particularly in the olfactory cortex, limbic cortex, frontal cortex, and the brainstem one year after initial infection.
3. Differences in frequency of neuropsychiatric symptoms between COVID patients one year after initial infection and controls who have never been infected as measured by self-reported questionnaires.
4. Differences in HRQoL between COVID patients one year after initial infection and controls who have never been infected measured using self-reported questionnaires.
5. Correlation of clinical characteristics of acute COVID, as retrieved from the electronic health record, with core neuropsychiatric symptom clusters, as measured by self-reporting questionnaire.
6. Correlation of socioeconomic factors with core neuropsychiatric symptom cluster(s) as measured by self-reporting questionnaires.
7. Correlation of vaccination status (type/number of doses) with core neuropsychiatric symptom

cluster(s) as measured by self-reporting questionnaires.
8. Differences in diffusivity and the index along the perivascular space (ALPS index) between COVID patients one year after initial infection who suffers from core neuropsychiatric symptom cluster(s) and those who do not as measured by MRI.
9. Differences in perfusion between COVID patients one year after initial infection who suffers from core neuropsychiatric symptom cluster(s) and those who do not as measured by MRI

Completion date
09/05/2024

Eligibility

Key inclusion criteria
COVID patients group
1. History of confirmed SARS-CoV-2 infection of any level of severity
2. SARS-CoV-2 infection occurred more than 1 year ago,before Omicron variant prevailed in Hong Kong in Feburary 2022
3. Aged between 18-65 years

non-COVID control group
1. No history of SARS-CoV-2 infection confirmed by lateral-flow test or PCR
2. Matched with COVID patients group in terms of the following 5 characteristics: age, gender, ethnicity, pre-COVID medical and psychiatric comorbidities, and socioeconomic status

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
Unable to give informed consent

Date of first enrolment
24/08/2022

Date of final enrolment
01/03/2023

Locations

Countries of recruitment
Hong Kong

Study participating centre
Prince of Wales Hospital
Shatin
Hong Kong
Hong Kong
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Sponsor information

Organisation
Shatin Hospital

ROR
https://ror.org/037s3ck33

Funder(s)

Funder type
Government

Funder Name
Research Grant Council, Hong Kong

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon reasonable request.
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IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Protocol file	31/08/2022	01/09/2022	No	No