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Long-term mental and brain health effects of COVID-19 from the Omicron strains among adult patients

Submission date
17/04/2023

Recruitment status
No longer recruiting

Registration date
19/04/2023

Overall study status
Completed

Last Edited
18/04/2023

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is the extension of the Phase 1 study. The current Phase 2 study explores the long-term neurological and psychiatric impact of COVID-19 in adults infected by the Omicron strains of the SARS-CoV-2 virus.

Who can participate?
People aged 18 to 65 years who had a confirmed COVID-19 infection that happened either in or after February 2022, or more than 1 year ago

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. The researchers will also ask for consent to check the COVID group participants' electronic health records for analysis. Selected participants will be invited to receive detailed neurocognitive assessment, sleep assessment and MRI brain imaging.

What are the possible benefits and risks of participating?
There are no benefits or risks expected.

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

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Neuropsychiatric ‘long-COVID’ in adult patients (Phase 2)

Acronym
NPLOC-HK (Phase 2)

Study objectives
1. Neuropsychiatric symptoms in patients infected with Omicron strains of COVID over a year ago showed a similar clustering pattern with symptoms in patients infected with pre-Omicron strain (which is derived from the result from Phase 1 of the study).
2. The risk of neuropsychiatric symptoms in patients infected with Omicron strains of COVID over a year ago is correlated with clinical characteristics of their acute COVID episode e.g severity.
3. The risk of neuropsychiatric symptoms in patients infected with Omicron strains of COVID over a year ago is correlated with their vaccination status before they got infected.

4. 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.
5. Patients reporting persistent neuropsychiatric symptoms, particularly the depression-anxiety-insomnia symptoms cluster, 1 year after initial COVID (Omicron) infection have increased frequency of new-onset mental illness as diagnosed by a specialist psychiatrist using DSM-5 criteria compared to those who do not.
6. Patients reporting persistent neuropsychiatric symptoms, particularly the fatigue-cognitive dysfunction symptoms cluster, 1 year after the initial COVID (Omicron) infection showed worse cognitive performance after cognitive exertion compared to those who do not.
7. Patients suffering from the fatigue-cognitive dysfunction symptoms cluster, 1 year after the initial COVID (Omicron) infection have sleep architecture abnormalities as measured by polysomnography, compared to those who do not.
8. There is a significant difference in grey matter volume between COVID (Omicron) patients 1 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.
9. There is a significant difference in white matter integrity between COVID (Omicron) patients 1 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.
10. There are significant differences in diffusivity and the index along the perivascular space (ALPS index) between COVID (Omicron) patients 1 year after initial infection who suffers from neuropsychiatric symptom cluster(s) and those who do not as measured by diffusion MRI.
11. There is a significant difference in perfusion between COVID (Omicron) patients 1 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 (0)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 (0)25053935; no email provided), ref: 2022.139

Study design
Cross-sectional case-controlled observational study with a nested case-control neurocognition sub-study, a nested case-control PSG sub-study, and a nested case-control MRI sub-study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions

The method of assessment will be an online survey. The following data will be collected via the online survey:
1. Demographic data
2. Pre-COVID physical and mental health status
3. Socioeconomic profile and social impact of COVID-19, including level of social deprivation and health behaviour
4. Clinical parameters of acute COVID-19 episode
5. Self-reported symptoms checklist for 'long-COVID', which includes items of neuropsychiatric dimensions e.g. cognitive complaint, fatigue, depression, anxiety, insomnia
6. Neuropsychiatric symptoms scales of mood, anxiety, post-traumatic stress, sleep and fatigue symptoms
7. Brief online cognitive tests with a focus on attention and memory
7.1. One-back memory test: subjects will be presented with a sequence of letters, and they are asked to decide whether the letter they see is the same as the last letter presented
7.2. Psychomotor vigilance test: the subjects are asked to press the button as quickly as possible when they see the display turn red
7.3. 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
7.4. Finger tap test

Separately, the researchers will ask for the 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, they 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
6. Attendance at clinics within the first 3 months of COVID diagnosis
7. The investigation and treatment record, including medication and other therapeutic interventions by clinics within the first 3 months of COVID diagnosis

Neuro-cognitive sub-study:
1. The presence of clinical neuropsychiatric disorders and their onset will be determined by a clinical interview. Diagnoses of mild cognitive impairment or dementia among those who score <22 in the Hong Kong version of the Montreal Cognitive Assessment (MoCA-HK) will be confirmed by clinician assessment. Chronic fatigue syndrome will be diagnosed according to the criteria of the National Academy of Medicine.
2. A semi-structured interview to ascertain diagnoses of various sleep disorders including insomnia, circadian rhythm disorder, RBD and narcolepsy; using 7 days of wearable actigraphy to measure rest-activity rhythm; and conducting an in-lab video-polysomnographic assessment (vPSG) of a subset of subjects to confirm the diagnosis of parasomnia, in particular RBD, which requires vPSG evidence of REM sleep without atonia.

PSG substudy:
Home PSG will be conducted to examine their sleep architecture.

MRI brain imaging sub-study:
The researchers will recruit three groups of subjects – a COVID patients group suffering from core neuropsychiatric symptoms clusters, and a matched COVID patients control group who do not have the 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: 2 shells (b = 1500/3000 s/mm²) 92-93 directions per shell, MB = 4, TR = 3.23 s, 1.5 mm voxels
4. Arterial spin labelling

Intervention Type
Other

Primary outcome(s)
Core neuropsychiatric symptom cluster(s) among COVID (Omicron) patients measured using self-reported questionnaires 1 year after the 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, at 1 year after initial infection
2. Differences in white matter integrity 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, at 1 year after initial infection
3. Differences in frequency of neuropsychiatric symptoms between COVID patients at 1 year after initial infection and controls who have never been infected, as measured by self-reported questionnaires
4. Differences in health-related quality of life (HRQOL) between COVID patients at 1 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 cluster(s) at 1 year post-infection, as measured by self-reporting questionnaire
6. Correlation of socioeconomic factors with core neuropsychiatric symptom cluster(s) at 1 year post-infection, as measured by self-reporting questionnaires
7. Correlation of vaccination status (type/number of doses) with core neuropsychiatric symptom cluster(s) at 1 year post-infection, as measured by self-reporting questionnaires
8. Differences in diffusivity and the index along the perivascular space (ALPS index) between COVID patients at 1 year after initial infection who suffer from core neuropsychiatric symptom cluster(s) and those who do not as measured by MRI
9. Differences in perfusion between COVID patients at 1 year after initial infection who suffer

from core neuropsychiatric symptom cluster(s) and those who do not, as measured by MRI
10. Differences in frequency of new-onset psychiatric disorders between COVID patients at 1 year after initial infection who suffer from core neuropsychiatric symptom cluster(s) and those who do not, as determined by clinical interview by psychiatrist
11. Differences in frequency of new-onset sleep disorders between COVID patients at 1 year after initial infection who suffer from core neuropsychiatric symptom cluster(s) and those who do not, as determined by semi-structured interview
12. Differences in frequency of olfactory dysfunction between COVID patients at 1 year after initial infection who suffers from core neuropsychiatric symptom cluster(s) and those who do not, as measured by olfactory identification test
13. Differences in grip strength between COVID patients at 1 year after initial infection who suffer from core neuropsychiatric symptom cluster(s) and those who do not, as measured by dynamometer
14. Differences in balance problem between COVID patients at 1 year after initial infection who suffers from core neuropsychiatric symptom cluster(s) and those who do not, as measured by clinical neurological examination
15. Differences in post-exertional cognitive performance between COVID patients at 1 year after initial infection who suffer from core neuropsychiatric symptom cluster(s) and those who do not, as measured by continuous vigilance test
16. Differences in sleep architecture between COVID patients at 1 year after initial infection who suffers from core neuropsychiatric symptom cluster(s) and those who do not, as measured by home PSG

Completion date
09/05/2024

Eligibility

Key inclusion criteria
1. History of RAT or laboratory-confirmed SARS-CoV-2 infection of any level of severity
2. First confirmed SARS-CoV-2 infection happened in or after February 2022 OR First confirmed SARS-CoV-2 infection occurred more than 1 year ago
3. Aged between 18-65 years

Participant type(s)
Patient

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
21/04/2023

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
Hong Kong

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

Organisation
Chinese University of Hong Kong

ROR
https://ror.org/00t33hh48

Funder(s)

Funder type
Research council

Funder Name
Research Grant Council, Hong Kong

Results and Publications

Individual participant data (IPD) sharing plan

An anonymised and cleansed dataset of subjects' socioeconomic data, past health data, self-reported symptoms and symptoms rating scale will be available after the result of the study is published upon request. For a subset of subjects, DSM-5-coded psychiatric diagnostic labels and their MRI image data will be available. Please contact Dr Steven Chau (stevenwaihochau@cuhk.edu.hk) for any request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes