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Long COVID: psychological risk factors and their modification

Submission date
28/11/2022

Recruitment status
No longer recruiting

Registration date
17/01/2023

Overall study status
Completed

Last Edited
24/06/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Studies suggest that after an infection with the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) has abated, a substantial portion of affected patients do not fully recover, and may be at risk of persistent somatic symptoms - a phenomenon often described as “Long COVID”. Results from previous studies indicate that the development of Long COVID involves both pathophysiological and psychological factors. Among psychological risk factors, illness-related anxiety and dysfunctional symptom expectations in particular seem to contribute to symptom persistence. Since both factors can potentially be modified by targeted interventions, this study will investigate whether Long COVID can be influenced by modifying illness-related anxiety and dysfunctional symptom expectations. Our primary hypothesis is that the therapeutic modification of illness-related anxiety and dysfunctional symptom expectations improves Long COVID symptom severity. Conceptually, this study is closely linked to the DFG-funded interdisciplinary SOMACROSS Research Unit “Persistent Somatic Symptoms Across Diseases” (RU 5211) which investigates risk factors and mechanisms of symptom persistence across ten medical conditions.

Who can participate?
Adults aged 18 years old and over with Long COVID suffering from at least moderate somatic symptoms.

What does the study involve?
To assess the extent to which Long COVID symptoms are modifiable in adult patients, we will conduct an observer-blinded, 3-arm randomized controlled proof-of-concept trial. A total of 258 patients with Long COVID will be randomly allocated into 3 groups of equal size: targeted expectation management aiming to reduce illness-related anxiety and dysfunctional symptom expectations in addition to treatment as usual (intervention 1), non-specific supportive treatment in addition to treatment as usual (intervention 2), or treatment as usual only (control). Both active intervention groups will comprise 3 individual online consultation sessions and a booster session after 3 months. The primary outcome is baseline to post-interventional change in overall somatic symptom severity. For outcome assessment, study participants complete online self-report questionnaires at four measurement points over 6 months.

What are the possible benefits and risks of participating?
There is a potential that participants in the two intervention groups of the SOMA.COV study will benefit from the interventions in terms of fewer somatic symptoms and reduced illness-related anxiety. The participants will also contribute to a better understanding of the effectiveness and mechanisms of action of a targeted expectation management intervention for patients with Long COVID and to the advancement of comprehensive care for affected patients. To the best of our knowledge, for the participants, there is no risk for serious adverse events caused by the application of the study interventions.

Where is the study run from?
SOMA.COV is being conducted by the University Medical Center Hamburg-Eppendorf, Hamburg, Germany. Since it is an online study, people with Long COVID from all over Germany can participate.

When is the study starting and how long is it expected to run for?
December 2021 to June 2025

Who is funding the study?
Deutsche Forschungsgemeinschaft, DFG (German Research Foundation)

Who is the main contact?
Dr. Petra Engelmann, p.engelmann@uke.de (Germany)

Study website
https://www.uke.de/english/departments-institutes/institutes/psychosomatic-medicine-and-psychotherapy/research/working-groups/working-group-for-5211/projects/associated-soma-cov/index.html

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
DFG project number 508447247

Study information

Scientific Title

Psychological risk factors for persistent somatic symptoms in Long COVID and their modification: a 3-arm randomized controlled trial

Acronym
SOMA.COV

Study objectives
Hypothesis 1: The therapeutic modification of illness-related anxiety and dysfunctional symptom expectations improves Long COVID symptom severity.
Hypothesis 2 (exploratory): In addition to illness-related anxiety and dysfunctional symptom expectations, further risk factors contributing to the persistence of Long COVID symptoms can be identified.
Hypothesis 3 (exploratory, using results from RU5211 SOMACROSS): Long COVID and other medical conditions share common risk factors for somatic symptom persistence.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/02/2022, Local Psychological Ethics Committee (LPEK) at the Center for Psychosocial Medicine of the University Medical Center Hamburg-Eppendorf (Martinistraße 52, 20246 Hamburg, Germany; +49 (0) 40 7410 24116; skuehn@uke.de), ref: LPEK-0446

Study design
Single-center nationwide interventional observer-blind three-arm randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Internet/virtual

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Persistent somatic symptoms in patients with Long COVID

Interventions
We will use a three-arm randomised-controlled trial (RCT) design. A fixed randomization schedule, stratified by gender, will be programmed and conducted electronically.

Experimental intervention 1 (COV.EXPECT + TAU):
This experimental intervention consists of an expectation management intervention (COV. EXPECT) in addition to treatment as usual (TAU). The manualized intervention primarily aims to reduce illness-related anxiety and to optimize expectations about symptoms, treatment outcomes, and coping strategies. The design and dose of the intervention are based on the demonstrated effectiveness of the expectation management intervention from the PSY-HEART trial, on the SOMA.GUT study within RU5211 SOMACROSS, and on other previous studies. The intervention consists of 3 individual online video consultation sessions at an interval of 2 weeks each and a booster session after 3 months, with each session lasting 45 minutes. Homework will be given after each session to deepen the acquired skills. The intervention thus addresses the topics of "dealing with anxiety", and "improving expectations" as well as patients' need for information about their disease.

Experimental intervention 2 (COV.SUPPORT + TAU):
This experimental intervention consists of a non-specific supportive intervention (COV. SUPPORT) in addition to TAU. COV.SUPPORT is identical to COV.EXPECT in terms of common and non-specific treatment elements, i.e. time, personal attention, and emotional support, but does not use specific interventions to modify illness-related anxiety and expectations.

Control intervention (treatment as usual):
The control intervention consists of TAU only. TAU in all study groups implies that patients receive their usual treatment without any interference from the study.

Intervention Type
Behavioural

Primary outcome measure
Overall somatic symptom severity assessed using the Patient Health Questionnaire 15 (PHQ-15) at baseline, after 6 weeks, after 3 months (post-interventional follow-up), and after 6 months

Secondary outcome measures
Current secondary outcome measures as of 24/08/2023:
1. SARS-CoV-2 infection and Long COVID measured using single items at baseline, after 6 weeks, 3 months, and 6 months
2. Long COVID symptoms measured using a self-developed screening questionnaire on Long COVID as well as other post-infectious symptoms called PHQ-15 PAIS at baseline, after 6 weeks, 3 months, and 6 months
3. Fatigue measured using the Fatigue Scale (FS) at baseline, after 6 weeks, 3 months, and 6 months
4. Post-exertional malaise measured using the DePaul Symptom Questionnaire Post-Exertional Malaise (DSQ-PEM) at baseline, after 6 weeks, 3 months, and 6 months
5. Pain measured using the Pain Disability Index – adapted (PDI) at baseline, after 6 weeks, 3 months, and 6 months
6. Risk factors for somatic symptom persistence measured using joint core instruments of RU5211 SOMACROSS at baseline, after 6 weeks, 3 months, and 6 months
7. Somatic Symptom Disorder according to DSM-5 measured by conducting a structured clinical interview (SCID) at baseline and after 3 months
8. Illness-related anxiety measured using the Somatic Symptom Disorder – B Criteria Scale (SSD-12) at baseline, after 6 weeks, 3 months, and 6 months
9. Treatment expectations measured using the Treatment Expectation Questionnaire (TEX-Q) at baseline, after 6 weeks, 3 months, and 6 months

10. Expectations of symptom severity measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months
11. Expectations of symptom burden measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months
12. Expectations of coping with symptoms measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months

Previous secondary outcome measures:
1. Fatigue measured using the Modified Fatigue Impact Scale-5 item version (MFIS-5) at baseline, after 6 weeks, 3 months, and 6 months
2. Shortness of breath measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months
3. Impairment of smell and taste measured using the Sinonasal outcome test (SNOT-22) at baseline, after 6 weeks, 3 months, and 6 months
4. Pain measured using the Pain Disability Index – adapted (PDI) at baseline, after 6 weeks, 3 months, and 6 months
5. SARS-CoV-2 infection and Long COVID measured using single items at baseline, after 6 weeks, 3 months, and 6 months
6. Long COVID symptoms measured using the COVID19 Yorkshire Rehabilitation Scale (C19YRS) at baseline, after 6 weeks, 3 months, and 6 months
7. Risk factors for somatic symptom persistence measured using joint core instruments of RU5211 SOMACROSS at baseline, after 6 weeks, 3 months, and 6 months
8. Somatic Symptom Disorder according to DSM-5 measured by conducting a structured clinical interview (SCID) at baseline and after 3 months
9. Illness-related anxiety measured using the Somatic Symptom Disorder – B Criteria Scale (SSD-12) at baseline, after 6 weeks, 3 months, and 6 months
10. Treatment expectations measured using the Treatment Expectation Questionnaire (TEX-Q) at baseline, after 6 weeks, 3 months, and 6 months
11. Expectations of symptom severity measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months
12. Expectations of symptom burden measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months
13. Expectations of coping with symptoms measured using a Numeric Rating Scale (NRS) at baseline, after 6 weeks, 3 months, and 6 months

Overall study start date
01/12/2021

Completion date
15/06/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/08/2023:
1. Self-reported resolved SARS-CoV-2 infection confirmed by a positive PCR, serology, or rapid antigen test
2. Long COVID according to the NICE/AWMF S1-guidelines
3. At least moderately severe ongoing symptoms (PHQ-15 ≥10)
4. Age ≥18 years
5. Informed consent

Previous inclusion criteria:
1. Resolved SARS-CoV-2 infection confirmed by a positive PCR or serology test
2. Long COVID according to the NICE/AWMF S1 guidelines
3. At least moderately severe ongoing symptoms (PHQ-15 ≥10)
4. Age ≥18 years old
5. Informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
258

Total final enrolment
269

Key exclusion criteria
Current exclusion criteria as of 24/08/2023:
1. Acute SARS-CoV-2 infection
2. Intensive care unit treatment for COVID-19
3. Psychotherapeutic treatment in the past 3 months
4. Necessity of acute emergency treatment
5. Acute suicidality
6. A substance use disorder
7. Acute psychosis
8. Cognitive incapacity to comprehend the study materials
9. Inability to complete outcome measures online
10. Insufficient German language skills

Previous exclusion criteria:
1. Intensive care unit treatment for COVID-19
2. Necessity of acute emergency treatment
3. Acute suicidality
4. Psychotherapeutic treatment in the last 3 months
5. Severe cognitive impairment
6. Inability to complete outcome measures online
7. Insufficient German language skills

Date of first enrolment
09/10/2023

Date of final enrolment
20/11/2024

Locations

Countries of recruitment
Germany

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University/education

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ROR
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Funder(s)

Funder type
Research organisation

Funder Name
Deutsche Forschungsgemeinschaft

Alternative Name(s)
German Research Association, German Research Foundation, DFG

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Results and Publications

Publication and dissemination plan

According to the WHO Statement on Public Disclosure of Clinical Trials (https://www.who.int/ictrp/reporting-on-findings), the main findings will be submitted for publication in a high-impact peer-reviewed journal within 12 months of study completion.

Intention to publish date
01/02/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study will be stored in a publically available repository (e.g., DRYAD Digital Repository; https://datadryad.org/stash). Study protocol and statistical analysis plan will be available at the ISRCTN registry. Individual participant data that underlie the reported results in a published article will be shared after de-identification beginning 3 months and ending 5 years following article publication. Data will be shared with researchers who provide a methodologically sound proposal to achieve aims in the approved proposal. Proposals should be directed to p.engelmann@uke.de. To gain access, data requestors will need to sign a data access agreement. Informed consent from participants was obtained.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		03/11/2023	07/11/2023	Yes	No
Statistical Analysis Plan	version 1	24/08/2023	24/06/2025	No	No