

# Long COVID: psychological risk factors and their modification

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<b>Registration date</b> 17/01/2023	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 24/06/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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.COVID 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.COVID 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>

## **Contact information**

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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.COVID

## **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  $\geq 10$ )
4. Age  $\geq 18$  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  $\geq 10$ )
4. Age  $\geq 18$  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

**Study participating centre****University Medical Center Hamburg-Eppendorf**

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**Study participating centre****University Medical Center Hamburg-Eppendorf**

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**Study participating centre****University Medical Center Hamburg-Eppendorf, II. Medical Clinic and Polyclinic**

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**Study participating centre****University Medical Center Hamburg-Eppendorf, Department of General Practice and Primary Care**

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**Sponsor information**



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**Sponsor type**

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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/ictcp/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](mailto: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?
<a href="#">Protocol article</a>		03/11/2023	07/11/2023	Yes	No
<a href="#">Statistical Analysis Plan</a>	version 1	24/08/2023	24/06/2025	No	No