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# Analysis of factors associated with the presence of persistent symptoms in people with a diagnosis of COVID-19: a case-control study

**Submission date**
15/03/2022

**Recruitment status**
No longer recruiting

**Registration date**
10/05/2022

**Overall study status**
Ongoing

**Last Edited**
29/05/2024

**Condition category**
Infections and Infestations

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

## Plain English summary of protocol

Background and study aims
The symptoms and consequences of persistent COVID-19 (long COVID) add to the impact from the interruption of access to medical care (such as arrangements for getting regular medications), basic personal routines (such as walking to local stores), social interactions (such as meeting friends) and support networks. Support should be personalized with input from the staff from multiple professions (e.g., primary care doctors, social workers). The aim of this study is to assess patients with and without persistent symptoms after a diagnosis of COVID-19 and analyze the factors associated with the persistence of the symptoms of COVID-19.

Who can participate?
People from Aragón who have been diagnosed with COVID-19 with and without persistent symptoms

What does the study involve?
Participants answer questions about their lifestyle, perceived quality of life, and in relation to the COVID-19 episode they suffered. A blood sample will be collected to measure diagnostic, inflammatory response, and immune-related markers. Participants with persistent symptoms will be asked about the list of symptoms they present, their duration and intensity, their functional capacity and state of mind. In addition, through blood tests, other types of diagnoses will be ruled out for people who are presenting persistent symptoms. The researchers will collect from their medical history if they suffer from any other type of chronic illness, and any drug treatments that they are taking. This first evaluation will last 45 minutes. A total of two visits will be required. Participants will have to travel to a care center that may not be close to their place of residence, for which there will be no financial compensation.

What are the possible benefits and risks of participating?
As this is a research study aimed at generating knowledge, it is unlikely that participants will obtain any personal benefit from participation, although they will contribute to scientific advancement and social benefit. Participants will not receive any financial compensation. Both for the evaluation and for the blood sample that will be done in this study, participants are not

at risk and should not have any discomfort. The questionnaires to be used do not involve any invasive or painful tests, and are widely used in research and in clinical practice. Both the evaluation and the extraction will be carried out by qualified personnel. The only discomfort participants may have is that of the blood sample, which is a small puncture and slight subsequent bleeding.

Where is the study run from?
Arrabal Health Center in Zaragoza (Spain)

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

Who is funding the study?
1. Instituto de Investigación Sanitaria Aragón (Spain)
2. Carlos III Institute (Spain)

Who is the main contact?
Dr Rosa Magallón Botaya
rosamaga@unizar.es

# Contact information

### Type(s)
Scientific

### Contact name
Miss Fátima Méndez-López

### ORCID ID
https://orcid.org/0000-0002-6409-9041

### Contact details
Aragonese Research Group in Primary Care (GAIAP)
Institute of Health Research
Avenue San Juan Bosco, 13
Zaragoza
Spain
50015
+34 (0)976506578
fmendez@iisaragon.es

### Type(s)
Principal Investigator

### Contact name
Dr Rosa Magallón-Botaya

### ORCID ID
https://orcid.org/0000-0002-5494-6550

### Contact details

Aragonese Research Group in Primary Care (GAIAP)
Institute of Health Research
Avenue San Juan Bosco, 13
Zaragoza
Spain
50015
+34 (0)976506578
rosamaga@unizar.es

# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
C.P. - C.I. PI21/278

# Study information

### Scientific Title
Analysis of factors associated with the presence of persistent symptoms in people with a diagnosis of COVID-19: a case-control study

### Acronym
Aralongcov

### Study objectives
The general objective of this study is to sociodemographically, clinically and biologically characterize patients with persistent symptoms versus those without persistent symptoms after the diagnosis of COVID-19 and analyse the factors associated with the persistence of COVID-19 symptoms.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 08/09/2021, Research Ethics Committee of the Community of Aragon (CEICA, Avda. San Juan Bosco, 13. 50009, Zaragoza, Spain; +34 (0)976 716584 / 976 715836; ceica@aragon.es), ref: C.P. - C.I. PI21/278

### Study design
Observational case-control study

### Primary study design
Observational

## Secondary study design
Case-control study

## Study setting(s)
GP practice

## Study type(s)
Prevention, Quality of life

## Participant information sheet
See additional files

## Health condition(s) or problem(s) studied
Long COVID/post COVID-19 condition

## Interventions
Current interventions as of 29/05/2024:

The research assistant will call patients who have shown an interest in participating in the study and an appointment will be made at their health centre. At first appointment, the study will be explained and the inclusion and exclusion criteria will be confirmed, the patient's file will be provided and the informed consent will be signed. If the participants meet the criteria, the research assistant will administer the different questionnaires and functional tests at the same appointment. Moreover, the researcher arranges a new appointment for a complete blood test.

The study is carried out in several visits, depending on the group assigned.
1. To carry out the cohort of patients with persistent covid. They will undergo 3 follow-up visits: visit 0 (baseline), visit 1 (at 6 months), visit 2 (at one year).
2. To create the control cases, only a single baseline visit will be made that allows us to collect data on the variables for both persistent covid patients and asymptomatic patients.
For the baseline visits, as in the case of the one-year visit cohort, the researcher will call the patients who have shown interest in participating in the study and will make an appointment for them at the reference health center (CS. Arrabal). At this appointment, the researcher in charge will explain the study and resolve any doubts that the potential participant may have. It will be verified that they meet the inclusion and exclusion criteria, the information sheet will be provided and the relevant informed consent for the study will be signed. After signing the consent, one of the team's researchers will be in charge of administering the different questionnaires and functional tests at the same appointment. Upon completion, a new appointment will be made for you to perform the complete blood test.
At the 6-month cohort visit, only the questionnaires will be assessed, but not the blood determination.

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Previous interventions:

The research assistant will call patients who have shown an interest in participating in the study and an appointment will be made at their health centre. At this appointment, the study will be explained and the inclusion and exclusion criteria will be confirmed, the patient's file will be

provided and the informed consent will be signed. If the participants meet the criteria, the research assistant will administer the different questionnaires and functional tests at the same appointment. Moreover, the researcher arranges a new appointment for a complete blood test.

## Intervention Type
Other

## Primary outcome measure
1. COVID-19 persistent symptoms measured with a battery of questions at baseline that include:
1.1. Approximate date of the beginning of symptoms
1.2. Duration
1.3. Intensity of symptoms
1.4. Frequency of each symptom
E.g. dysgeusia, dyspnea, neuromuscular conditions; measured at baseline, and revised with symptomatology
2. The severity of the first episode of COVID-19 measured with a battery of questions at baseline:
2.1. Approximate date of the beginning of symptoms
2.2. The first symptom and the most relevant symptom in their first contact with COVID-19
2.3. Hospitalization (Yes/No) or ICU (Yes/No)
2.4. Diagnosed confirmed with or without laboratory tests, and the date of the tests (CRP /antigenic test/serology)
2.5. Severity of the episode: mild/moderate/serious/critical (SEMI Classification)

## Secondary outcome measures
1. Sociodemographic variables (sex, age, place of residence, occupation, habitability, ethnicity, origin) measured with a battery of questions at baseline.
2. Lifestyle variables:
2.1. Perceived quality of life measured using SF-12 scale at baseline
2.2. Consumption measured using a battery of questions at baseline
2.3. Diet measured using the PREDIMED scale at baseline
2.4. Sedentary lifestyle measured using the International Physical Activity Questionnaire (IPAQ) questionnaire at baseline
2.5. Sleeping habits measured using Pittsburg questionnaire at baseline
3. Comorbidity measured using ECH with medical records at baseline, including previous cardiovascular disease (chronic heart disease, heart failure, myocardial infarction, peripheral vascular disease, stroke), hypertension, dyslipidemia, respiratory diseases (COPD, asthma, chronic bronchitis), chronic renal disease, chronic liver disease, chronic neurological disorders, previous immunosuppression/transplant, chronic hematological diseases (leukemia, lymphoma, myeloma), cancer/neoplasm, HIV and others immunodeficiencies, obesity, malnutrition, diabetes, dermatological diseases, rheumatologic diseases, mental disorders and dementia, thyroid pathology, autoimmune pathology.
4. Clinics and treatment variables:
4.1. TA, Sat $O_2$ %, body mass index (BMI) and temperature measured at baseline
4.2. Use of pharmacotherapy, nutritional supplements, and probiotics measured using a battery of questions (active ingredient, dose, medication schedule, approximate date from the beginning) at baseline
5. Emotional affective variable measured using the Patient Health Questionnaire-9 (PHQ-9) scale at baseline
6. Functional ability:
6.1 Functional status post-COVID 19 measured using Post-COVID-19 Functional Status (PCFS) at baseline

6.2 Functional physical skills measured using 1-min stand-sit test and 6-minute walk test at baseline
6.3 Respiratory function measured using spirometry at baseline
7. Cognitive ability:
7.1 Attention capacity measured using the Stroop test and Symbol Digit Modalities Test (SDMT) at baseline
7.2 Long-term memory measured using the Rey–Osterrieth complex figure test (ROCF) at baseline
7.3 Cognitive ability measured using the CogniFit app at baseline
8. Analytics measured using a complete blood count at baseline:
8.1. Basic biochemistry, hemogram, and coagulation
8.2. Inflammatory markers
8.3. Cytokines
8.4. Serology
8.5. Protein
9. Other variables:
9.1. Pain measured using the Pain Catastrophizing Scale (PCS) at baseline
9.2. Fatigue severity measured using the Fatigue Severity Scale (FSS) at baseline

### Overall study start date
25/05/2021

### Completion date
31/12/2025

## Eligibility

### Key inclusion criteria
Aged 16 to 75 years

Case Group:
Meet the diagnostic criteria of long COVID/post-COVID-19 condition (LC): complex multiorgan symptoms that affect patients who have suffered from COVID-19 (diagnosis confirmed with or without laboratory tests) and persist after the acute phase of the disease, after 4 or even 12 weeks

Control Group (CG):
Have been infected by COVID-19 as confirmed by RT-PCR, antigenic test or serology, from a duration no more than 4 weeks, without symptoms later

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
16 Years

### Upper age limit
75 Years

### Sex
Both

### Target number of participants
400

### Total final enrolment
170

### Key exclusion criteria
1. Symptoms already existed before SARS-Cov-2 infection
2. Refusal to take part

### Date of first enrolment
28/03/2022

### Date of final enrolment
31/12/2024

## Locations

### Countries of recruitment
Spain

### Study participating centre
**Servicio Aragonés de Salud -Unidad de Investigación Atención Primaria**
Aragonese Research Group in Primary Care (GAIAP)
Institute of Health Research
Avenue San Juan Bosco, 13
Zaragoza
Spain
50015

## Sponsor information

### Organisation
Instituto de Investigación Sanitaria Aragón

### Sponsor details
Institute of Health Research
Avenue San Juan Bosco, 13
Zaragoza
Spain
50009

+34 (0)976716818
info@iisaragon.es

**Sponsor type**
Research organisation

**Website**
https://www.iisaragon.es/

**ROR**
https://ror.org/03njn4610

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
Instituto de Investigación Sanitaria Aragón

**Funder Name**
Instituto de Salud Carlos III

**Alternative Name(s)**
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, ISCIII

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
Spain

# Results and Publications

**Publication and dissemination plan**
Planned publication in a high-impact peer-reviewed journal and exhibition at international conferences.

**Intention to publish date**

01/05/2025

## Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | version 3 | | 21/03/2022 | No | Yes |
| Protocol file | | | 11/10/2022 | No | No |