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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
Completed

Last Edited
25/06/2026

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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?
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Scientific

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Additional identifiers

Protocol serial number
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

Primary study design
Observational

Study design
Observational case-control study

Study type(s)
Prevention, Quality of life

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(s)
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)

Key secondary outcome(s)

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

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

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
75 Years

Sex
All

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
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Sponsor information

Organisation
Instituto de Investigación Sanitaria Aragón

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, La misión del Instituto de Salud Carlos III (ISCIII), ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan

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?
Results article		30/08/2024	05/05/2026	Yes	No
Results article		24/06/2026	25/06/2026	Yes	No
Protocol article		24/03/2026	25/03/2026	Yes	No
Participant information sheet			21/03/2022	No	Yes
Protocol file	version 3		11/10/2022	No	No