Supplementary material

Supplementary methods

Process of patient recruitment by Rare Patient Voice and PRC Corporation

1. Recruiters invited potentially eligible patients to participate via email or telephone, using institutional review board-approved language.

2. Those interested in participating communicated with a trained recruiter via phone or email and confirmed whether they met the inclusion/exclusion criteria.

3. Patients were asked to provide verbal consent for their contact details to be provided to a Modus researcher and to participate in the study. Written informed consent was obtained electronically prior to patients' participation in the study. All patients were provided a copy of the fully signed consent form.

4. Patients were also asked to provide written confirmation from their clinician of their long coronavirus disease 2019 (COVID-19) diagnosis.

Screener form eligibility criteria

Inclusion criteria

- ≥18 years of age

- Clinically confirmed diagnosis of long COVID-19

- Initial COVID-19 infection must have been at least 180 days ago (documented via a positive polymerase chain reaction test)

- Currently experiencing long COVID-19 symptom(s) that cannot be explained by an alternative diagnosis
- The patient was not vaccinated at the time of the COVID-19 infection or 90 days thereafter
- The patient has received their last COVID-19 vaccination (including booster shot) at least 4 weeks prior to scheduling the interview
- Willingness and ability to participate in up to one 60-minute audio-recorded telephone or online interview in English
- Willingness and cognitive ability to provide electronic, informed consent
- Ability to speak, read, write and understand English
- Patient has any of the following risk factors for severe COVID-19:
  - Age ≥50 years
  - Obesity, defined as body mass index (BMI) ≥30 kg/m^2, or BMI (kg/m^2) ≥95^{th} percentile for age and sex based on Centers for Disease Control and Prevention growth charts
  - Cardiovascular disease, including hypertension
  - Chronic lung disease, including asthma
  - Type 1 or type 2 diabetes mellitus
  - Chronic kidney disease, including those on dialysis

– Immunosuppressed (cancer treatment, bone marrow or organ transplantation, immune deficiencies, HIV (if poorly controlled or evidence of AIDS), sickle cell anaemia, thalassaemia, or prolonged use of immune-weakening medications

Exclusion criteria

- Patient has concomitant illness(es) that in the recruiter or investigator's judgment would confound researchers' understanding and description of the long COVID-19 disease experience

Patient Information Collected

Patients' demographic information, including age, weight, height, sex, ethnicity, race, education level, employment status, occupation, living situation, marital status and household income, were collected. Comprehensive health information was also collected, including general health status at the time of interview, time since the beginning of COVID-19 symptoms, any hospitalisation due to COVID-19 and time since hospitalisation, smoking status, existing chronic disease or conditions, treatment with a monoclonal antibody, and COVID-19 vaccination status.

Saturation Analysis

Saturation refers to data adequacy, ie, the point at which no new relevant information emerges from additional qualitative data [1-3]. Within patient-reported outcomes research, saturation has been defined as "*the point in the data collection process when no new concept-relevant information is being elicited from individual interviews or focus groups, or no new information is deemed missing during cognitive interviewing*" [4]. In the present study, the adequacy of the sample size was evaluated by a saturation

analysis. Saturation analysis was conducted by grouping interviews chronologically and comparing the emerging sub-domains that reflected the conceptual categorisation of the codes. The sub-domains that emerged from the second quintile were compared with the sub-domains that emerged in the transcripts from the first. This comparison was repeated for each additional quintile. The cycle of data collection and analysis was continued until additional data collection produced no or minimal new information to further confirm or challenge the conceptual model.

Analysis

SAS software version 9.4 (SAS Institute, USA) was used for descriptive analysis. Continuous variables were described by their frequency, mean, standard deviation, median, first and third quartiles, extreme values (minimum and maximum values), and the number of missing values. Categorical variables were described by the frequency and percentage of each response choice, with missing data included in the calculation of the percentage.

Patient Interview Guide

Patient-centered outcomes research in long COVID-19 disease: Patient interview guide

Introduction

Before the interview begins, you should confirm the completion of the Participant Screener and Informed Consent Form for each participant.

Introduce yourself and the purpose of the study

Hello, my name is [Interviewer name] and I work for Modus Outcomes. Modus Outcomes is a company that talks to people about health various health conditions. Currently, we are working with a pharmaceutical company to find out more about your experience with long COVID-19. We define long COVID-19 as symptoms resulting from a COVID-19 infection that last longer than 4 weeks that are not explained by an alternative diagnosis. There are several symptoms you may suffer from, e.g., brain fog, fatigue or shortness of breath. There are many other symptoms, too.

Interview procedures including access to SE-LC19 using REDCap:

During this interview, you will have the opportunity to tell me about your personal experience with long COVID-19. I will ask you open-ended questions about the symptoms you experience and how those symptoms impact your life. After we discuss these questions, I will ask you to access the SE-LC19 weblink which you have received via email. I will ask you to provide me with your feedback on the questions you are required to answer.

The interview will last approximately 1 hour. You can stop this interview at any time, and it will have no impact on your compensation.

There aren't any "right" or "wrong" answers to the questions I will ask you today. We are really interested in knowing what YOU think about your long COVID-19 experience, so we appreciate anything you can tell us.

You will also be asked general demographic and health questions.

Audio recording

This interview will be audio recorded to make sure we capture all the information you share with us. Please try to speak clearly. If you need to take any breaks, please let me know. I can pause the recording at any time.

Anonymity and data handling

Audio recordings will be transcribed by an independent transcription agency. All information that could identify you will be left out of the transcriptions. These de-identified transcripts will be shared with the study sponsor and used in our analysis. Results of this interview will be anonymized, so no answers are attributable to any specific individual.

Adverse event reporting

If during the interview you happen to mention experiencing a medical event while receiving certain treatments developed by the study sponsor, we are required to report this to the company even if it has already been reported by you directly, your physician to the company, or the regulatory authorities. You will remain anonymous and only be identified by your participant ID number.

Closing

Do you have any questions for me?

Answer any questions that the participant may have. Ensure that they agree to have the interview audio recorded for the designated amount of time. Turn on the audio recording. Mention your name and the participant ID of the person you are interviewing along with the current date and time of the interview.

This is [Interviewer name] with participant [participant ID]. It is [date] at [time]. Do you agree to have this interview audio recorded? If *yes*, begin audio recording. If *no*, do not progress with interview.

Concept elicitation

Symptoms of long COVID-19

Can you begin by telling me about the symptoms you have experienced with long COVID-19? Please keep in mind that we are focusing only on symptoms that have lasted or appeared at least 4 weeks past your initial COVID-19 infection and are not explained by any other conditions you may be suffering from.

- What persistent symptom(s) did you notice?
- How would you describe those symptoms in your own words?

What symptoms have progressively disappeared after being persistent for more than 4 weeks?

Are there any other symptoms that have gotten worse over time? Please describe these symptoms.

What other new symptoms have you experienced since you have experience long COVID-19?

[If a clear description of symptom was not provided ask participant to describe the symptom:] What does the symptom feel like?

For each symptom:

How long have you experienced this symptom?

How has [symptom] changed since you first experienced it?

- In what ways has it improved/worsened/remained the same?

Does [symptom] change from day to day? During the course of the day? In what ways does it change?

Can you describe how severe [the symptom] is/was? Did the severity change since you were diagnosed?

Additional questions and probes:

Which symptom/s of long COVID-19 are most bothersome for you?

- Can you tell me more about [symptom mentioned]?
- Why is [symptom mentioned] more bothersome than others?

Which symptom/s of long COVID-19 are the least bothersome for you?

- Can you tell me more about [symptom mentioned]?

- Why is [symptom mentioned] less bothersome than others?

Impacts of long COVID-19 symptoms/diagnosis

How do your long COVID-19 symptoms affect your day-to-day life?

Can you describe to me what a regular/normal day was like for you *prior* to experiencing long COVID-19 symptoms?

- What did you do on a day-to-day basis during the period of COVID restrictions?

In what ways has your day-to-day life changed since you began to experience long COVID-19 symptoms?

- How does this compare to your 'normal' life before you experienced long COVID-19 symptoms?

Are there day to day activities that you engage in differently since experiencing long COVID-19 symptoms? Please note that we are interested in learning about any changes that are foremost due to suffering from long COVID-19 and not restrictions imposed due to the pandemic.

Why did you have to change how you engaged in these activities?

How has your life changed since you started experiencing long COVID-19?

How has your work been impacted by experiencing long COVID-19?

Which impacts/change bothers you the most and why? Which bothers you the least and why?

Which symptoms have affected your quality of life/daily activities the most? Why?

Examples for additional probes on broad activities:

- Ability to engage in physical activities such as exercise routines
- Emotional well-being (e.g. anxiety, depression)
- Caring for other people or your pets
- Household chores
- Doing your usual exercise routine (within the duration of the pandemic)
- Doing your usual hobbies (within the duration of the pandemic)
- Spending time with others (remotely or in person)
- Going grocery shopping to collect your medications or food

Which of your daily activities that were impacted by long COVID-19 have you been able to resume?

Closing and DHIF completion

Opportunity for participant to share additional information

Those are all the questions I have for you today. Is there anything else you want to tell me about your long COVID-19 experience that is important for researchers to know?

Follow up as appropriate.

Closing the interview

Thank you very much for helping us with this research. We appreciate your time and effort. The information you shared with us today will help researchers to learn about long COVID-19 symptoms and how best to measure them in the future. Findings and data from this research may be published so that the scientific community can learn more about long COVID-19 and how it affects people's lives. No personal identifiers will be included in any published material.

Conclude audio recording and close the interview. Ask participants the questions within the Demographic and Health Information Form (DHIF) and record their answers.

Table S1. PubMed search strategy

Search	Term(s)	Results
1	Post-acute sequelae of SARS-CoV-2 infection OR long COVID-19 *Field: Title/Abstract*	134
2	Symptoms	7,204,054
3	Impact	1,262,676
4	Qualitative	325,386
5	Functioning	14,448,823
6	Health-related quality of life	445,770
7	1 AND 2 OR 3 OR 4 OR 5 OR 6	171
8	Filters: English, human participants	115

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S2. Overview of clinicians' backgrounds

Current position(s)	Specialty/training	Number of years practicing	Number of long COVID-19 patients treated per week
Attending physician at academic medical centre	Pulmonary and critical care	30	40
Private practice	General medicine	20	20
Attending physician in emergency department	Emergency medicine	15	Missing
Registered nurse at a hospital	Registered nurse	30	10–20
Registered nurse at a hospital	Registered nurse	26	Missing

COVID-19, coronavirus disease 2019.

Table S3. Saturation analysis of sub-domains: Symptoms

Group 1 (interviews 1–8) 24 concepts	**Group 2 (interviews 9–16) 7 concepts**	**Group 3 (interviews 17–24) 7 concepts**	**Group 4 (interviews 25–32) 1 concept**	**Group 5 (interviews 33–41) 2 concepts**
Altered or loss of smell	Chest pain	Digestive problems (abdominal pain, bloating, diarrhoea, constipation)	Difficulty swallowing	Challenges with fine motor skills
Altered or loss of taste	Dizziness	Skin changes		Stiffness
Body aches and pains	Dry mouth	Joint pain		
Brain fog	Fever	Lightheaded		
Chills	Vision changes	Decrease in appetite and weight loss		
Cough	Pins and needles	Muscle pain		
Difficulty breathing	Numbness	Changes in menstrual cycle		
Concentration	Fever			
Difficulties finding the right word				
Fatigue				
Hair loss				
Headache				
Heart palpitations				
Haziness				
Forgetfulness/ memory problems				
Nausea				
Phlegm				

Red or dry eyes
Ringing in ears
Runny nose
Shortness of breath
Sneezing
Sweats
Weakness

Table S4. Saturation analysis of sub-domains: Impacts

Group 1 (interviews 1–8) 10 concepts	**Group 2 (interviews 9–16) 11 concepts**	**Group 3 (interviews 17–24) 1 concept**	**Group 4 (interviews 25–32) 0 concepts**	**Group 5 (interviews 33–41) 0 concepts**
Anxiety	Sleep disturbance	Challenges caring for pets		
Depression	Bathing			
Childcare	Independently moving around			
Irritability	Feeling like a burden on families			
Cautious about travel	Housebound			
Cooking	Drinking			
Exercise	Eating			
Household chores	Fear of reinfection			
Isolation	Stress			
Engaging in fewer social activities	Shopping			
	Loss of independence			

References

1. Morse JM. The significance of saturation. *Qualitative Health Research* 2016;5:147-49.

2. Strauss A, Corbin J. *Basics of Qualitative Research*. Thousand Oaks, CA: SAGE Publications, 1990.

3. Meyrick J. What is good qualitative research? A first step towards a comprehensive approach to judging rigour/quality. *J Health Psychol* 2006;11:799-808.

4. Rothman M, Burke L, Erickson P*, et al.* Use of existing patient-reported outcome (PRO) instruments and their modification: the ISPOR Good Research Practices for Evaluating and Documenting Content Validity for the Use of Existing Instruments and Their Modification PRO Task Force Report. *Value Health* 2009;12:1075-83.