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Experiences and challenges faced by patients with COVID-19 who were hospitalised and participated in a randomised controlled trial: a qualitative study

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ABSTRACT

Objectives As part of a randomised controlled trial, this qualitative study aimed to identify experiences and challenges of hospitalised patients with COVID-19 during illness and treatment (objective 1: COVID-19-related perspectives; objective 2: trial participation-related perspectives).

Design Semistructured interviews following a prespecified interview guide, transcribed verbatim and analysed in accordance with the grounded theory process. Investigator triangulation served to ensure rigour of the analysis.

Setting Interviews were embedded in a multicentre, randomised, active-controlled, open-label platform trial testing efficacy and safety of experimental therapeutics for patients with COVID-19 (Austrian Corona Virus Adaptive Clinical Trial).

Participants 20 patients (60±15 years) providing 21 interviews from 8 June 2020 to 25 April 2021.

Results Qualitative data analysis revealed four central themes with subthemes. Theme 1, 'A Severe Disease', related to objective 1, was characterised by subthemes 'symptom burden', 'unpredictability of the disease course', 'fear of death' and 'long-term aftermaths with lifestyle consequences'. Theme 2, 'Saved and Burdened by Hospitalization', related to objective 1, comprised patients describing their in-hospital experience as 'safe haven' versus 'place of fear', highlighting the influence of 'isolation'. Theme 3, 'Managing One's Own Health', related to objective 1, showed how patients relied on 'self-management' and 'coping' strategies. Theme 4, 'Belief in Medical Research', related to objective 2, captured patients' 'motivation for study participation', many expressing 'information gaps' and 'situational helplessness' in response to study inclusion, while fewer mentioned 'therapy side-effects' and provided 'study reflection'. Investigator triangulation with an expert focus group of three doctors who worked at the study centre confirmed the plausibility of these results.

Conclusions Several of the identified themes (2, 3, 4) are modifiable and open for interventions to improve care of patients with COVID-19. Patient-specific communication and information is of utmost importance during clinical trial participation, and was criticised by participants of the present study. Disease self-management should be actively encouraged.

Trial registration number NCT04351724.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study's methodology, of gathering patient perspectives, is well suited to identify issues that matter to individuals who, in future, require hospitalisation for COVID-19.
⇒ Patient perspectives regarding trial participation are of general interest to other researchers who conduct clinical trials, potentially also non-COVID-19 related.
⇒ Coding was done by several team members, which renders the findings plausible, and our qualitative data analysis applied two types of triangulation, increasing the study's trustworthiness.
⇒ The sample size is limited, as it was difficult to gain access to patients hospitalised with COVID-19.
⇒ Our analysis aimed less at developing a theory than at identifying categories and themes relevant to improving patient care in a pandemic with many unknowns.

INTRODUCTION

SARS-CoV-2,[1] the virus that causes COVID-19, was first detected in December 2019 in the city of Wuhan (Hubei province, People's Republic of China).[2] As of November 2021, a total of 1907 COVID-19 drug studies were registered at ClinicalTrials.gov, alongside an additional 542 registered vaccine studies.[3] Drug studies are being conducted with the ultimate aim of identifying COVID-19 treatment options. However, as of January 2022, the recommended pharmacological treatment for patients hospitalised with COVID-19 and requiring only supplemental oxygen

included only remdesivir or dexamethasone or dexamethasone plus remdesivir.[4] (Baricitinib or tocilizumab was at that time recommended for those with rapidly increasing oxygen needs.[4]) One interesting randomised trial found that awake prone positioning for acute hypoxaemic respiratory failure significantly reduced the incidence of treatment failure (intubation or death) and the need for intubation, without any signal of harm.[5] That study and others[6] provide information of interest to laypeople and can improve self-management of disease.

Since the start of the pandemic, many reports have described results regarding COVID-19 pharmacological treatment, while analyses of patient experiences are scarce. This discrepancy is unfortunate, as information from patients is valuable for understanding the challenges and opportunities of disease management, and can lead to improved care for others.[7] A previous review by experts in community medicine, disaster medicine and psychiatry emphasised major emotional distress related to the lack of effective treatments[8] but did not include direct patient evidence. One of the few qualitative interview studies was conducted early in the pandemic with hospitalised patients with SARS-CoV-2 from China, and described different stages of attitude towards the disease—ranging from early fear, to denial and, finally, to acceptance.[9] That study identified major sources of stress, including quarantine measures and concerns regarding the health of family members.[9] A more recent interview study from the UK was conducted among patients suffering from Long COVID[10] (here termed Post-COVID, according to WHO). The authors reported that patients had difficulty being taken seriously, and suggested that quality principles for Post-COVID service should include providing continuity of care.[10] To our best knowledge, there are no other qualitative studies that might have explored overall experiences of individuals with COVID-19, and especially those related to hospitalisation.

Randomised controlled trials are the gold standard for examining the effectiveness of new drugs,[11 12] but their success depends on patients' willingness to participate. Recruitment problems are a common obstacle, which may affect statistical power[13] as well as internal and external validity[14–16] due to the possibility of selection bias.[17–20] As in other areas of medicine, advances in COVID-19 treatment cannot be achieved without human participants, who, importantly, must not be harmed for the sake of research.[21] To ensure maintenance of participants' right to self-determination, the investigators must obtain informed consent for their research by presenting information about a new therapeutic measure and asking the potential participants to read and sign a detailed written consent document.[22]

Here we aimed to explore the experiences and perspectives of patients who were hospitalised with SARS-CoV-2 and simultaneously participated in a randomised controlled trial. Our first objective was to capture COVID-19-related perspectives, while our second objective was to capture trial participation-related perspectives. As part of the present study, the results were also discussed with an expert focus group comprising three doctors who had been taking care of the interviewed patients with COVID-19 during their hospitalisation.

METHODS

Study design, setting and participants

All participants in the present qualitative interview study were recruited from the Austrian Corona Virus Adaptive Clinical Trial (ACOVACT). The design of the qualitative study that is presented here, and which was embedded in ACOVACT, is further described below. ACOVACT itself was designed as a multicentre, randomised, active-controlled, open-label platform trial on the efficacy and safety of experimental therapeutics for patients with COVID-19. At the start of the study in 2020, the different treatment arms of ACOVACT comprised hydroxychloroquine (subsequently deactivated due to safety concerns), lopinavir/ritonavir and camostat. Several substudies for adjunctive treatments were designed simultaneously, and foresaw additional treatment with rivaroxaban for thromboprophylaxis, candesartan (for renin-angiotensin system blockade) versus nitrendipine/doxazosin, asunercept and Pentaglobin.

Per the ACOVACT inclusion criteria, participants had to be hospitalised due to SARS-CoV-2 infection; require oxygen support; have given informed consent indicating their understanding and agreement to comply with the study; be ≥18 years of age; and, for female patients of childbearing potential, be willing to take effective contraception measures during the study. Patients were excluded if they were moribund or had an estimated life expectancy <1 month; were pregnant or breast feeding; had severe liver dysfunction; were allergic or intolerant to any of the experimental substances; and/or anticipated discharge from the hospital within 48 hours after inclusion. As of November 2021, ACOVACT was still ongoing.

To qualify for inclusion in the present qualitative interview study, ACOVACT participants had to feel physically and emotionally able to be interviewed, be willing to be interviewed at the time of study inclusion or to schedule interview appointments and be fluent in German or English. Practically speaking, patients who became hospitalised for COVID-19 in Vienna were asked by the ACOVACT recruitment team if they were willing to participate in an interview at the time or shortly after their study inclusion into ACOVACT. If they agreed, they were contacted by the investigators of the present study (mainly LH, VT and HM) during the following days via telephone or video call. The interviews were supposed to be conducted with participants treated at two of the ACOVACT study centres: the 'Klinik Favoriten' and the 'AKH Wien'. Although the initial plan was to conduct an interview at inclusion and another interview after discharge, with corresponding questions, most patients were ultimately interviewed after discharge, as they were often weakened by the disease or not contactable by

phone (further details presented in the Results section). Ultimately, only one participant was interviewed twice. The interviews were conducted by telephone or video call, digitally recorded and typed up verbatim. Any names mentioned during the interviews were removed. Interviews were terminated early when necessary due to health complications.

Details of the data collection

Authors LH, VT and HM were medical students at the Medical University of Vienna, had access to both study sites and conducted interviews in German and, in one case, in the English language. Before the interview, patients were informed about the aim of this qualitative study, the audio recording and the data processing, and were again asked to give their verbal consent. Additionally, the ACOVACT written informed consent form had already included a paragraph about the interview study being part of ACOVACT. A targeted sampling strategy was planned, with the aim of ensuring that the sample of interview participants would be diversified according to demographic and clinical characteristics. It was planned that recruitment would be stopped after saturation was reached, that is, at the point where no further concepts could be expected from additional interviews.[23 24]

Table 1 shows the interview guide, which was based on the available literature—although scarce, as only one paper was published at the time of the study planning[9]—and discussions among the team. Author AT designed the first version of the interview guide.

Details of the data analysis and investigator triangulation

Anonymised transcripts from the interviews were thoroughly read by the authors (LH, VT, HM, AK, UK and MH) and were subsequently coded and summarised into categories following the principles of the grounded theory process.[25 26] For this purpose, the transcripts were entered into one Microsoft Word document by LH, VT and HM, and then sorted using a previously described text sorting technique for qualitative data analysis[27] based on the Microsoft Word program, with author UK leading the latter process. Authors LH, VT, HM, AK and MH conducted several coding sessions to identify meaningful concepts through open, axial and selective coding, which were then grouped into termed concepts. To obtain grounded categories with higher conceptual strength, similar codes and categories were constantly compared and merged into new categories representing essential patterns and relationships in the data set. All of the resulting categories and subcategories are illustrated in figure 1. The study complies with the Consolidated Criteria for Reporting Qualitative Research.[28]

To ensure rigour of the analysis, we arranged two triangulation settings: first, a coder triangulation with author UK and, second, a focus group or support team triangulation consisting of three doctors from the Department of Infectiology at the Klinik Favoriten, who had been taking care of patients during the time of the interviews. Specifically, preliminary coding results were presented to author UK for cross-checking at multiple occasions (first form of triangulation (coder triangulation)). Moreover, the main categories were presented to the expert focus group participants with whom we had a sincere discussion about the accuracy of the results and possibilities to improve care (second form of triangulation). Regarding the selection process of the focus group, anyone working at the ACOVACT sites in Vienna was eligible for participation. However, we hypothesised that the most meaningful outcomes would be obtained if the focus group included predominantly those doctors who were relatively active in recruiting ACOVACT participants. Only verbal consent was obtained from the participants of the focus group. The outcomes from the discussion were protocolised, summarised and added to this manuscript's Results section. Those manuscript sections and sentences describing the focus group discussion were corrected several times, until all those participating in the focus group were satisfied with the final version.

Patient and public involvement

It was the nature of this qualitative study to involve patients directly about their experiences with COVID-19 and the ongoing ACOVACT trial, but the development of the research questions was done without direct patient involvement. The manuscript was sent to all participating patients who provided their email addresses when the interviews were conducted.

RESULTS

Patient characteristics and details of the recruitment process

Among 314 patients who were hospitalised with COVID-19 and included into ACOVACT (218 from 'Klinik Favoriten' and 96 from Vienna General Hospital), 50 were asked to participate in the interview study, of whom 20 agreed. One patient was interviewed twice, once in hospital and once after discharge. Six interviews were conducted while the interviewees were still in hospital (at least halfway through the individual hospitalisation period) and 15 interviews were conducted after their discharge. The interviewing authors LH, VT and HM reported that recruitment was particularly difficult for the first interview while ACOVACT participants were hospitalised. The most common reasons for ACOVACT participants to not agree to being interviewed during their hospitalisation included experiencing physical difficulty, feeling too stressed out and being unfamiliar with the hospital environment.

The interviews were conducted from 8 June 2020 to 25 April 2021. Among the 20 interviewed participants, the average±SD age was 60±15 years, 10 were women (table 2) and one participant was interviewed twice.

Eighteen interviews were conducted by telephone, two by videoconference and one in person at the hospital. The interviewed participants were hospitalised for a median time of 13 days in total (IQR: 10, 17). Most participants

Table 1 Interview guide

Interview 1	
1.1 Experiences with COVID-19	Introduction: If it is alright for you, I would like to talk about the experiences you made during your COVID-19 disease.
1.1.1	How did it occur that you got positively tested? What went through your head as you waited for the test result?
1.1.2	What happened after you received your positive test result? How did your life go on?
1.1.3	How do you manage with the disease in general? Are there any problems which concern only you?
1.1.4	As you were admitted to hospital, what experiences did you make (a) at admission, (b) with the hospital itself, and (c) the hospital staff?
1.2 Study recruitment and expectations on interventions	
1.2.1	How did you learn about the study?
1.2.2	Can you say in your own words what the aim of the study is? How easy or difficult was the decision to participate?
1.2.3	How did you decide to participate? Did you ask for the opinion of other people—was it something else?
1.2.4	What did you consider? Were there any fears or concerns?
1.2.5	What are your personal expectations towards the study?
1.2.6	How were you informed about the (antiviral) therapy? Do you feel well educated about it?
1.2.7	Do you have any concerns regarding therapy risks?
1.2.8	Which potential benefits do you see for yourself?
1.3 Recovery	
1.3.1	If you look into the future—for your remaining time in the hospital—are there any concerns?
1.3.2	And what about the subsequent time at home?
1.3.3	What are your hopes towards the disease course and the remaining time in the hospital?
1.3.4	At which point of condition do you see yourself as recovered/healthy again? What does it take to get there?
Interview 2	
2.1 Experiences with COVID-19	Introduction: A lot has happened since our last conversation. How have you been?
(2.1.0 if no first interview was taken)	How did it occur that you got positively tested? What went through your head as you waited for the test result? What happened after you received your positive test result? How did your life go on?
2.1.1	Can you tell me about your experiences since our last talk? How was the hospital care? Please also elaborate on any negative experiences.
2.1.2	What impact did COVID-19 have on you personally? What was very bad? What was kind of harmless?
2.1.3	How did you cope with spending a long time in the hospital?
2.1.4	What was the most difficult time for you since your infection?
2.1.5	How did you manage? Did you have any help/support? Who helped you during that difficult time?
2.2 Study participation and experiences with intervention	
2.2.1	What was the best/worst about your study participation? Please explain why and how this came about.
2.2.2	Were your experiences with the study as expected? Were there any surprises/something special? Did you miss anything? Based on your experiences, do you have any advice?
2.2.3	Were there any therapy side effects? If so, can you explain them in more detail?
2.2.4	How satisfied were you with the hospital care? Did you experience a difference in care since you were included in the study? Do you think that it was an advantage/a disadvantage for you?
2.2.5	Were there any doubts over the course of the study? Did you regret having participated? If so, why?
2.2.6	Is it important for you to get informed about the study results and to receive them? Are there any open questions concerning the study? Did you have contact to other study participants?
2.3 Recovery	
2.3.1	Whenever you think about recovery, at which point do you see yourself healthy again? Do you need some kind of confirmation for that?
2.3.2	After hospital release, what were your biggest challenges to overcome and your most important sorrows/concerns?
2.4 Final questions	Is there something you would like to add? Did I forget anything to ask?

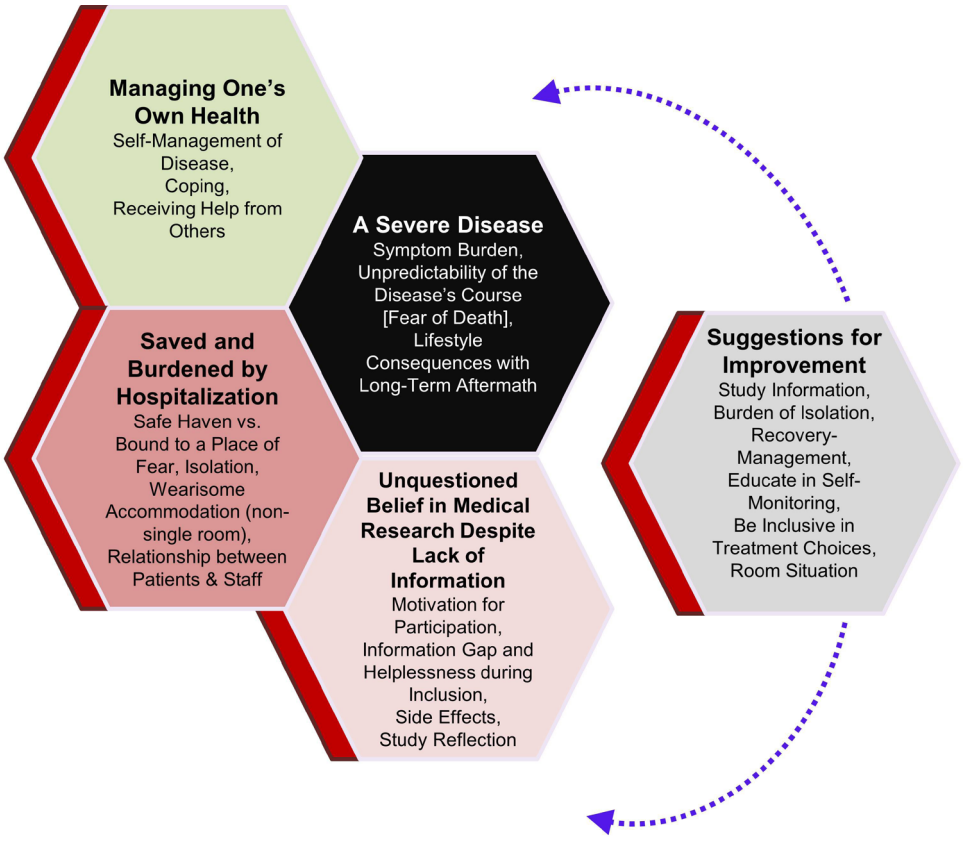

Figure 1 Thematic schema showing themes and subthemes arising from qualitative analysis. 'Suggestions for improvement' were developed by reflecting on the content of the qualitative interviews and through discussions among the clinicians.

(n=19) had required oxygen supplementation for a minimum of 3 days during their in-hospital stay, of whom seven had received high-flow nasal oxygen or continuous positive airway pressure. One participant was admitted to the intensive care unit (ICU) but not intubated. The average duration of the interviews±SD was 25±13 min. Table 2 lists the details of the ACOVACT-specific treatment of the interviewed participants. Besides their study medication, 14 patients received glucocorticosteroids for a median duration of 9 days while in hospital.

Themes and subthemes

We identified four main themes with a range of three to six subthemes for each theme, which are presented in table 3 with representative quotations (in addition to the text that follows here below). The first three themes belong to the first study objective (COVID-19-related patient perspectives) while theme 4 belongs to the second study objective (trial participation-related patient perspectives).

Figure 1 presents conceptual links.

Theme 1: a severe disease (belongs to objective 1 (COVID-19 related))

Symptom burden

The majority of patients reported symptoms including high fever, often accompanied by hallucinations and sleeping problems, cough, shortness of breath, dizziness, nausea, fatigue, weakness, exhaustion and gustatory dysfunction. In some cases, loss of taste and smell had made participants aware of a possible SARS-CoV-2 infection early in the course of their disease. Some participants also reported having lost their appetite and, in combination with the gustatory dysfunction, having lost a great deal of weight over the disease course. In some cases, the infected were not prepared; they did not expect the intensity and severity of the virus and were caught off guard:

> That was at the limit. I have never experienced something comparable. I was so weak; I felt very bad.

For those patients who spent time at home with the disease prior to hospitalisation, the symptoms were a great burden. It was a challenge to remain self-reliant. Everyday life, like climbing the stairs or even cooking, turned out to be rather difficult. Self-treatment at home was also difficult. The use of household remedies against infections and over-the-counter antipyretics often did not have a sufficient therapeutic effect.

Unpredictability of the disease course (fear of death)

In addition to the heavy physical symptoms, many participants felt mental strain. The positive test result left some of the affected feeling baffled and surprised, and it took some time for them to realise what an infection with COVID-19 actually meant and what consequences might follow. Along with the new disease came uncertainty and concerns, especially over how the course of the disease might develop. Some patients feared the possibility of

Table 2 Characteristics of hospitalised participants in a COVID-19 clinical trial

Characteristic	Total (n=20)
Demographic	
Age in years, n (%)	
30–39	3 (15)
40–49	1 (5)
50–59	5 (25)
60–69	6 (30)
70–79	4 (20)
80+	1 (5)
Mean age in years (SD)	60 (15)
Female, n (%)	10 (50)
Location, n (%)	
Klinik Favoriten	19 (95)
Vienna General Hospital	1 (5)
Preferred interview in English, n (%)	1 (5)
Socioeconomic	
Type of education, n (%)	
Secondary level 1	4 (20)
Secondary level 2	8 (40)
Postsecondary college/short tertiary	2 (10)
University	4 (20)
Preferred not to say	2 (10)
Marital status, n (%)	
Married/partnered	15 (75)
Single	1 (5)
Divorced/separated	3 (15)
Widowed	1 (5)
Number of children, n (%)	
0	2 (10)
1	2 (10)
2	10 (50)
3+	6 (30)
People in household, n (%)	
1	4 (20)
2	9 (45)
3–4	5 (25)
5+	2 (10)
Clinical	
Symptoms on admission, n (%)	
Cough	11 (55)
Sore throat	5 (25)
Fever	11 (55)
Chills	6 (30)
Shortness of breath/difficulty breathing	9 (45)
Pain/pressure in the chest	2 (10)
Fatigue	11 (55)
Nausea, loss of appetite, stomach-ache	7 (35)
Diarrhoea	4 (20)
Myalgia	4 (20)
Dysgeusia	6 (30)
Anosmia	5 (25)
Pre-existing conditions, n (%)	
Diabetes	3 (15)
Hypertension	12 (60)
Cardiovascular disease	7 (35)
Chronic lung disease	5 (25)
Obesity (BMI>30)	8 (40)
Other	10 (55)
Treatment for COVID-19, n (%)	
Camostat (SOC)	12 (60)
Hydroxychloroquine/chloroquine	1 (5)
Lopinavir/ritonavir	6 (30)
Asunercept	4 (20)
Remdesivir	6 (30)
Glucocorticoids	14 (70)
No antiviral treatment	1 (5)
Oxygen	
Oxygen, n (%)	12 (60)
Non-invasive ventilation or high-flow devices, n (%)	7 (35)
No oxygen, n (%)	1 (5)

BMI, body mass index; SOC, Standard of care.

death, and were concerned about how to survive and how to get better as fast as possible. Patients feared death and the possibility of having to be transferred to the ICU for intubation, which gave them the motivation to avoid this possible scenario at all cost:

> [As you received your positive test result, about what did your worry most?]—surviving, that was my only thought.

The interviewees often worried more about their family, friends and close ones than about themselves. The possibility that they might have infected others was another reason to worry, and distressed many participants. Before their hospitalisation, they had already isolated themselves from the rest of their family in order to avoid spreading the disease. Consequently, their hospitalisation represented some relief, taking away the risk of infecting their household members. In some cases, the spreading of

Table 3 Themes, subthemes and illustrative quotes from patients hospitalised due to COVID-19

Theme 1: a severe disease	
Symptom burden	'I got a fever during the night. It was very unpleasant. I was alone in bed, I felt incredibly sick; I couldn't sleep. I almost hallucinated. I couldn't lie still and I had to move all the time. It was a terrible night.' 'It got worse in these 6 days and the fever was high—38.5 to, once even, 40—and paracetamol tablets did not help anymore. The fever did not go down. Ibuprofen did not help either.' 'The first night was terrible, because I also had this depressive attack somehow and also …, that was very strange, almost like hallucinations. And after the first night, I asked for a sleeping pill.' 'I only sleep 4 … 5 hours and then it's over, despite the sleeping pills.'
Psychological impact	'That scared me, on the psyche, it scared me.' 'The worst thing about COVID-19 was that you had no contact with your people.' 'In 1996, I had depression. I was afraid that I would fall into it again.' 'Yes, at the beginning, after the diagnosis, I have to admit that it really hit me. I sat there for a while and said nothing.'
Long-term aftermaths with lifestyle consequences	'I don't have much trouble with walking uphill, but the lungs aren't what they used to be.' 'One is so weak. The interest and the ability to concentrate are as well.' 'Slow and exhausting. But knowing that you can do it on your own, and that it will probably get better with time, is a good feeling.'
Theme 2: saved and burdened by hospitalisation	
The hospital as a safe haven	'It was all very great. I am so satisfied, really, amazing. They [the hospital staff] do it so well, so efficiently, so super!' 'When I was pushed into my room in the hospital, I somehow had the feeling that I was now more or less saved. That was a very strong feeling and that's how it was. That also proved to be true.' 'The hospital is not really my business, but in that case I was glad to be admitted.' 'It would not be possible without the hospital.' 'The most important thing, of course, was the time in the intensive care unit. That was very exhausting. But I felt very well taken care of; everyone took great care of me, the nurses, the doctors, it was really fantastic.'
In isolation	'The smallest is a daddy's child and when daddy is not at home, it is always a bit difficult.' 'You know what else was bad? I was not allowed to have any visitors at all.' 'It was a psychological burden because I didn't see the family for so long, for months.' 'I missed the personal contact. Telephone is not the same.'
Bound to a place of fear	'I was in a panic. There was nothing I could do but push the button to get someone to come. I said, "That woman is suffocating next to me".' 'So, we had two half-dead women in the room.' 'Yes terrible. Imagine such a night! A woman of 75 who cries for her mother half the night because she doesn't know where she is. You have to process all that first.'
Relationship between patients and medical staff	'The doctors were very nice. But every day, someone else came. Maybe that's normal. But that was quite a burden for me.' 'I explained that as a COPD patient, I would not get more than 93 [oxygen saturation], which was ignored. I was always told, "No, no, 96 or 97." It was a relatively tedious thing in the hospital.'
Theme 3: managing one's own health	
Self-management of the disease	'Yes, positive and yes, then I called again 1450 and asked for a doctor and they then sent the ambulance.' '[And where did you get the information about the oxygen measurement?]—I have acquaintances who are doctors and I have also informed myself.' 'The first thing I did, when I knew that I was positive, I bought an oxygen oximeter and checked it and took my temperature and as soon as I got below 90 with the oxygen saturation, I called the ambulance and we went to the hospital.' 'And I always saw that when I turned to the side, the lung function was immediately much worse, the lung performance, the oxygen saturation went down, 10 or 20%. That's why I quickly switched to the prone position and took the oxygen mask. And I saw on the devices that something was happening, in the important parameters.' 'And I have also demanded the [oxygen] mask during the day, even though everyone said I didn't need it.' 'I checked my breath, of course, because I had been told, "Watch out, if you find it hard to breathe, you'll have to see that you get to the hospital." I then naturally huffed my breath, as humans are—that's not so conducive either. My daughter is a doctor and she brought me a device for oxygen saturation. We measured again and again and there was an increasing deterioration and then she admitted me.'
Seeking help from others	'My son and husband then decided that I had better come to the hospital so I would be safe.' 'Because I knew that I belonged to the vulnerable group, I was voluntarily quarantined. The children and grandchildren brought me food.' 'I was already so psychologically battered that my daughter got special permission [to visit] on a Sunday, a week before my release. We were then able to meet in this room where people get together. At a distance, we were able to see each other in person.' 'My doctor also told me that I could approach my wife without worrying, that I was not contagious. So we spent a really nice time. She took care of me exclusively.' 'I had the telephone with me in the intensive care unit. It gave me a lot of strength when I spoke to or texted my wife.' 'My son. He saved the whole family. When he was no longer positive [for COVID-19], he took care of everyone else.'

Continued

Table 3 Continued

Theme 1: a severe disease	
Coping	'[Is there anything that helps you getting better?]—Yes, I will talk to my kids, I wrote it down and maybe I will do therapy, I don't know yet.' 'You live along and you get used to the situation with time.' 'In the end, I went in very optimistically and noticed that the course could only be moderately severe, according to the symptoms—no shortness of breath, no pain in the limbs, etc. Then I thought to myself: You're lucky and you'll pull through.' 'But I didn't worry about it. I accepted it as it is and made the best of it.'
Theme 4: unquestioned belief in medical research despite lack of Information	
Motivation for study participation	'I said "Why not?". If I already have it [COVID-19], then let them try it [the study medication], it's only good to get new drugs on the market.' 'Others should be able to learn [through the study]. Maybe others can be helped. I stand behind it. I would do anything.' 'Concerning the study, I signed because Mr. X is an incredibly sympathetic person whom I know from television. How or what I got there—no one told me anything about it.' 'I didn't think about it for long. I'm fine and I participated out of principle. I didn't think about whether it would be better for me to survive or not. Of course, I thought to myself: they won't kill me.' 'I had the feeling that it would be ungrateful of me if I said "No!".' 'I just, out of affect, said yes, because it's ok. But I didn't know what kind of study that was or what they do to you.' 'I agreed because it's important to the whole picture, but I can't tell you what they actually did.' 'This was an easy decision because I didn't feel there were any alternatives at all.'
Lack of information and helplessness at inclusion	'They told me it's a drug that I'm getting that's been used for other diseases for a longer time and where they hope it will work well for COVID-19. I don't even know what it's called.' 'I got some piece of paper where they told me "Sign it!" and then I signed it.' 'The only thing I did not like was, that I was kind of overrun. You sign some papers, but you don't really have the time to read it through, and you are not able to read in that situation.'
Side effects of study treatment	'I was then given tablets that are over 1 cm in size, 8 a day, and just as I popped this tablet on top, I had to go to the loo and I was, really true, suffering from it until yesterday!'
Study reflection	'I would actually be vividly interested in what was studied and attempted in that study.' 'I would like to know if it [the treatment] made a difference.'

COPD, chronic obstructive pulmonary disease.

COVID-19 could not be avoided due to the late onset of symptoms, which left those patients feeling guilty:

> I was worried for my cousin and his wife; they are both over 60 and it was obvious that I infected them.

Long-term aftermaths with lifestyle consequences

For many patients, the impact of COVID-19 did not end with their hospital release. Many participants remained tired and exhausted, with some reporting that they could not do anything but sleep for days. The relief of returning to their families, and the happiness of having overcome the infection, often overweighed the burden of tiredness. However, having spent a long time in bed with little to no physical activity resulted in loss of strength and muscle mass. Dealing with everyday tasks, such as shopping for groceries or even climbing the stairs, was a challenge and quickly led to exhaustion and shortness of breath.

Participants also reported receiving support from their family and friends. Participants' biggest wish was to return to their initial physical level and to regain their self-reliance. To regain their strength, some went for long walks, did minor physical workouts or just tried to climb the stairs higher and higher, slowly increasing the intensity day by day:

> I have lost a lot of muscles. But I saw the progress; I could go to the toilette by myself, down to the yard, and up the stairs. It was so exhausting; I have felt 15, 20 years older. Everything was so slow and exhausting. But to know, that I can do it alone and that it might get better with time, was a good feeling.

Some participants still experienced uncertainty and did not know how to proceed to improve and accelerate their recovery. They worried about disease recurrence and an increased vulnerability to other infectious diseases. They expressed their wish for better instructions on how to manage their recovery—specifically whether any physical examination or future X-ray follow-ups were recommended, and who could be contacted in case of worsening or unanswered questions.

Theme 2: saved and burdened by hospitalisation (belongs to objective 1 (COVID-19 related))

The hospital as a safe haven

Before hospital admission, many patients were in despair and stressed out. They realised their critical medical condition and reported being aware that they were suffering from a new and deadly disease. Some of the participants were afraid to stay alone at home, dealing with that serious disease, and said that as soon as they entered the hospital and were transferred into their rooms, they felt like they were saved. They saw the hospital as their safe haven and gladly took that chance. The patients felt rescued and were relieved to be able to place their fate into the hands of professionals:

> As I was brought to my hospital room, I had the feeling that I am saved now. It was a strong feeling and it turned out to be true.

Most patients felt well cared for and well treated at the hospital. According to them, the hospital staff handled the exceptional COVID-19 situation professionally. The majority of the subjects had confidence in the competence of the physicians and nurses, and in the decisions they made for them (eg, concerning treatment options):

> I told them: 'Without you, I would be dead!' I told it everyone, the cleaning staff and the doctors, amazing work, and all the time with these plastic suits on, that is insane!
>
> I felt that I was in good hands, that they all knew what they were doing.

In isolation

On the other hand, the hospitalisation also brought isolation and loneliness. Due to COVID-19 restrictions, no visitors were allowed. The contact with medical staff was kept short. The necessary safety wardrobe of the caretakers (suits and face masks) rendered the situation impersonal, making it difficult to build a personal relationship:

> The people come in like Martians. That is a very strange situation.

The patients usually communicated with their families by telephone or video calls, and some described that it did not have the same positive social effect as meeting someone in person. In particular, some of the elderly patients felt very lonely and sad. For most patients, social support from the outside was very important because it gave them a perspective and motivation to overcome this difficult situation. One patient was heavily affected by the isolation and showed depressive symptoms; therefore, an exception was made and her daughter was allowed to meet her in an isolated room:

> I was so mentally strained, that my daughter got on Sunday, one week before my release, a special visitor permit. We were allowed to meet in a room. With some distance, we could see us in person. That was the worst about COVID, that you cannot have contact to other people.

Bound to a place of fear

Another stressful factor for patients was the wearisome accommodation if they were not placed in a single room. In one particular case, a patient who was placed into the same room with another patient with COVID-19 witnessed this stranger struggling for life. She saw her roommate suffering, crying, screaming and fighting for breath, which disturbed her deeply:

> I was in panic. I could not do anything, but press the button for someone to come. I said: 'The woman next to me is suffocating.' I asked, if I can get another

room, so that I would not notice it. It was horrible. She was retching. I must not think about. That was really wearing.

Many participants reported that sleeping and resting were difficult in the hospital, and nearly all said they had received sleeping pills. This was because of the noise caused by other people in the room and ventilators, and due to the psychological stress.

The patients were confined to their beds. They reported that the many hours of just lying around doing nothing felt gruelling and wearisome. Participants suffered from being restricted in their movements due to medical equipment on the one hand and by distance and isolation measures on the other:

> The bed is very tight—you are wired with ECG cables, infusions everywhere. But tied to the bed all the time, that is grueling.

A few of the interviewees were also discontent with the care they received and, to a certain degree, regretted their hospital stay:

> My luck was that the last virologist I talked to was very nice and competent. He explained everything to me and read my medical history and said that I can go home tomorrow. That was my stroke of luck. But the rest was just terrible!

Relationship between patients and medical staff

The majority of patients felt well cared for and treated in the hospital, but some participants perceived the relationship between the doctors and the patients as difficult. This predominantly resulted from the fact that hygiene measures and safety precautions allowed only very short and impersonal ward rounds. Many patients also reported that they were treated by many different doctors, but would have preferred a unified team. Representing a special case, some patients suffered from certain pre-existing conditions, such as chronic obstructive pulmonary disease or diabetes, and felt incapacitated with regard to their treatment.

> I felt like I was incapacitated when it came to diabetes. I've had it since 1984, and there's almost nothing I don't know. I know my body best. It also messed me up that I wasn't allowed to inject, even though I had almost 300 [mmHg] of sugar. It was like a horror movie.

> A different virologist came every day—I have never seen so many in my life. The virologists in the hospital grow like mushrooms. Every day there was a so-called visit of one minute or one and a half minutes—that was it.

Theme 3: managing one's own health (belongs to objective 1 (COVID-19 related))

Self-management of the disease

Participants reported knowing the common COVID-19 symptoms, and most of them had closely watched their body signals and well-being before, during and after their hospitalisation. The participants observed parameters, including body temperature (fever), breathing and oxygen saturation. Some had privately purchased a pulse oximeter. Observing their oxygen saturation gave them a feeling of safety, and enabled them to realise when hospitalisation was needed. After noticing symptoms, many of them had called the Austrian health consultation helpline to find out if they might have COVID-19. At home, many patients had tried home remedies, including tea, herbs, homeopathy and antipyretics. Many of the participants reported that they had been in contact with their primary care physician, or doctors within their circle of family and friends, to get more information and recommendations on how to deal with the infection:

> The first thing I did, as I knew that I am positive, was buy a pulse oximeter to monitor myself and measuring my temperature. As soon as my saturation dropped under 90%, I called an ambulance.

While in the hospital, the patients followed the recommendations of the medical staff to improve their breathing, by staying in the prone position. Beyond their compliant behaviour, they closely monitored their own health parameters and, in the event of worsening oxygen saturation, reverted themselves to the prone position and reached for their oxygen masks to improve their condition. Following these instructions, and witnessing that their oxygen saturation improved with these measures, gave them a feeling of safety and the motivation to struggle on. The possibility of making a small difference for and by themselves, towards a faster positive outcome, boosted their morale.

Receiving help from others

The majority of interviewees reported that they had been dependent on the help and support of others ever since the onset of the disease. Quite often, their family members had been the ones to decide that the participants should get to a hospital to receive proper care, rather than staying home in bad health any longer:

> My husband and my son decided for me to get to the hospital—to be in safety.

Coping

Although most of the participants knew the severity and danger of SARS-CoV-2 infection, many of them stayed calm and tried to think positive. After getting the positive test result, they reported preparing themselves to endure the next days to weeks, and knowing that it might become a tough time. One person also reported that he did not mind the isolation at all because he liked being alone:

> I was not like 'Oh my god! What am I going to do?' I am a positive thinking person, I was more like 'How stupid, I was always cautious and now I am innocently infected. Well let's see, it will be alright.'

Theme 4: unquestioned belief in medical research despite lack of information (belongs to objective 2 (trial participation related))

Motivation for study participation

The patients had different motives for participating in ACOVACT. Many participated in order to contribute to science and thus advance research. The majority also reported that they were motivated by wanting to do something beneficial for society:

> I think I do it for the [progress of] medicine, to find a drug against it soon. If there are some persons, who do the study, so you can gather experience and information and can progress better. It is also good for science to research further.

Apart from altruistic reasons, a few patients also recognised a personal benefit from participating in the study. These reasons included expecting better treatment and monitoring, as well as access to new treatment options:

> My god, I simply tried to get better as soon as possible. I didn't realized if it was any new medication. I automatically said yes, because I had the hope that it might help me. I was very concerned to get back to health.

Many patients also reported that one reason they participated in the study was because they had confidence in the physicians, and that those physicians would provide them with the best possible healthcare. Thus, when asked by the physicians to participate in the study, the patients trusted them so much that they agreed without further consideration:

> You automatically say yes to it because you have the hope that it will make you healthy again.

A small proportion of interviewees could not report a clear motivating factor. They participated in the study for no specific reasons:

> I had no motive at all. I mean, put yourself in the position—you have a fever of 38/39, you're glad that you're in the hospital now, that they're going to give you the right medication or something—and then you just say 'yes', although you don't know what kind of study it is.

Information gap and helplessness at study inclusion

The probands also voiced very mixed messages regarding how well they were informed about the clinical trial on study inclusion. Most patients said that they were inadequately educated at the beginning of the study. They reported a general lack of information and could only recall that they signed 'some kind of papers'. Additionally, most patients had little knowledge of how exactly the drug trial was conducted or what the goal was:

> Somebody asked me, if I would like to participate in a study. I said 'Yes!', but that was it! No Information! Nothing!

The majority of patients were in a critical health situation when they were admitted to the hospital and enrolled in the study, and were often confused or found it difficult to respond due to fever and weakness. In this condition, patients found it difficult to understand and recall the information they received at study inclusion. Many patients were overwhelmed by the wealth of information they were given, especially given their many other concerns and fears at the moment of hospitalisation:

> I was not even aware that I was taking part in a study. They just kept taking blood from me. I was told: 'For antibodies.' But what exactly was meant by that or was done, I didn't know at all. Or I didn't realize it… could be. I don't know. I miss a few days in my head.
>
> It was on the first day that they talked to me about [the study]. At that time, I was not really receptive.

Only a few participants were satisfied with the amount of information they had received, and felt well educated and instructed by the doctors. They reported that the doctors had taken their time to explain everything, and had repeated incomprehensible information on request:

> I feel like I was really educated—especially by the attendings—about the dangers and what was being done.

Side effects of the study treatment

The different experimental therapies in ACOVACT were perceived as having little to no side effects. The worst reported side effect was strong diarrhoea caused by the pharmaceutical 'Kaletra' (lopinavir/ritonavir). However, many subjects reported problems with the large amount of medication they were given, or rather the size of the tablets they had to swallow. As a result, some patients struggled to take their medication on a daily basis:

> The medication box that everyone gets in the hospital—in the morning, at noon, and at night—was suddenly pumped full of drugs.

Study reflection

With few exceptions, the patients did not regret having participated in ACOVACT. Only one patient reported that she had discontinued the study early because she suffered from severe side effects of 'Kaletra' (lopinavir/ritonavir), and felt that she was not sufficiently cared for. The majority of subjects pursued the strong interest in contributing to society and science through their participation, and also hoped for the best possible treatment and chance of cure for themselves:

> [So, you don't regret your study participation?]—'No, not in any way. If it has helped me, then I am very grateful.'

However, in retrospect, many participants reported that they had been insufficiently informed about the design and purpose of the study when they had entered it, and

some were not even aware that they were participating in a study. We also asked patients for suggestions for future improvement. Since many patients were not very receptive at the time of study inclusion, due to symptoms of illness and general excessive demands, they would have liked to be informed about the study in detail a second time, at a later point during their hospital stay.

For all patients, it was important to identify and understand the purpose and goal of the study. They unanimously agreed that they had strong interest in the results of the study, because the study outcome would give meaning to their participation:

> I would really like to know what the purpose of this study was. Are they using people as guinea pigs or does this have a therapeutic purpose? Or anything else? How is this being evaluated? That's important to me, really.

Investigator triangulation with an expert focus group

The discussion among focus group participants, three doctors who had been taking care of the interviewed patients at the Department of Infectiology at the Klinik Favoriten and the closer study team (authors LH, VT, HM, AK, UK and MH) was sincere and meaningful. Focus group participants confirmed the plausibility of these results. The doctors, however, also concluded that the patients' poor state of health was partially responsible for their reported uninformedness about their trial participation.

DISCUSSION

In the present qualitative interview study with patients who were hospitalised for COVID-19 and participated in the ACOVACT randomised trial, we identified meaningful themes with implications for care. Among the non-modifiable or only partially modifiable themes, belonging to our objective 1 (to capture COVID-19-related perspectives), patients reported suffering from the uncertainty and severity of COVID-19 and the burdensome hospital situation due to isolation, although hospitalisation was initially considered a salvation. Notably, a key finding was that many participants expressed appreciation for being able to self-manage their disease course. Specifically, they reported that they had treated their disease symptoms independently at home, and later proactively participated in their treatment at the hospital, benefiting from additional support by healthcare professionals. The participants greatly appreciated information regarding breathing positions in relationship to oxygen saturation values, as well as emotional support from family. Although this finding is seemingly self-evident, we believe that such care was of high value, especially since a patient's breathing position has proven benefit in terms of outcomes.[5 6]

We also gained knowledge (related to our objective 2) about how the study subjects perceived their participation in a randomised trial on pharmacological COVID-19 treatment options. For most patients, agreeing to participate was a matter of principle, with primary motivations including altruism, and belief and trust in science. Many participants also hoped that access to the trial medication would bring them back to health more quickly. However, the majority complained about inadequate education regarding the study itself. This finding is crucially important. The process of obtaining informed consent is based on disclosure of adequate information, the patient's intellectual ability and voluntariness, and is not just a matter of documentation.[29] Additionally, patients should be so actively involved into the study discussion that they can make an autonomous decision regarding the proposed study treatment.[30 31] However, even outside of COVID-19 research and its unusual circumstances, there is growing evidence that the informed consent process does not fully meet the needs of clinical research participants.[32–35] Although process of informed consent has become increasingly regulated and standardised, its challenges are difficult to tackle.[36] The consent form itself has been criticised for becoming longer and more complicated, obscuring important details and being geared towards the interests of institutions and sponsors. Data show that even after signing an informed consent form, participants have limited understanding of the information about the study.[22 36]

As an important validation requirement of qualitative studies, we discussed our results with an expert focus group of three doctors who worked at one study centre, asking them for their interpretation of the themes and ways to improve care. The focus group concluded that the patients' poor state of health was partially responsible for their reported uninformedness about their trial participation. It is entirely possible that patients with COVID-19 who were thus sickened by a systematic febrile disease potentially causing hypoxia and dehydration had a poor comprehension of the purpose and goal of the study, or had impaired powers of recall of the consent process which was provided by good clinical practice (GCP)-trained investigators and found to be adequate at that particular time. Communication barriers by masked caregivers and the fact that many patients did not speak German as their first language could have adversely contributed. Stressful and insecure hospital life during the pandemic, isolation measures and the doctors and nurses' fears of becoming infected might also have contributed to the reported lack of information and poor doctor–patient relationships. The short daily visits with limited patient contact hindered communication, which was also described as regrettable from the doctors' side. Focus group members suggested repeating trial education after inclusion to increase the knowledge of the trial participants and avoid misunderstandings. From the knowledge gained, a list of suggestions (box 1) was created to improve the future treatment of COVID-19, and the implementation of clinical trials in times of crisis.

To our knowledge, only few qualitative studies with patients suffering from COVID-19 have previously

Box 1 Suggestions for improvement

Clinicians' perspective

Trial information: Re-educate patients after a few days, ask several times if everything was understood, ideally in a calm setting with less stress and more receptivity than on the day of admission. If possible, hand out an extra information sheet with briefly summarised study issues in simple language for the layperson to understand.

Burden of isolation: Ease the isolation by increasing contact with family and friends through daily phone or video calls. Also support elderly people, who might have problems applying video chat programs, to enable face-to-face chatting. Educate patients about the possibility of professional psychological support if needed, and establish an available team of psychotherapists for the given task.

Recovery management: Instruct patients on the recommended next steps and, particularly, where to turn for further information and support in the hospital's discharge letter or in a discharge conversation. The aim should be a multidisciplinary rehabilitation plan, with general practitioner (GP) check-up, respiratory and cardiac consultants, physiotherapists and psychologists, which can be even more important for Post-COVID.

Patients' perspective

Educate in self-monitoring: Educate all patients about the simplest health parameters, especially the understanding of oxygen saturation and its importance in the disease course of COVID-19. Show patients how saturation levels change depending on the position in which they lie in bed, and the positive effect of lying in the prone position on physiological ventilation. After hospital release, advise patients, who are unsure about possible relapse or recovery progress, to get a pulse oximeter for monitoring and reassurance.

Be inclusive in treatment choices: Be aware of the special needs of patients with diabetes or chronic obstructive pulmonary disease (COPD), and of their higher level of medical knowledge. Provide enhanced patient–doctor communication to elaborate patients' previous knowledge about self-therapy.

Accommodation: More quickly isolate healthier patients from patients with critical medical conditions to avoid them witnessing disturbing incidents. Pay close attention and communicate openly with patients to avoid wearisome and unpleasant accommodation and interference with roommates, especially because patients are tied to their beds and isolated with strangers in the same room for a long time, which already leads to lower resilience concerning stressful events. Perfect accommodation for everyone can hardly be accomplished, but should be pursued as far as possible.

been published, of which two were conducted in the UK,[10 37] another one in China[9] and also Denmark.[38] Patients from the Danish study described COVID-19 as a threat to existence, and expressed disbelief and surprise of being affected by the unthinkable.[38] An interview study from the UK investigated the experiences of older people with household isolation and social distancing during COVID-19.[37] Finally, a Latinx study,[39] conducted at two public hospitals in Colorado and San Francisco, identified people's disbelief and misinformedness regarding the virus, as COVID-19 was described as not real or as an invention of the government.

A strength of the present study is that qualitative studies with patients suffering from COVID-19 are scarce compared with clinical research, and patient-reported experiences may define important areas for improved care and potentially better outcomes. The recruited patients exhibited a wide range of ages, had different social backgrounds and experienced individual disease courses with differing disease severity. Our research team included both clinicians and social scientists. Coding was done by several team members, which renders the findings plausible. Our qualitative data analysis applied two types of triangulation, increasing the study's trustworthiness. Moreover, the study is unique, as there is currently no comparable literature describing the experiences of patients hospitalised with COVID-19 in a clinical trial. However, the sample was limited, and the results may not have fully captured the perspectives of some minority ethnic groups. Furthermore, in the planning phase of the study, the difficulty of conducting interviews during the patients' hospitalisation was not expected. Therefore, the interview guides for time point 1 (hospital) and time point 2 (after hospital release) were merged to avoid missing information, as the interview often could not be conducted early enough during hospitalisation. As the interviews were conducted from June 2020 to April 2021, it is not clear how well the results that belong to our study objective 1 will relate to more contemporary phases of the pandemic. Finally, on study objective 2, it is not clear how well can the challenges of fully informed research participation be carried over to other settings: other trials testing completely different interventions, and again patients with COVID-19 in more recent phases of this pandemic.

In summary, our study shows what patients went through after having been infected and hospitalised with SARS-CoV-2 (study objective 1), and how they experienced their participation in a clinical trial during the COVID-19 pandemic (study objective 2). Patients were altogether grateful for the medical support and felt safe during their in-hospital stay, but substantial efforts should be made to care for their mental well-being during isolation, as the hospital was also seen as a 'place of fear'. Importantly, our analysis related to our objective 2 suggests that communication about trial participation was insufficient. Specifically, our interviewees expressed their appreciation of research, but criticised being not adequately informed about the trial's design and objectives. This finding needs to be confirmed by other groups and in additional study settings, in the unfortunate, virtual absence of qualitative research on COVID-19. In contrast to qualitative studies, quantitative clinical research (including clinical trials) is massive. If other groups can confirm that many of these trial participants have felt underinformed, then an ethical discussion on the future of COVID-19 research is needed. Besides better communication with patients, the results of our study also point to the importance of self-management of disease, which should be much more actively encouraged, as long as an immediate cure for COVID-19 is not within reach.

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