



Lessons from Long COVID: working with patients to design better research

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The perspectives of people with lived experience of any condition being researched must actively inform the research questions asked and the way in which we go about answering them. The experience of Long Covid gives a contemporary example of how working together with patients is integral to medical research.

When ‘Long COVID’ emerged as a concept in Spring 2020, it was those with lived experience of the disease who gave it its name and characterized it to the world, initially through use of social media¹. Even though chronic illness induced by viral infection is not a new phenomenon, awareness of this potential outcome of the COVID-19 pandemic was entirely absent from public messaging, even at a time when large numbers of people were becoming infected with SARS-CoV-2.

During most of 2020, it was mainly those with lived experience of Long COVID, including people working in health care and medical research, who were alerting the world to this illness². While dealing with their own impaired health, patients became activists advocating for two interlinked things: for their illness to be better recognized, researched and cared for; and for the prevention of additional people being affected by Long COVID. Many people with Long COVID felt the need to share their personal stories with the world, however uncomfortable that may be, to draw attention to the problem of prolonged ill health from COVID-19, even after so-called ‘mild’ initial disease. I was one of those people³.

With my two positions as both a public health academic and a person living with Long COVID, I learned a few lessons. An important one is how much better we can do in health research if our understanding and questions are enriched by the lived experiences of patients right from the start of the research cycle⁴. I aim to gradually apply the lessons I have learned to my own research and hope that other researchers will also benefit from my sharing of these reflections.

Let us start with the framing of the research question. Traditional ways of shaping the research agenda may miss the obvious from a patient perspective, particularly if people with lived experience do not inform that agenda at the research concept and design stage. The language used to frame research questions is particularly important, as bias can creep in at an early stage.

I take as an example a widely quoted, published study carried out in France⁵, which framed the research question as such: “Are the belief in having had COVID-19

infection and actually having had the infection as verified by SARS-CoV-2 serology testing associated with persistent physical symptoms during the COVID-19 pandemic?” The way the question is phrased suggests that it is already decided that ‘true’ infection is verified by a positive result of a laboratory test, namely a SARS-CoV-2 anti-spike protein IgG antibody test, otherwise it is merely a ‘belief’. However, this type of serology test is not an accurate way to assess the presence or absence of past infection, particularly in those experiencing persistent symptoms. Antibodies may be undetectable in some individuals infected with SARS-CoV-2 (REF.⁶). Also, having Long COVID is in itself associated with a weaker antibody response to infection and immune dysregulation^{7–9}. Thus, it is not scientifically sound to use antibody testing to classify the exposure (past SARS-CoV-2 infection) in relation to the occurrence of the outcome (persistent symptoms), because the method used for classification itself may be causing the outcome if the aetiology of Long COVID is related to the nature of the immune response to the infection. The assumptions underlying both the research question and the study design are problematic.

Why is the research question framed in such a way that a low accuracy laboratory test is to be believed — as a default — more than patients’ testimonies about their own health? The burden of proof should not be on ill people every time that a study implies that Long COVID is imagined. Framing illnesses that we still lack sufficient knowledge about as ‘beliefs’ can be harmful. Involving patients in shaping the question is essential for the research to be relevant to them. Also, researchers and science journals should take responsibility for how the framing of studies they publish can disadvantage people’s lives, in terms of the stigma attached to their condition and the type of care and support they receive. We have seen this happen with similar conditions such as myalgic encephalomyelitis/chronic fatigue syndrome, and it is time for the medical research community to learn from these mistakes. Particularly for chronic conditions that are still poorly understood, we risk further biasing that understanding

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by assuming that we — as researchers — know how to ask the right questions.

The legacy of how research was carried out in the past in relation to post-viral illnesses should not dictate the present and future. Co-producing the relevant research questions with patients can help to correct the legacy of dismissal, which has tended to assume a predominant psychosomatic explanation for things we do not yet understand. Now that research funding for Long COVID has started to increase, it presents an opportunity to think with patients outside the box in terms of both the research questions and study designs.

For a condition that is still emerging, with poorly defined characteristics and underlying mechanisms, involving people with lived experiences can help to design studies that truly capture the reality of the condition. In Long COVID, the classical epidemiological approach of using health-care-based studies does not work well on its own, because there is huge variation and significant deficiency in diagnosis, clinical coding and management strategies¹⁰. A health-care-based study sample in this case is not a representative sample, because — in the absence of prescriptive clinical guidelines — simply being recognized and labelled with the condition may involve substantial health literacy and resources on the part of the patient. This may result in widening inequalities with regards to access to health care and representation in health-care-based samples of patients with Long COVID. Community-based studies can fill this gap by recruiting a wider range of people with lived experience. We need the input of those who are struggling to access traditional health-care services to help us design more inclusive studies.

Truly listening to patients is not a ‘tick box’ exercise. It means having more than one patient representative within the research team and thinking about how to take their input into account even if it potentially leads to added complexity such as a significant change of research plan. Within people with lived experience of Long COVID, diverse intersectional voices are needed. Also, in any research about children and young people, listening to people from this age group, also with a diverse intersectional lens of gender, ethnicity, disability and socioeconomic status, is crucial.

The way in which we label conditions that we do not fully understand yet is important. That may mean using different definitions for research, surveillance and clinical practice. The clinical case definitions need to be the most inclusive because patients’ health care, social care, employment, financial benefits or penalties, how they are perceived in society and how they perceive themselves depend on these definitions. Although research case definitions may strive to be more specific, they often inform clinical case definitions. Thus, research definitions should be grounded in the everyday reality of those living with the conditions being defined.

Going back to my previous example⁵, the researchers have in effect applied their own beliefs to a case definition of ‘true’ COVID-19, and imply that, in the majority of cases, not having antibodies to SARS-CoV-2 spike protein equals a false belief in having had COVID-19. We all have beliefs and assumptions, researchers or not. This is part of being human. However, when we are in a position of power such that our beliefs can influence other people’s lives, health care and living conditions, we must make room for those concerned to challenge them. One of the central roles of co-producing research with patients is to challenge our beliefs and assumptions that project onto the research.

In summary, people with lived experience of chronic conditions from diverse backgrounds and characteristics must have a central role in conceptualizing and phrasing the research question, shaping the study design, and co-producing innovative ways to capture real-life experiences, as well as defining and labelling their conditions in a way that serves their wellbeing. Scientific research sets the medical and care agenda for patients with chronic illnesses. It also influences the wider social and economic agenda for people living with these conditions. The more socially and economically disadvantaged people are, the greater the potential influence on their lives. This is a huge responsibility that researchers are only able to fulfil with sharp awareness of the power structures involved in conducting research, with humility and with an openness to see things from different perspectives.

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Competing interests

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