

TITLE: Patient-Led Research for COVID-19: Embedding Patients in the Long COVID Narrative

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SUMMARY

This article discusses the value of patient-led research, the formation of Patient-Led Research for COVID-19, and how to improve Long COVID care and research.

ABSTRACT

A large subset of COVID-19 patients are experiencing symptoms well beyond the claimed two-week recovery period for mild cases. This long-term sequelae has come to be known as Long COVID. Originating out of a dedicated online support group, a team of patients formed Patient-Led Research for COVID-19 and conducted the first research on Long COVID experience and symptoms. This article discusses the history and value of patient-centric and patient-led research; the formation of Patient-Led Research for COVID-19 as well as key findings to date; and calls for the following: the acknowledgement of Long COVID as an illness, an accurate estimate of the prevalence of Long COVID, publically-available basic symptom management, care and research to not be limited to those with positive PCR and antibody tests, and aggressive research and investigation into the pathophysiology of symptoms.

INTRODUCTION

During the first few months of the COVID-19 pandemic, a false narrative was presented to the public: the vast majority of infected people would recover within two weeks [19]. However, a large subset of COVID-19 patients, many of whom are young and previously healthy, continued to experience symptoms well past two weeks [3–6,9,10,26]. These patients have what is now referred to as Long COVID [22], which we define as being symptomatic from COVID-19 for over three weeks, with many experiencing debilitating symptoms for months.

On April 13th 2020, Fiona Lowenstein published an op-ed in the *New York Times* about Long COVID recoveries, which brought thousands of people to the support group she had created for patients experiencing these prolonged symptoms, called the Body Politic COVID-19 Support Group [17]. Each of the authors of this article joined, looking for support and for answers. Out of the support group, a research team was born with the initial goal to gather and document people's various experiences with this illness. By being patient-driven and patient-centric, the Patient-Led Research for COVID-19 team has been able to better understand patient concerns, document what patients are experiencing, and create surveys that reflect these concerns and experiences.

This article discusses the importance of patient-led and patient-involved research, the formation of the patient-led research group, and the gaps that still exist in the provision of care in patients with Long COVID.

PATIENT-LED RESEARCH

In conventional medical research, doctors and researchers decide what outcomes matter and what hypotheses should be tested. When patients with the illness being studied are not included in these decisions, there is often a discrepancy between the research that patients want and the research that actually happens [12,13,23]. Several medical establishments and leading publishers advocate for research that involves patients in decision-making. For example, the *British Medical Journal* has set up a partnership with patients and the public to encourage this type of work [28], and PCORI, the Patient-Centered Outcomes Research Institute, promotes research guided by patients in the U.S. [21].

A step beyond this work is patient-led research, in which patients are not only involved, but actually lead the research. While some critics say that patients are not educated enough to do their own research [1], there is no degree that can give you the lived experience of an illness or the collective knowledge of an online community [27]. People experiencing the illness are best able to identify the questions to ask and issues to investigate that matter to them, and also to design effective solutions based on their intimate familiarity of the illness. Too often conventional research tests hypotheses that do not address the urgent needs of patients, and research that does often takes too long for many patients to benefit. Patient-led research, on the other hand, attempts to answer the questions that will most help patients while being able to release results quickly and publicly. After all, the point of research is to provide access to trusted information, and to contribute to our shared knowledge and understanding of an illness while finding treatments that improve patients' quality of life. Patient-led research does this effectively and efficiently.

There are countless examples of patients who have led their own research to date, many stemming from online health communities [15]. Patients with ALS, Parkinson's disease, and diabetes have paved the way in conducting research for and with their communities [32]. Their findings have made a large impact on the communities they are part of, and highlight the critical importance of patient-led research.

PATIENT-LED RESEARCH FOR COVID-19

Creation of the Research Group

The Body Politic COVID-19 Support Group [25] initially started on WhatsApp but quickly moved to Slack as the number of members increased beyond WhatsApp's capacity. People were eager to share their story and see if their symptoms aligned with others', particularly because there was little public health, medical, or media attention on this extended version of the illness. This type of support group is not a new phenomenon. When doctors are at a loss for answers or provide diagnoses of anxiety without also providing treatment, patients of unresearched or ignored illnesses often seek out others who are experiencing their same symptoms - for validation, for advice, for treatment [2, 11, 14, 16, 20]. The Body Politic support group's reach expanded particularly quickly because the nature of COVID led to a large number of people having similar experiences at the same time.

The Slack group is organized into dedicated channels for different topics and symptoms. There are over 60 channels as of November 2020, with topics ranging from "neurological" to "victories" to "resources and tips." Despite this organization, there was an overflow of information that needed to be aggregated in order to be useful and properly compare symptoms, pre-existing health conditions, and treatments. The members of the research team recognized that recording these experiences could be a powerful tool to highlight that this extended illness is not just happening to a select few COVID-19 cases, but is happening to many across the world. We recognized that the number of people with Long COVID (dubbed "long haulers") was only going to increase as the number of COVID-19 cases increased, and yet no one except patients seemed to be trying to figure out what was going on at the time.

Our research team came together in the Slack group shortly after the support group was formed, seeking answers to the questions we were asking of each other and of our doctors. Gina Assaf created the research group and launched the first survey on April 21, 2020 with the help of several other members. Shortly thereafter the other core team members - Hannah Davis, Hannah Wei, Athena Akrami, and Lisa McCorkell - joined efforts to help analyze results and write the first report. All team members had relevant skills directly applicable to the work, and our diverse backgrounds blended together to create a multidisciplinary team that is female-led and spans three countries.

Our first survey was open from April 21 to May 2, 2020. We had a total of 640 respondents. We worked quickly to analyze the data and publish our first report because we understood how critical it was for this information to be public - not only did we want to work quickly to honor our respondents' time and energy, but we also had a personal stake in it. Our first report was published on May 11th [29] - only nine days after we began analyzing the data despite us all working through debilitating symptoms.

As we analyzed the survey, we paid attention to the questions the support group members had about their own data and the questions we were curious about ourselves. We recognized that a large portion of our respondents - 47.8% - were unable to be tested, and 27.5% tested negative despite exhibiting a similar symptom course. Instead of removing this valuable data from our survey, we utilized it. We found that the main difference between people who tested positive and people who tested negative was not necessarily the symptoms they experienced, but how early in their illness they were able to be tested (day 10 of being symptomatic for those who tested positive vs. day 16 for those who tested negative). We found that symptoms fluctuated and were not just respiratory, but spanned many bodily systems including neurological, cardiovascular, and gastrointestinal. We found that neurological symptoms were commonly reported by our respondents, despite being underreported in other COVID research. Importantly, the symptoms were not limited to fever, shortness of breath, and cough, indicating that restricting testing to only those experiencing all three of these symptoms missed out on a subset of COVID-19 patients.

Reception

Our report was the first research on Long COVID, released at a time when there was little discussion about long haulers and what recovery of COVID-19 could actually look like. We posted our report on the Body Politic Support Group, and we received messages from support group members who found validation in seeing their experience reflected in a study of hundreds of other people. Many used the study to prove to their doctors that their symptoms are, in fact, real.

We paired our research with advocacy to better inform patients, doctors, medical organizations, and the general press, and our research was discussed in the first mainstream piece on Long COVID [34]. Our research connected us with myalgic encephalomyelitis (ME) advocacy groups who have been experiencing similar symptoms but have been largely ignored by the research and medical community for decades. We presented our research to the WHO [30], CDC, and NIH [7,30], and were cited in the UK Parliament's first mention of Long COVID [7,30,31]. We have been cited in major medical journals such as the *British Medical Journal*, *JAMA*, and *Fatigue*; in publications such as *The Atlantic*, *MIT Tech Review*, and *CNN*; and in the first guidelines put out for treatment of people with Long COVID [23].

Additional Research

While we knew our first report captured important information, respondents who had not yet recovered had only been experiencing symptoms for an average of 40 days. As the months went by, our symptoms continued well beyond 40 days. Each of us experienced relapses and new symptoms, and those experiences were reflected in the support group. New information was being shared by members - antibody results, MRI results, diagnoses. More and more people were joining our ranks as long haulers, and yet there were still few answers from the medical and research community on the science behind Long COVID and how best to treat the illness. While the UK, Italy, and several other countries have started to follow up with

hospitalized COVID-19 patients after they are released from hospital, little is known about the clinical course and return to baseline health for patients with outpatient illness and those with milder symptoms at the beginning that did not result in hospitalisation.

Our second survey [8] focuses on issues that many long haulers were discussing and sharing: antibody testing, the constellation of complex symptoms specifically neurological and cognitive, mental health and coping, diagnostics, and treatments. We made efforts to increase the diversity of our respondents by translating the survey into nine languages and reaching out to communities hit hardest by COVID-19.

Our surveys are a reflection of our own experience and the experiences we read about in our support group. We thoughtfully chose each question, knowing that each one is critical. Our second survey took approximately an hour for respondents to complete - an amount of time that we know many patients with Long COVID would have difficulty completing in one sitting due to extreme fatigue. To account for this, we encouraged breaks at several points throughout the survey. We also email patients their responses if they request it so they can keep this valuable information in their records to share with their doctors. Our partnerships with Long COVID community leaders in other countries, support groups, and BIPOC patient advocates helped to disseminate our survey, and we responded to feedback from participants regarding inclusive and accessible questions.

In our future work, we hope to partner with BIPOC community leaders in performing their own research, send follow-up surveys to track patients over time, and continue to advocate for patient-led research.

GAPS IN CARE AND RESEARCH

Despite our progress, many gaps remain in research and patients' provision of care. Long COVID patients still need the following:

1. **Acknowledgement that this is an illness:** While the media and many public health professionals have acknowledged the existence of Long COVID, we are still experiencing gaslighting from doctors and loved ones. We hear of (and personally experience) countless reports of doctors claiming patients' symptoms are caused by anxiety or are all in their head despite research documenting the existence of post-viral illnesses [18]. Many patients in our support group are being turned down for disability benefits and are not being believed by employers. Long COVID can be a debilitating illness, with many patients unable to work. Supportive policies must be in place to ensure that these patients are able to care for themselves and their families, and the recognition of Long COVID is the first step.
2. **An accurate estimate of the prevalence of Long COVID:** While there have been attempts at estimating the prevalence of Long COVID [4,6,26], most are flawed; one of the major estimates assumes those with four or less symptoms are recovered, even if

those symptoms are debilitating fatigue or cognitive issues [24]. Knowing how many patients Long COVID is affecting is critical for determining healthcare resources and estimating future impacts to employment. Moreover, the wider appreciation of the Long COVID prevalence and its implications would likely influence the public behavior around compliance to measures against the transmission of the virus. One way to estimate Long COVID more accurately is to have contact tracers follow up with patients for several months after their isolation period ends to ask if they are still experiencing symptoms. However, it must be noted that this would miss out on the portion of the population that is not tested or does not respond to contact tracers.

3. **Basic symptom management:** The medical community must provide publicly-available guidelines for basic symptom management, similar to what is provided in the *British Medical Journal* [12,23], by seeking input from Long COVID patients and patients of other post-viral illnesses. All symptoms that Long COVID patients experience should be covered, particularly neurological symptoms which have so far largely been unaddressed. These guidelines must be accessible and in all languages. This will be especially useful for patients who may not have access to healthcare.
4. **Provision of care and research, being inclusive of all who show symptoms:** There are only a handful of post-COVID clinics worldwide, and only a few known studies being conducted on Long COVID. Many clinics and research studies require a positive PCR or antibody test to receive care and participate; this prevents a large proportion of patients with Long COVID from receiving the care they need and being represented in research. Not everyone has access to testing, not everyone wants to be tested, and testing is not 100% accurate. Medical professionals and researchers must consider these political, social, and physiological aspects of COVID in order to prevent the unintentional construction of barriers.
5. **Aggressive research and investigation into the pathophysiology of symptoms:** Since the beginning of the COVID-19 pandemic, hundreds of clinical trials have started to investigate how SARS-COV-2 impacts the body. However, most of the focus has been on the acute illness. The pathophysiology of Long COVID, which may differ from that in the acute phase of COVID-19, warrants detailed investigation. The first step requires acknowledgement of the complexity and diversity of symptoms experienced by Long COVID patients. Given the multi-organ impact of COVID-19 [33], it is not clear whether the long term sequelae will develop as unique complications or divergent pathophysiologies. Patients' insights about their phenotypic heterogeneity of symptoms should be incorporated into studies of pathogenesis and treatments.

Nearly a year into the COVID-19 pandemic, there is still more unknown than known. It is clear, however, that as patients, we are intimately aware of what we are experiencing. As the number of long haulers increases, it is critical for doctors, researchers, public health professionals, and policymakers to include patients in the conversation and support patient-led research. There is too much at stake not to.

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