

Long COVID: Emerging Research and Gaps in Canada

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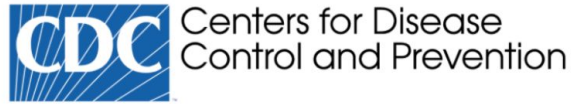
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I. Patient-Led Research - Team



- Long COVID patients, **still sick**
 - Formed April 2020 in Body Politic Support Group's data channel
- **30+** patient-researchers across 3 continents
 - Academic and industry research experience
- **Interdisciplinary** background
 - Medicine, participatory design, neuroscience, public policy, cognitive science, research engineering, data science & machine learning, biostatistics, virology & immunology, psychiatry, neurology, pediatrics, social epidemiology
- **IRB** from University College London

I. Patient-Led Research - Contributions



Post-COVID Conditions: *Information for Healthcare Providers*

The CDC includes **post-exertional malaise** in a list of Post-COVID symptoms, and acknowledges health effects persisting after **mild or asymptomatic SARS-CoV-2 infection**.



In the wake of the pandemic *Preparing for Long COVID*

A detailed policy brief outlining existing research and *three new ICD-10 codes* for use with Long COVID (page 19), including a link to **probable COVID-19 infection** and **multisystem inflammatory syndrome**.

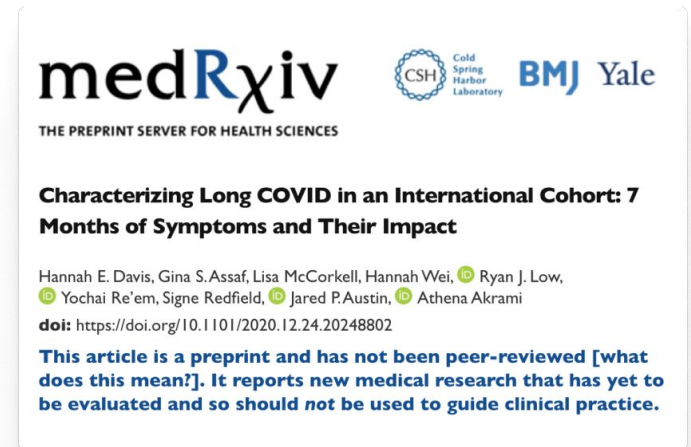


Living with COVID-19 *Second review*

A dynamic review of the evidence around Long COVID, with recommendation that **"people living with Long Covid (who are experts by experience) should be equal partners in setting the research agenda"**.

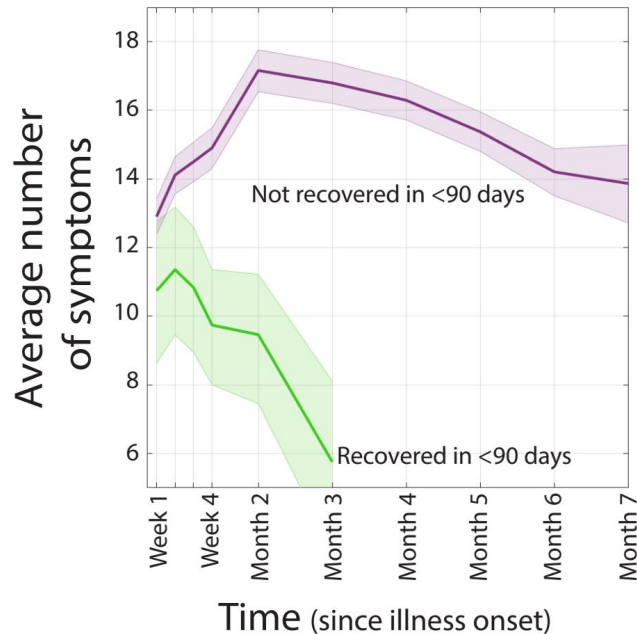
I. Patient-Led Research - Research Timeline

- **May 2020:** “*What Does COVID-19 Recovery Actually Look Like?*” | [Report available on our website](#)
- **December 2020:** “Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact” | [Preprint on Medrxiv](#)
 - Tracked 205 symptoms in total over 7 months
 - Survey questions are open sourced, 9 translations available on our website and Figshare
- **April 2021:** [Vaccine Experience Study](#)
 - Ongoing survey study
 - Current and future collaboration with immunology labs



I. Patient-Led Research - Recovery

c. Average number of symptoms over time



3,762 patients

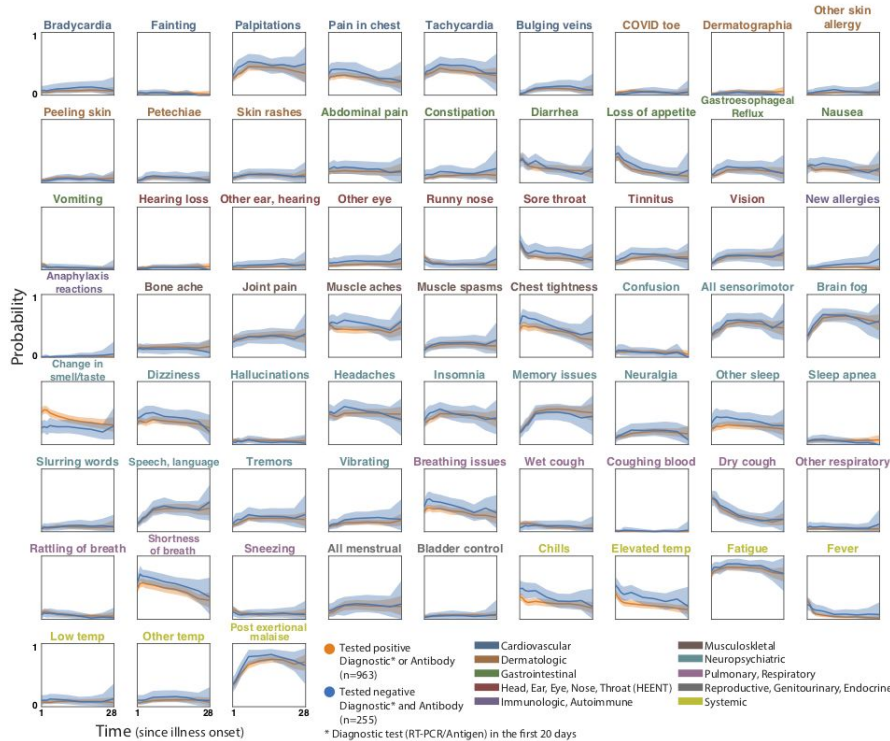
92% not hospitalized

18% health care workers

Symptoms lasting **> 28 days** after initial onset

- **65.2%** reported **experiencing symptoms over 6 months**
- **14 symptoms on average** for those reported *not recovered* by their 7th month of illness
- **21%** reported **severe** or **very severe** after month 6

I. Patient-Led Research - Testing

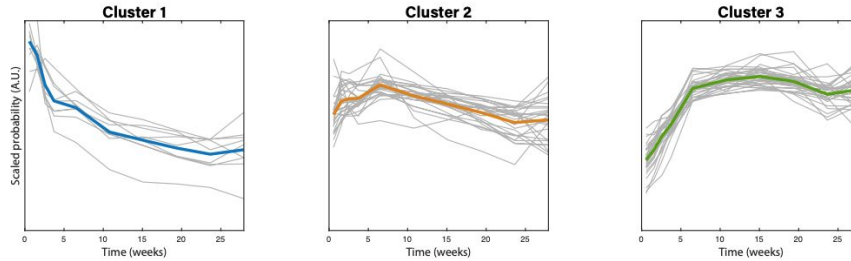


Symptom time courses for respondents who were **confirmed COVID positive** vs those **without a positive confirmation**

- **205 symptoms** sorted into affected organ systems
- Blue: 95% confidence band
- **Statistically insignificant** symptom timecourses between COVID positive and everyone else

If a patient experienced loss of smell and taste, **they were more likely to test early.**

I. Patient-Led Research - Symptom Timecourse



Cardiovascular	25. Fainting 19. Pain/burning in chest 33. Tachycardia	49. Bradycardia 38. Palpitations 64. Visibly inflamed/bulging veins
Dermatologic	30. COVID toe	53. Dermatographia 55. Other Skin and Allergy 42. Peeling skin 54. Petechiae 44. Skin rashes
Gastrointestinal	9. Diarrhea 2. Loss of Appetite 4. Vomiting	45. Constipation 43. Gastroesophageal reflux
HEENT (Head, ears, eyes, nose, throat)	7. Runny nose 6. Sore Throat	48. Hearing loss 51. Other ear/hearing issues 39. Other eye symptoms 58. Tinnitus 59. Vision symptoms
Immunologic/ Autoimmune		65. New allergies 63. New anaphylaxis reaction
Musculoskeletal	32. Bone ache or burning 21. Muscle aches 15. Tightness of Chest	37. Joint pain 40. Muscle spasms
Neuropsychiatric	20. Acute (sudden) confusion/disorientation 12. Changes to sense of smell and taste 22. Dizziness, unsteadiness or balance issues 31. Hallucinations 29. Headaches and related symptoms 35. Insomnia	41. All sensorimotor symptoms 47. Brain fog 61. Memory issues 50. Neuralgia (nerve pain) 62. Speech/language issues 52. Tremors

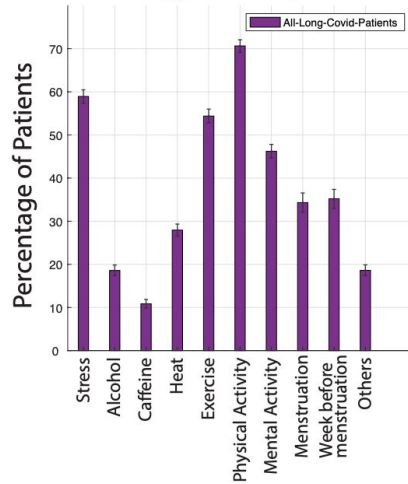
Symptom clusters based on **temporal similarities**

- **Cluster 1:** Acute COVID symptoms
- **Cluster 2:** Peak after 6 weeks. Tapers off slowly over time
- **Cluster 3:** Not prevalent during acute COVID. Persistent

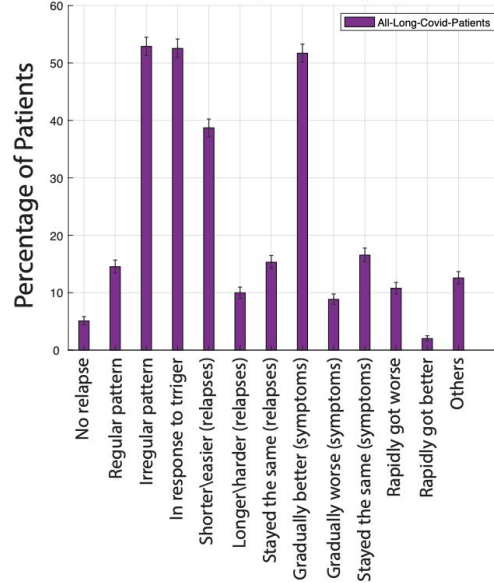
Long COVID symptoms have **variable onsets** and **heterogeneity in presentation** across multiple organ systems

I. Patient-Led Research - PEM & Relapse

d. Triggers of relapses



e. Experiences with relapses and symptom course

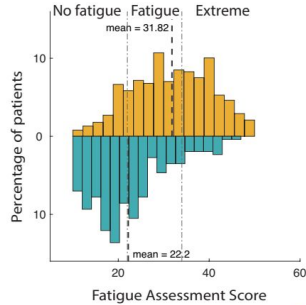


Recovery is **NOT** linear!

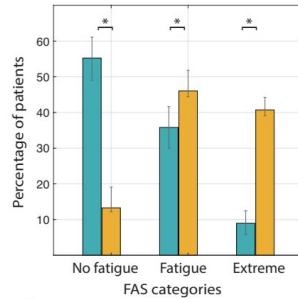
- 85.9% reported experiencing **symptom relapses**
- 52.8% reported **irregular** relapses
- Triggered by physical and/or cognitive **exertion**
- **72.2%** reported experiencing post-exertional malaise after **6 months**

I. Patient-Led Research - Quality of life

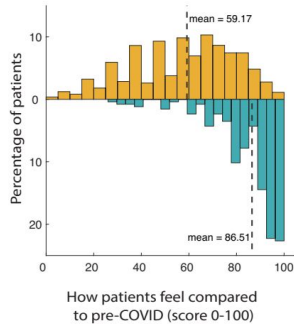
a. Fatigue Assessment Scale (FAS)



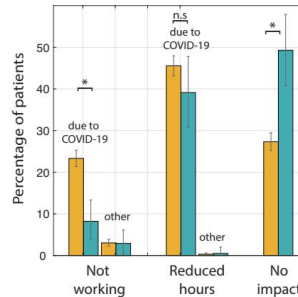
b. FAS categories (No fatigue, Fatigue & Extreme)



c. Return to pre-COVID baseline



d. LONG COVID impact on work



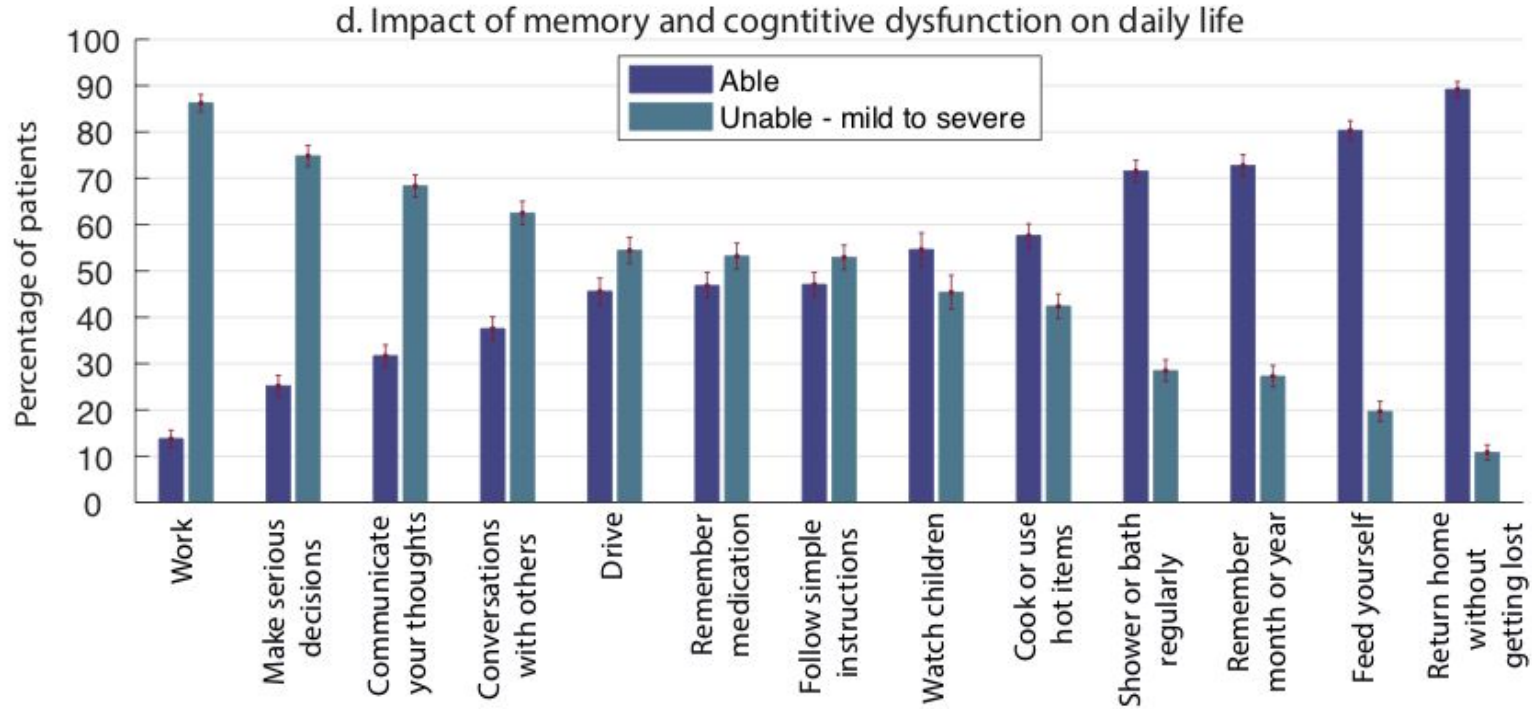
Long COVID is a **debilitating, relapse-remitting condition** with socio-economic consequences

- **45.2%** reduced workload after illness
- **22.3%** no longer working due COVID-19

Focus on:

1. Biological/immunological underpinnings of relapses and PEM
2. Tracking patients over time. Overlaying quality of life measures
3. Build on top of research on post-viral illnesses

I. Patient-Led Research - Cognitive Dysfunction





II: Long COVID Research Priorities and Emerging Fields



National
COVID
Cohort
Collaborative



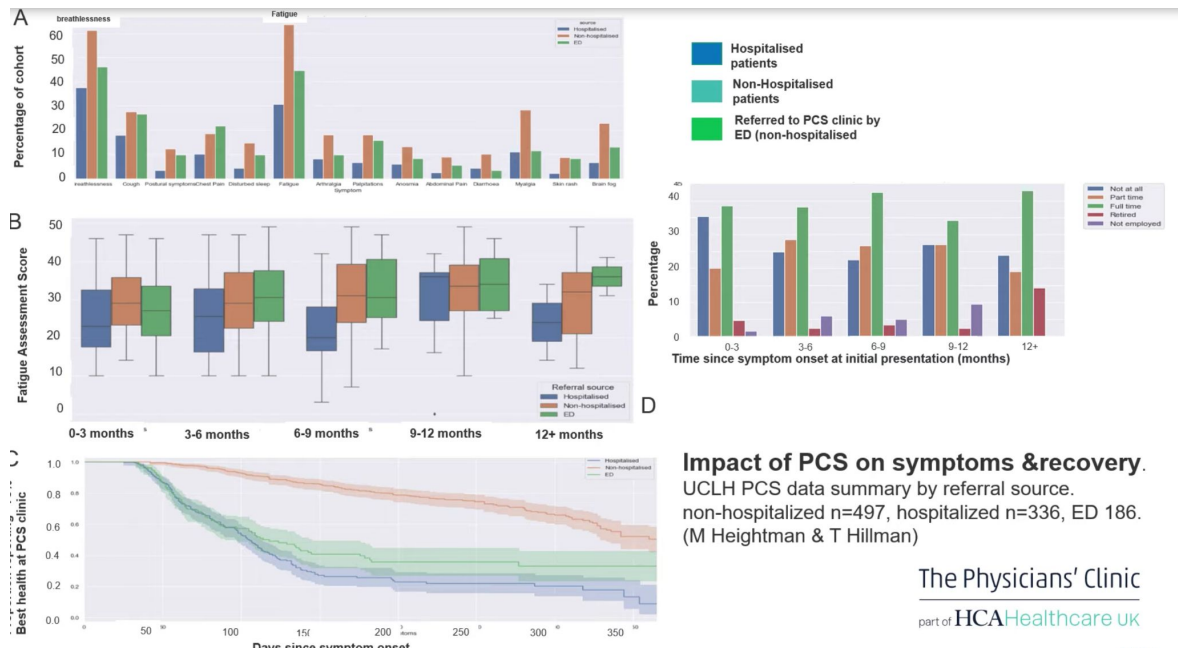
Yale University
School of Medicine



RUTGERS
New Jersey Medical School

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II. Research Priorities - Non-Hospitalized Cohort



Outpatient population from Long COVID clinic in UCLH

- Non-hospitalized patients experience **greater fatigue, took longer to recover**
- Predominantly female, 20-60 years old
- Previously fit, **no pre-existing conditions**

Impact of PCS on symptoms & recovery.
UCLH PCS data summary by referral source.
non-hospitalized n=497, hospitalized n=336, ED 186.
(M Heightman & T Hillman)

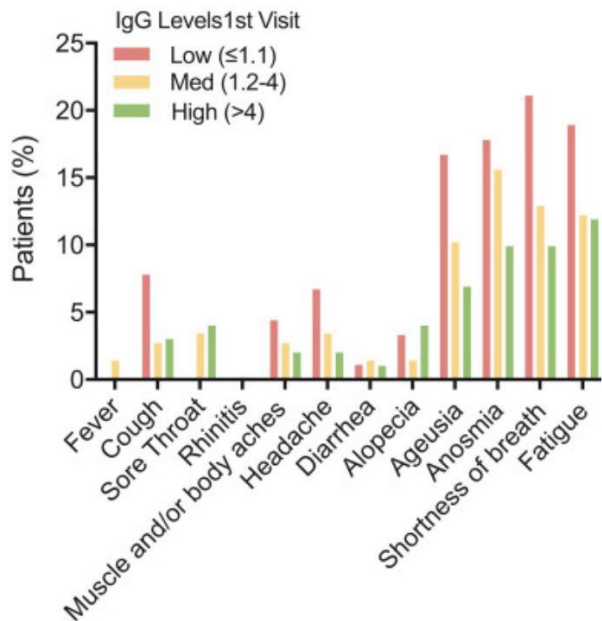
The Physicians' Clinic
part of HCA Healthcare UK

Post-COVID assessment in a specialist clinical service: a 12-month, single-centre analysis of symptoms and healthcare needs in 1325 individuals

II. Research Priorities - Post-Viral Experts

- **Brain inflammation, brainstem inflammation, appropriate neuroimaging techniques** (Dr. Jarred Younger, Dr. Michael VanElzakker, Dr. David System, Harvard)
- **Neuroimmunology** (Dr. Avindra Nath, NIH)
- **Metabolic profiling** (Dr. Oystein Fluge, Dr. Ron Davis, Dr. Jarred Younger)
- **Impaired endothelial function in POTS** (Dr. Alfred Gamboa, Vanderbilt)
- **Mitochondrial fragmentation, antiviral & metabolic phenotypes in ME** (Dr. Bhupesh Prustry)
- **Hypoperfusion/cerebral blood flow** (Dr. Peter Rowe, Johns Hopkins)
- **Two-day exercise testing & other PEM research** (Workwell foundation, Dr. Leonard Jason)
- **Nanoneedle diagnostic test** (Dr. Ron Davis, Stanford)
- **Overlaps with connective tissue disorders, including Ehlers-Danlos Syndrome** (PolyBio Research, Dr. Peter Rowe, Johns Hopkins, Dr. Bjorn Bragee, Karolinska Institutet)
- **Circulating microRNAs** (Dr. Moreau)
- **Autoimmunity, autoantibodies** (Dr. Franziska Sotzny)
- **Viral/microbial persistence** (Dr. Amy Proal, Dr. Bhupesh Prusty)
- **Intracranial hypertension, hypermobility, craniocervical obstructions** (Karolinska Institutet, Dr. Bjorn Bragee, Dr. Nicolas Higgins)
- **Altered T cells and B cells, Metabolomics and Proteomics** (Dr. Maureen Hanson, Cornell University)
- **Elevated blood lactate** (Dr. Alaa Ghali)
- **Reactivations, difference in early vs late post-viral years** (Dr. Nancy Klimas)

II. Research Priorities - Immunological Profiling

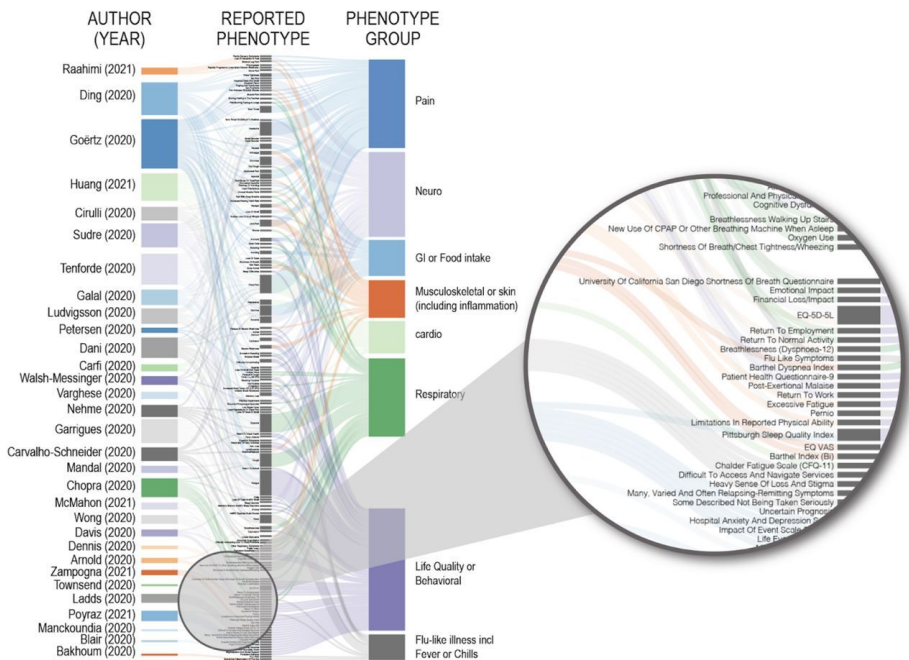


Augustin M, et al found lower baseline serum IgG titers **associated with persisting symptoms** in non-hospitalized patients

- What are the effects of vaccination on Long COVID symptoms?
- Are those with Long COVID producing autoantibodies?
- How are B cells / T cells altered and could these be a more accurate diagnostic for Long COVID?

[Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study](#)

II. Research Priorities - Deep Phenotyping



Identify potential Long COVID patients and disease patterns

- Combine biomarkers, imaging data, EHR data, claims data, patient-reported data to develop Long COVID phenotypes
- Use models to detect early at clinical sites and predict patient outcomes
- Enable more precise care management at scale

[Challenges in defining Long COVID: Striking differences across literature, Electronic Health Records, and patient-reported information](#)

III: Patient Partnership & Collaboration Models



**LONG COVID
ALLIANCE**

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III. Patient Partnership - PLRC Model

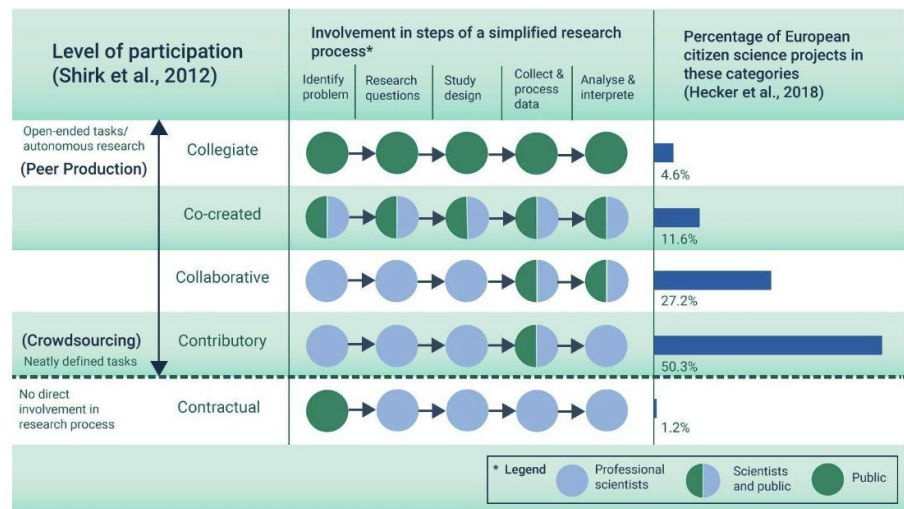


Figure 1. Involvement of the public in the steps of the research process according to Shirk et al. (2012)'s typology of public participation in science

[Kloppenborg, Katharina, et al. "Peer Production Practices: Design Strategies in Online Citizen Science Platforms." SocArXiv, 23 May 2021.](#)

At PLRC patients are involved at every step of the research process

- Patient-researchers *set research agendas* based on **emerging priorities that directly serve patients**
- Patient community *raise research questions* based on **lived experiences**
- Patient-researchers and collaborators *conduct analysis and publish reports*

III. Patient Partnership - Best Practices



OPEN

Patient-Led Research Collaborative: embedding patients in the Long COVID narrative

Lisa McCorkell¹, Gina S. Assaf¹, Hannah E. Davis¹, Hannah Wei¹, Athena Akram^{1,2,3,4}

Abstract

A large subset of patients with coronavirus disease 2019 (COVID-19) are experiencing symptoms well beyond the claimed 2-week recovery period for mild cases. These long-term sequelae have come to be known as Long COVID. Originating out of a dedicated online support group, a team of patients formed the Patient-Led Research Collaborative 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 Collaborative 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, publicly available basic symptom management, care, and research to not be limited to those with positive polymerase chain reaction and antibody tests, and aggressive research and investigation into the pathophysiology of symptoms.

Keywords: Long COVID, COVID-19, Patient-led research, Patient-centric, Long haulers, Post-acute sequelae of SARS-CoV-2 infection, Post COVID-19 syndrome, Patient-centered

1. Introduction

During the first few months of the coronavirus disease 2019 (COVID-19) pandemic, a false narrative was presented to the public: most infected people would recover within 2 weeks.¹⁻⁴ However, a large subset of patients with COVID-19, many of them young and previously healthy, continued to experience symptoms well past 2 weeks.^{4,7,11,12,24} These patients have what is now referred to as Long COVID,²⁵ which we define as being symptomatic from COVID-19 for more than 28 days, with many experiencing debilitating symptoms for months.¹⁰

On April 13, 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 her organization created for patients experiencing these prolonged symptoms, called the Body Politic COVID-19 Support Group.²⁶ 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 Collaborative (PLRC) 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 PLRC; and the gaps that still exist in the provision of care in patients with Long COVID.

2. 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.^{16-18,27} 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 the Patient-Centered Outcomes Research Institute (PCORI) promotes research guided by patients in the United States.²⁷

A step beyond this work is patient-led research, in which patients are not only involved, but actually lead the research. Although some critics say that patients may not have the education needed 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.²⁹ 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

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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PMID 342014613

https://doi.org/10.1097/PR9.0000000000000013

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Best practices when working with Long COVID patients:

- Understand that many of us, like ME/CFS patients, are **traumatised by medical gaslighting and neglect**
- Understand the debilitating consequences of Long COVID on energy levels, attention, ability to work and provide for family. **Limit long meetings, pay patients for their time**
- A lot of us have or had fulfilling education and/or careers prior to illness. **Respect our areas of expertise and lived experiences**

III. Patient Partnership - Work with us, Canada!



“Your team really helped us to capture the broader experience and to adapt questions to the unpredictable nature of Long Covid.

We really wouldn't feel confident in our questions without it, and these changes and others will hopefully give people a study experience that feels like they're really part of the study and that their condition is understood and paid attention to.”

-- Collaborator at Yale School of Medicine

Long COVID patients **want a seat at the table** for research concerning our health outcomes and treatment.

Get in touch with PLRC or other Long COVID patient groups with presence in Canada for collaboration:

- **PLRC:** patientledresearch.com
- **Long COVID Canada:** longcovidcanada.ca
- **Body Politic:** wearebodypolitic.com
- **Long COVID Alliance:** longcovidalliance.org
- **Long COVID Kids:** longcovidkids.org



**PATIENT-LED
RESEARCH
COLLABORATIVE**

Thank you!

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