



June 26, 2023

Lauren K. Roth
Associate Commissioner for Policy
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Submitted electronically through regulations.gov.

Re: Patient-Focused Drug Development for Long COVID; Public Meeting; Request for Comments; FDA-2023-N-0363-0001

Lauren Roth,

Introduction

Thank you for the opportunity to comment on the U.S. Food and Drug Administration's (FDA) efforts to facilitate patient-focused drug development for long COVID. I am writing to you on behalf of Pandemic Patients, which is a 501(c)(3) non-profit patient advocacy organization that works to relieve the harm caused by COVID-19 and Post-COVID Conditions. In partnership with the COVID-19 Health and Safety Taskforce (CHeST),¹ Pandemic Patients developed a survey to solicit information from long COVID patients on the impact of long COVID on their daily life, their views on treatment approaches, and decision factors they consider when selecting a treatment.² We collected responses to this survey through June 21, 2023, and received 270 responses. We have attached a spreadsheet to this comment containing the data we collected.³ We respectfully submit this data to the FDA to elevate the perspectives and experiences of long COVID patients as the agency prioritizes the advancement of patient-focused drug development for this population.

Data Collection

The survey instrument was distributed to respondents through the Pandemic Patients website,⁴ social media channels, and targeted email between February 24 and June 21, 2023. The survey exclusively collected responses digitally. The survey did not collect location data or any personally identifiable information.

¹ <https://pandemicpatients.org/home/chest/>

² See Attachment A. Patient-Focused Drug Development for Long COVID Survey Instrument.

³ See Attachment B. Patient-Focused Drug Development for Long COVID Survey Responses.

⁴ <https://www.pandemicpatients.org/>

Survey Responses

1. Demographic Information

Survey respondents were primarily middle-aged white women who have completed a bachelor's degree or above. Younger populations and non-white populations were underrepresented among survey respondents. Respondents' use of digital communications tools and social media may have influenced these demographic elements.

a. Gender⁵

Survey respondents were predominantly (78.1%) female. A very small portion of survey respondents (1.9%) did not identify as either Male or Female.

b. Age⁶

Over half (51.9%) of the survey respondents were between the ages of 40-59. No survey respondents were under the age of 18 and a minority of respondents (3.7%) were between the ages of 18 and 29.

c. Ethnicity⁷

Most survey respondents (90.7%) were White / Caucasian. A very small portion of survey respondents were either American Indian, Alaska Native, Native Hawaiian, or Pacific Islander. Respondents were able to select multiple ethnicities to indicate mixed race.

d. Education Level⁸

Over two-thirds of survey respondents (70%) have completed a bachelor's degree. Roughly one-third of survey respondents (30.7%) have completed a master's degree or above. The respondents who selected "Other," (8.5%) described their education level as an associate degree, some college, trade school, or other professional certification.

2. Which symptoms of long COVID have the most significant impact on your life?⁹

Survey respondents were asked to assess the severity of their symptoms by how significantly they impact their life. The responses were assigned a weight according to the severity of each symptom. "I don't have this symptom" is assigned 0 points. "Little or no impact" is assigned 1 point. "Some impact" is assigned 2 points. "Significant impact" is assigned 3 points. "Extreme impact" is assigned 4 points. The total score for each symptom provides context on how much it impacts patients' lives relative to other symptoms. The symptoms that scored the highest include fatigue, exercise intolerance, cognitive symptoms, joint or muscle pain, and sleep disorders. Seizures, persistent fever, and fainting scored the lowest.

a. Are there any symptoms not listed above that have a significant impact on your life? If so, describe each symptom and the impact it has on your life.

Respondents were asked to describe other symptoms that have a significant impact on their life. The most common symptoms cited by survey respondents, in order of significance, include fatigue, nerve

⁵ See Fig. 1. Gender.

⁶ See Fig. 2. Age.

⁷ See Fig. 3. Ethnicity.

⁸ See Fig. 4. Education Level.

⁹ See Fig. 5. Daily Impacts of Symptoms.

pain, post-exertional malaise, cognitive deficits, muscle weakness, gastrointestinal symptoms, temperature dysregulation, anxiety, neuropathy, and hair loss.

Other symptoms were mentioned less frequently, including anaphylaxis, histamine intolerance, joint subluxations and dislocations, bruising, temperature intolerance, gastroparesis, kidney and uterine tumors, blisters on the skin and mouth, blurred vision, loss of voice, loss of hearing, medication intolerance, panic disorder, swelling of the lymph nodes, new and worsening cysts, polyps, and nodules, difficulty managing blood pressure, heightened sensory sensitivity, including smells, light, and sound, hypoxic anemia, thyroid issues, weakened immune system, sleep disorders, low sex drive, mucus in the throat, asthma, panic disorders, hypervigilance, burning sensations, vibrations, muscle spasms, tremors, dehydration, dysphasia, loss of appetite, numbness and tingling, blood clots, recurring infections, and weight gain or loss, among others. Survey respondents also described the worsening of underlying conditions, including fibromyalgia, Ehlers-Danlos Syndrome (EDS), and Mast Cell Activation Syndrome (MCAS), which contribute to lower quality of life.

b. Would you say your long COVID today is well-managed?¹⁰

Most (65.9%) survey respondents indicated that their symptoms are not well managed, with nearly a quarter (21.5%) not knowing whether their symptoms are well managed. Importantly, only 5.2% of respondents felt that their symptoms are well-managed. Respondents who selected “Other” (7.8%) commonly described their symptoms as fluctuating over time, with some symptoms improving and others worsening.

c. How has your long COVID changed from original diagnosis to now?¹¹

Over three-quarters (77.4%) of survey respondents indicated their symptoms have stayed the same or worsened. Less than one-quarter of respondents (22.6%) indicated their symptoms have improved.

d. Are there specific activities that are important to you that you cannot do at all or as fully as you would like because of your Long COVID?

Survey respondents discussed various activities they are unable to do because of their long COVID symptoms. These activities are associated with the following general categories: physical activities (such as exercising, walking, running, lifting, hiking, cycling, swimming, yard work, and yoga), work and volunteer activities (working, volunteering, managing finances, managing medications, managing schedules, studying, hobbies, and problem solving), social activities (socializing, dining at restaurants, attending concerts, writing, reading, communicating, watching movies, maintaining relationships), household activities (completing household chores, preparing food and cooking, gardening, grocery shopping, cleaning, caring for children, and caring for pets), and activities of daily living (getting out of bed, staying upright, bathing and maintaining personal hygiene, and driving).

e. Is there a particular impact of Long COVID (such as need to work a reduced work schedule, inability to complete daily tasks, anxiety, or depression) that worries you? If so, what worries you most?

Survey respondents expressed concern across several domains, including physical discomfort, cognitive decline, decreased productivity, inability to work, loss of income, difficulty maintaining their energy levels, declining mental health, the need for treatment, inability to complete daily tasks, poor sleep,

¹⁰ See Fig. 6. Symptom Management.

¹¹ See Fig. 7. Symptom Change.

reduced social life, increased susceptibility to other infections and other health risks, risk of death and disability, and the fear of unknown future health outcomes.

3. Treatment Approaches

a. Please describe how your treatment regimen has changed over time.

Survey respondents shared information about the treatments, medications, and supplements they have used to manage their symptoms. This includes amphetamines, massages, chiropractic care, acupuncture, physical therapy, movement therapy, breathing therapy, cognitive therapy, relaxation therapy, psychotherapy, transcranial magnetic stimulation, neurofeedback, intravenous ozone infusions, medications to manage heart rate and chest pain, laser treatment, beta blockers, antidepressants, sleep medications, electrolytes, low-dose naltrexone (LDN), immunoglobulin therapy (IVIG), nattokinase, diets and dietary supplements, antihistamines, heartburn medications, antibiotics, anti-fungal medications, anti-nausea medications, anti-inflammatory medications, antivirals, and antioxidants. Some survey respondents have received rehabilitation, home health care, and occupational therapy. Several survey respondents referenced pacing as a helpful strategy.

b. What factors influenced your decision when selecting a course of management for your Long COVID?

When selecting a treatment for long COVID, survey respondents highlighted the following considerations: health care coverage, cost, availability, side effects, time off from work, travel to treatment location, history of treatment efficacy, and the severity of the illness. Survey respondents also valued referrals to specific practitioners and the risk-benefit profile of different treatments. However, many respondents experienced challenges obtaining treatment due to insurance coverage barriers.

c. Assuming there is no complete cure for Long COVID, what specific things would you look for in an ideal treatment for Long COVID?

When discussing ideal treatments for long COVID, survey respondents emphasized their desire to manage specific symptoms, including fatigue, post-exertional malaise (PEM), cognitive impairment, dysautonomia, pain, anxiety, muscle weakness, and shortness of breath. Survey respondents also highlighted the need for greater awareness of long COVID among medical professionals. Beyond treatments, survey respondents identified other supports that would be helpful, including financial support, job protection, and other forms of aid that would help them recover. Ideal treatments would provide pain relief without using narcotics, they would have a high probability of improving quality of life, and they would benefit all people affected by long COVID.

d. Is there a particular symptom of Long COVID that you would prioritize for treatment? Please describe the symptom you would most like to have treatment options for.

The symptoms survey respondents would prioritize for treatment include fatigue, PEM, cognitive impairment, breathing difficulties, cardiovascular symptoms, pain, anxiety, depression, and other mental health symptoms. Other responses include postural orthostatic tachycardia syndrome (POTS), heightened sensory sensitivity, low blood oxygen levels, vision issues, gastrointestinal symptoms, loss of taste and smell, hearing loss, headaches, tinnitus, asthma, muscle weakness, and dizziness.

e. What would you consider a successful treatment outcome for Long COVID?

Survey respondents characterized successful treatment outcomes broadly, with responses associated with the following categories: Full Recovery (including the ability to return to work, hobbies, and daily life), Improvement in Symptoms (through medication or other treatments, to enable patients to be

more active and reduce the severity of symptoms), Research (generating more answers and solutions to long COVID that improve patient outcomes alongside increased public understanding and acceptance of long COVID), and Prevention (including protective measures to prevent people from developing long COVID).

4. Clinical Trials

- a. Have you considered participating or have you participated in a clinical trial for Long COVID? If so, please describe your experience.**

Regarding their participation in clinical trials, many survey respondents have considered participating in clinical trials, with some having already participated. A handful of survey respondents have not yet considered participating in a clinical trial. A significant number of survey respondents indicated they would be willing to participate in a clinical trial if one was available or accessible to them.

- b. What factors (if any) of the clinical trial enabled you to participate?**

Factors that contributed to survey respondents' ability to participate in clinical trials include ease of participation, wanting to help themselves and/or others, the trial location and access to the trial site, personal connections with researchers, and receiving compensation.

- c. What factors (if any) of the clinical trial made it more difficult for you to participate?**

Factors that made it difficult for survey respondents to participate in clinical trials include distance from the trial location, in-person visit requirements, lack of communication, disabling long COVID symptoms or other chronic health conditions, disqualification due to pre-existing conditions, difficulty accessing or understanding trial information, needing a positive COVID-19 test, and financial barriers.

- d. How does the clinical trial intervention (side effects of the medical intervention, how the intervention is administered etc.) weigh into your decision to participate in a clinical trial?**

Many survey respondents expressed concern about potential side effects of a proposed clinical trial intervention, which may dissuade them from participating in a clinical trial. Some survey respondents expressed concern about being exposed to COVID-19 when visiting the clinical trial location. Respondents also consider the risk-benefit profile of the proposed intervention, potential long-term side effects, the possibility of receiving a placebo, and the opinions of patient advocates. Respondents expressed concern about the risks associated with graded exercise therapy (GET) and cognitive behavioral therapy (CBT) specifically.

- e. How does the logistics of the clinical trial (duration of the trial, whether the trial is fully remote or requires clinic visits, the number of in-person clinic visits required, distance from home to clinic site, or whether you might receive a placebo or not) weigh into your decision to participate in a clinical trial?**

Survey respondents identified several logistical factors that influence their decision to participate in a clinical trial. Respondents expressed various preferences or challenges related to travel and in-person visits, and many indicated that it is helpful trials to have virtual and remote options. Specifically, respondents called attention to physical limitations associated with fatigue and other impairments that make it difficult for them to travel long distances or attend multiple in-person appointments. Respondents also emphasized the importance of enforcing masking and other safety protocols at trial sites. Respondents also mentioned the need to consider the cost-benefit profile of the trial and how it might affect their overall health.

f. What outcomes for Long COVID are most important to measure in a trial setting?

Regarding the outcomes for long COVID that are most important to measure in clinical trials, survey respondents expressed a strong desire to return to their normal functioning. Many respondents mentioned specific symptoms including fatigue, pain, cognitive impairment, exercise intolerance, and difficulty breathing that would need to improve for them to regain their previous function. Improvement in quality of life was also emphasized heavily in the responses. Respondents placed high value on treatments that can help them improve their level of functioning, both physically and mentally.

Conclusion

Thank you for providing us with the opportunity to submit additional information on the experiences of long COVID patients. Based on the results of this survey, long COVID patients feel that their symptoms are severe, they inhibit function across many critical areas of their life, their symptoms have rarely improved over time, and their symptoms are not well managed. Despite attempting a variety of treatment approaches, an effective treatment strategy remains elusive. These challenges emphasize the importance of patient-focused drug development for long COVID patients. We hope the information we have provided is helpful.

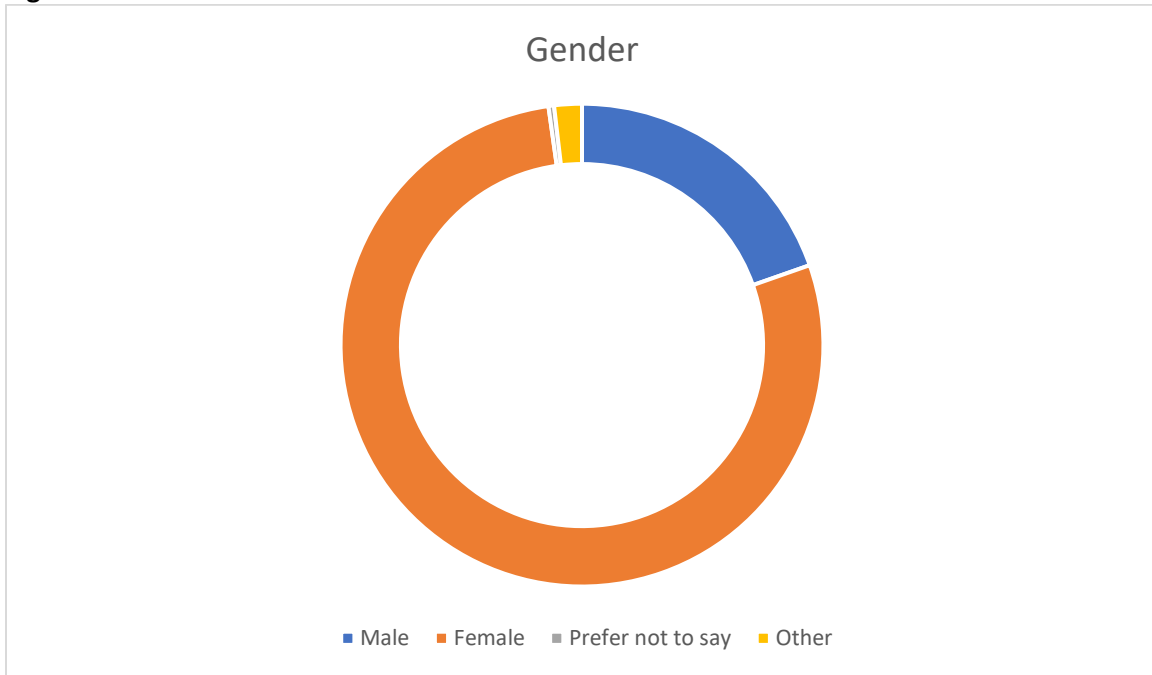
If you have any questions or need additional information, please contact me at a.wylam@pandemicpatients.org.

Sincerely,

A stylized, handwritten signature in black ink, consisting of the letters 'A' and 'W' intertwined.

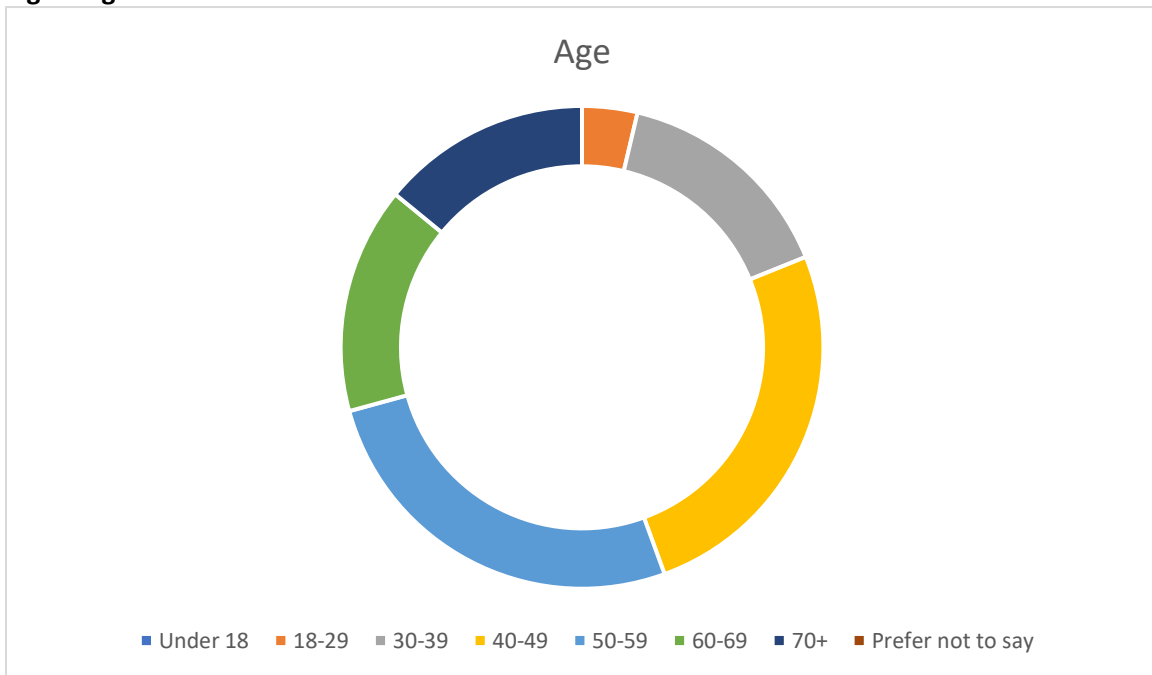
Andrew Wylam
President
Pandemic Patients

Fig. 1. Gender



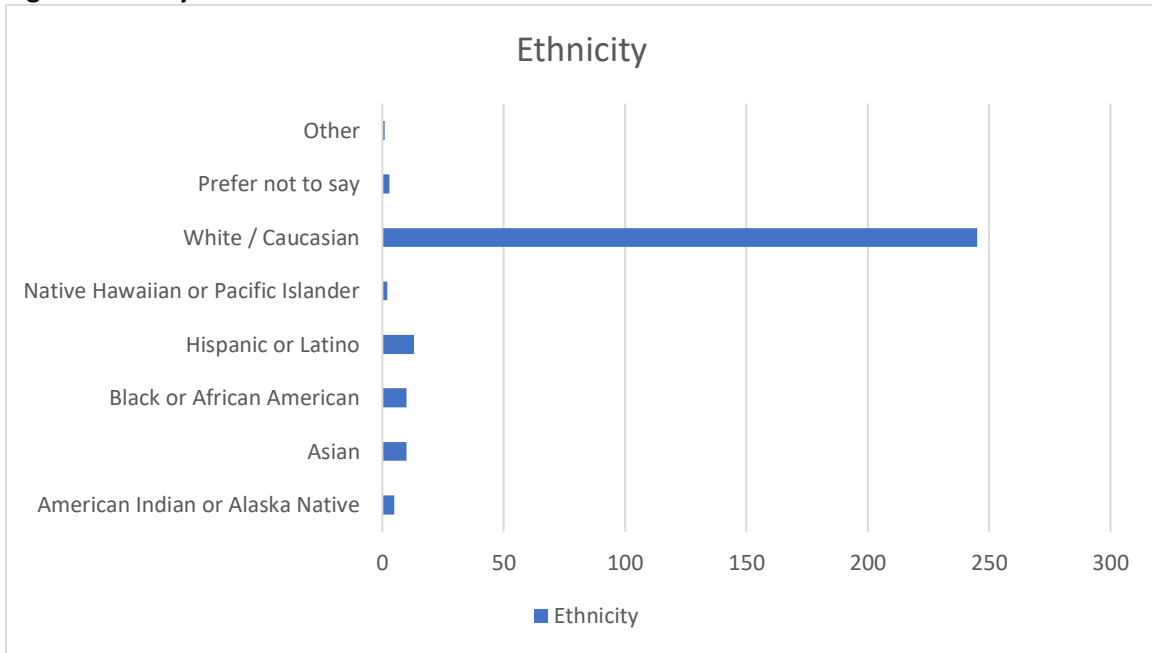
Male	Female	Prefer not to say	Other
53	211	1	5

Fig. 2. Age



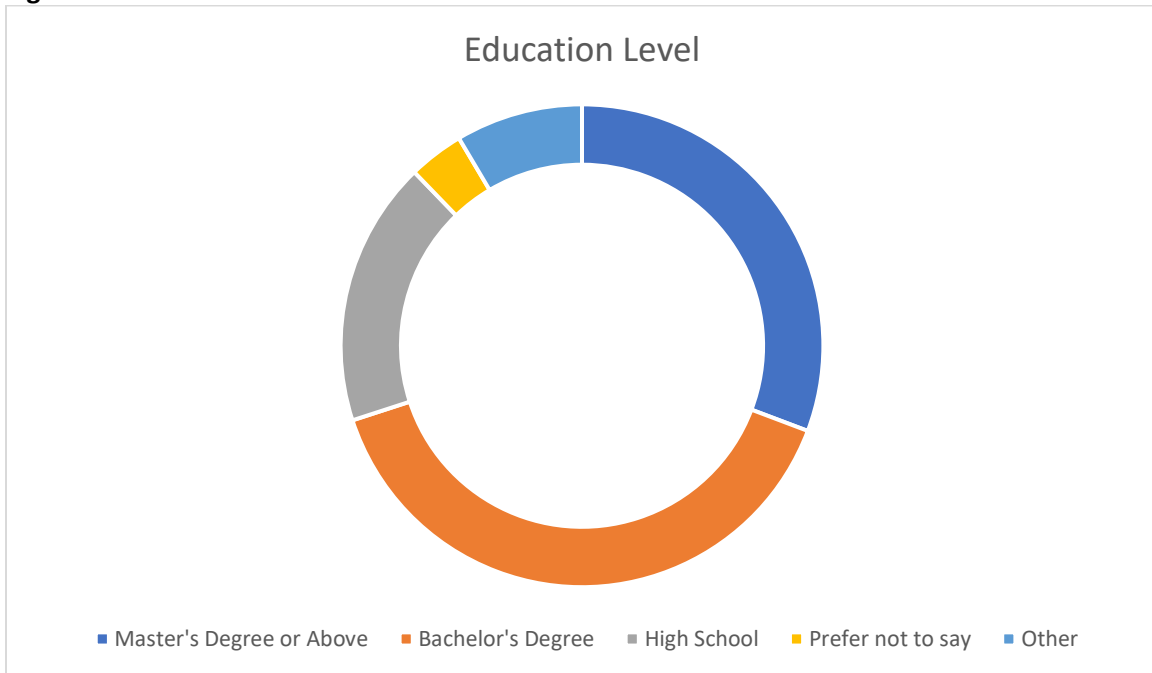
Under 18	18-29	30-39	40-49	50-59	60-69	70+	Prefer not to say
0	10	41	69	71	41	38	0

Fig. 3. Ethnicity



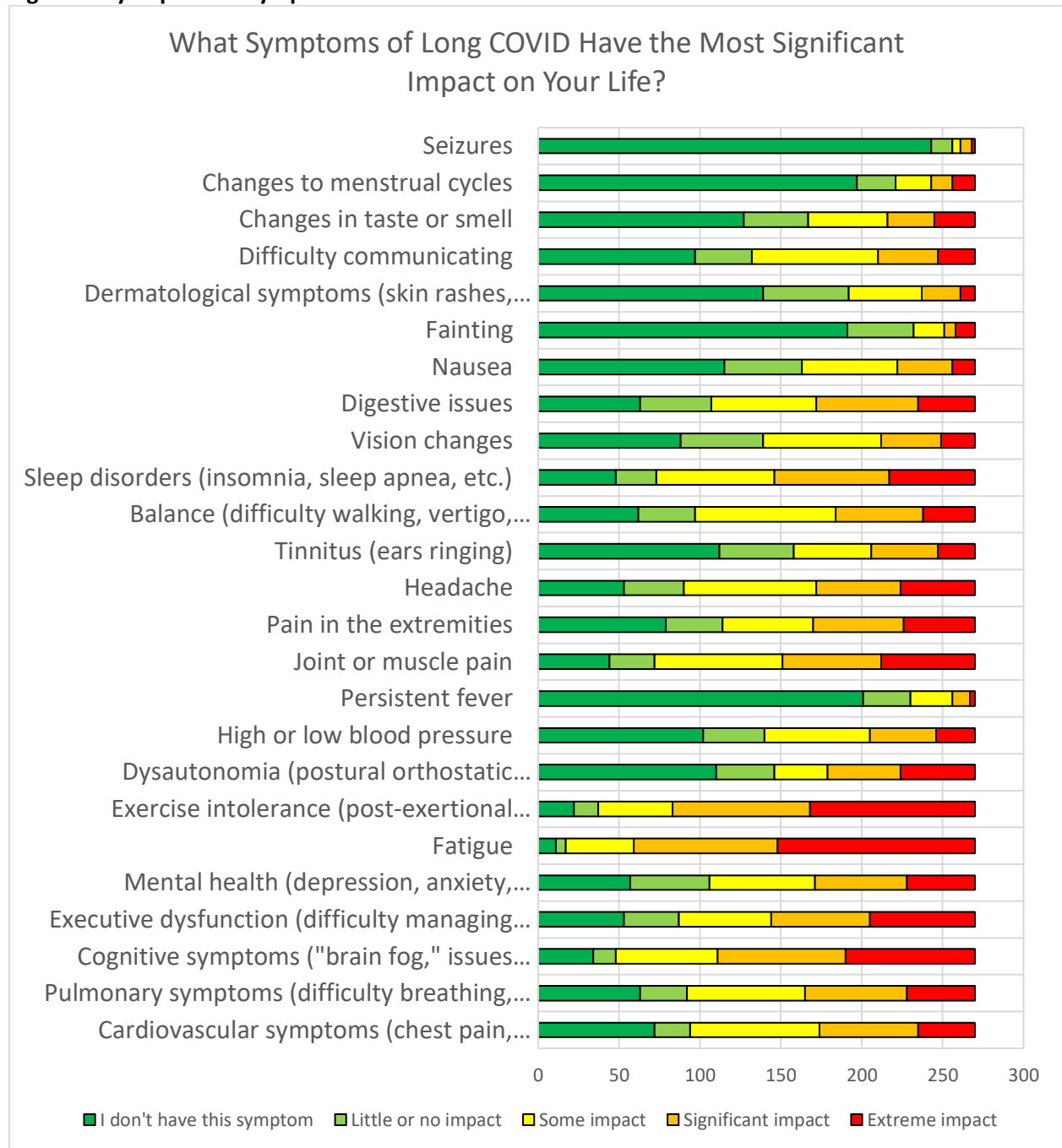
American Indian or Alaska Native	Asian	Black or African American	Hispanic or Latino	Native Hawaiian or Pacific Islander	White/Caucasian	Prefer not to say	Other
5	10	10	13	2	245	3	1

Fig. 4. Education Level

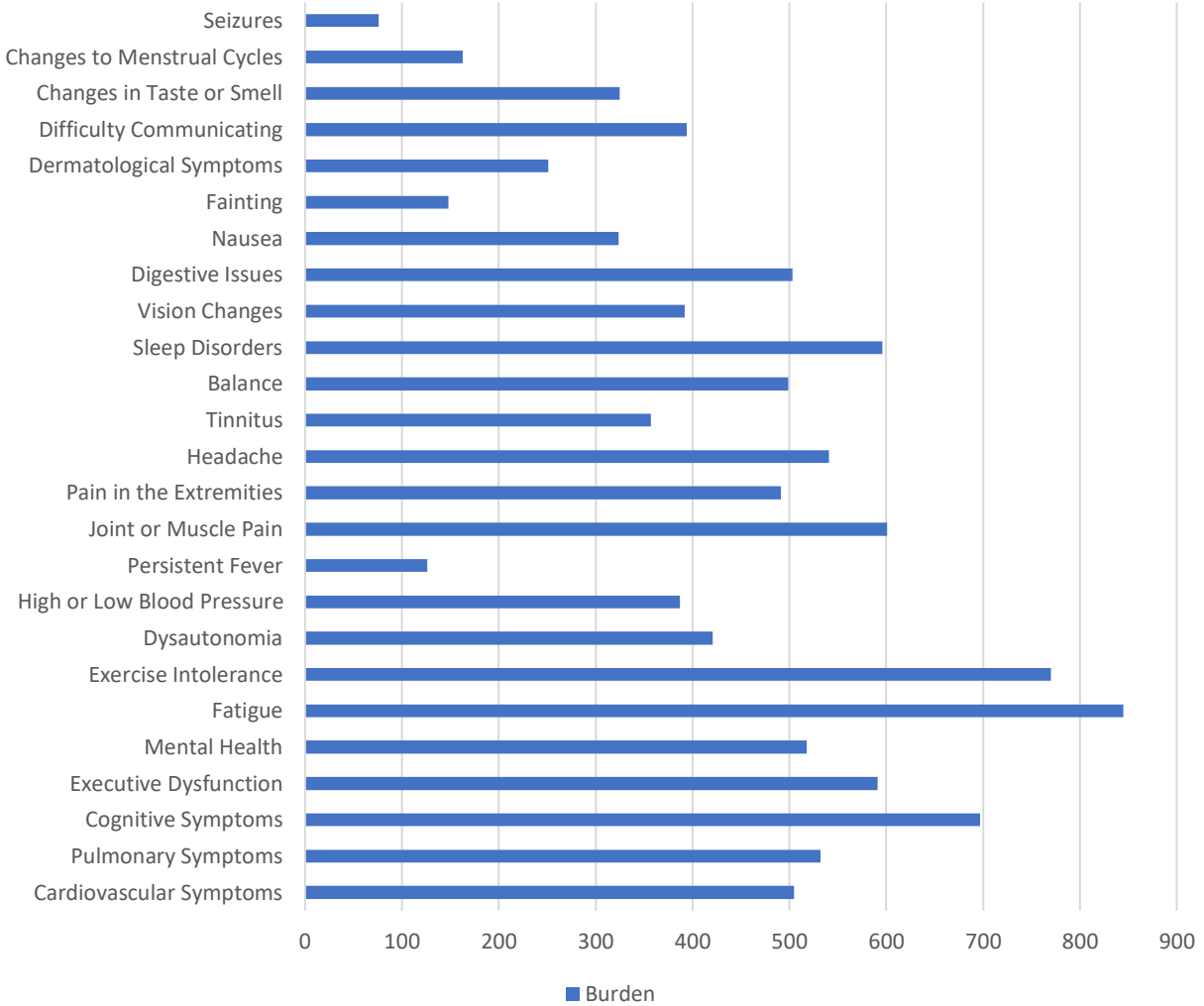


Master's Degree or Above	Bachelor's Degree	High School	Prefer not to say	Other
83	106	48	10	23

Fig. 5. Daily Impacts of Symptoms



What Symptoms of Long COVID Have the Most Significant Impact on Your Life?



	Cardiovascular Symptoms	Pulmonary Symptoms	Cognitive Symptoms	Executive Dysfunction	Mental Health
I don't have this symptom	72	63	34	53	57
Little or no impact	22	29	14	34	49
Some impact	80	73	63	57	65
Significant impact	61	63	79	61	57
Extreme impact	35	42	80	65	42
Weighted score	505	532	697	591	518

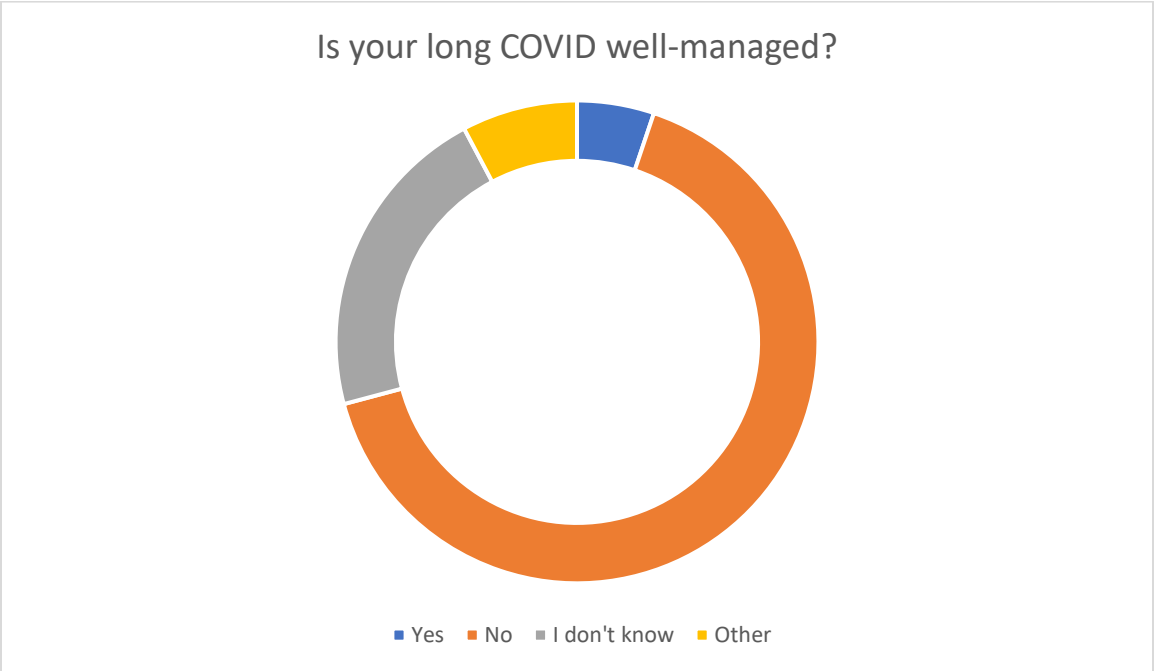
	Fatigue	Exercise Intolerance	Dysautonomia	High or Low Blood Pressure	Persistent Fever
I don't have this symptom	11	22	110	102	201
Little or no impact	6	15	36	38	29
Some impact	42	46	33	65	26
Significant impact	89	85	45	41	11
Extreme impact	122	102	46	24	3
Weighted score	845	770	421	387	126

	Joint or Muscle Pain	Pain in the Extremities	Headache	Tinnitus	Balance
I don't have this symptom	44	79	53	112	62
Little or no impact	28	35	37	46	35
Some impact	79	56	82	48	87
Significant impact	61	56	52	41	54
Extreme impact	58	44	45	23	32
Weighted score	601	491	541	357	499

	Sleep Disorders	Vision Changes	Digestive Issues	Nausea	Fainting
I don't have this symptom	48	88	63	115	191
Little or no impact	25	51	44	48	41
Some impact	73	73	65	59	19
Significant impact	71	71	63	34	7
Extreme impact	53	53	35	14	12
Weighted score	596	392	503	324	148

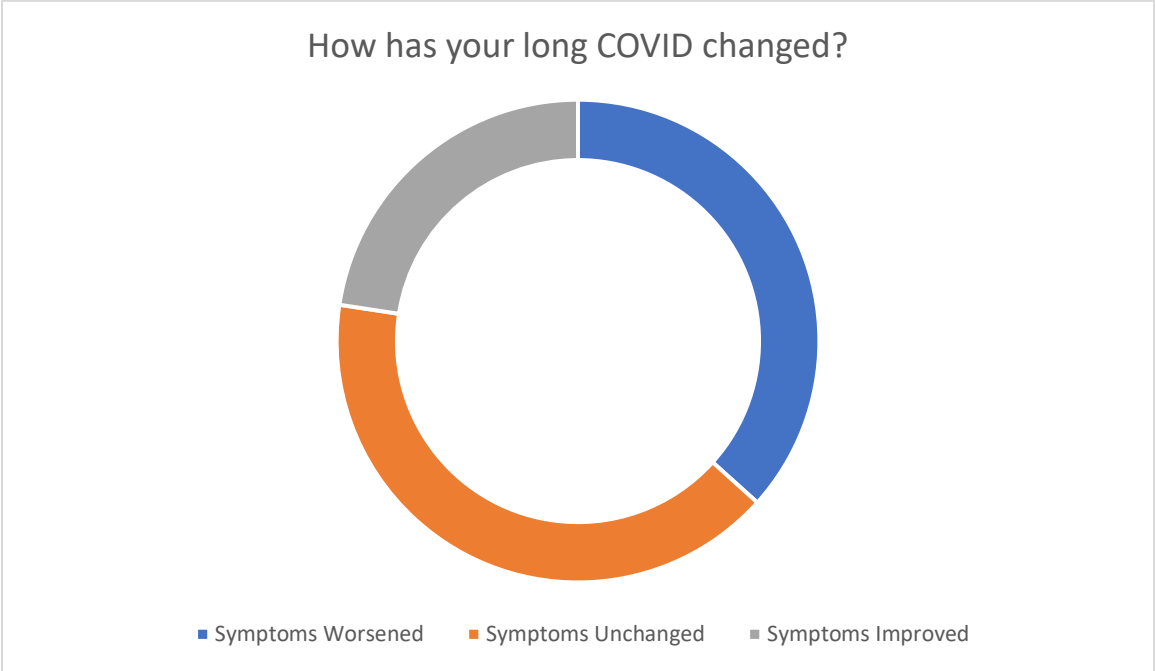
	Dermatological Symptoms	Difficulty Communicating	Changes in Taste or Smell	Changes to Menstrual Cycles	Seizures
I don't have this symptom	139	97	127	197	243
Little or no impact	53	35	40	24	13
Some impact	45	78	49	22	5
Significant impact	24	37	29	13	7
Extreme impact	9	23	25	14	2
Weighted score	251	394	325	163	76

Fig. 6. Symptom Management



Yes	No	I don't know	Other
14	178	58	21

Fig 7. Symptom Change



Symptoms Worsened	Symptoms Unchanged	Symptoms Improved
99	110	61