

Review

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Long COVID Treatment No Silver Bullets, Only a Few Bronze BBs

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Keywords: long COVID; COVID



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Review

Long COVID Treatment. No Silver Bullets, Only a Few Bronze BBs

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Abstract

Long COVID is the consequence of having had COVID. Long COVID has many other names including Long-haul COVID, Post-COVID conditions (PCC), Post-COVID-19 syndrome, Post-acute sequelae of SARS-CoV-2 condition (PASC) and Chronic COVID. Long COVID is the name most frequently used. COVID is not alone in having severe post infection consequences. Influenza, Ebola, Marburg, Dengue, and Lyme Disease are other infections with severe post infection consequences. Long COVID has emerged over the past few years and is ill-defined. Long COVID's underlying science and treatments are rapidly evolving. There is no diagnostic test for it. The most-often reported lower bound on its prevalence is about 7%. Seven percent doesn't sound like much, but under the assumption that 75% of the people in the world have had COVID, that means 420 million people in the world have Long COVID which is about 5 times the number of people killed or injured in the 20th and 21st century wars. There are several root causes for Long COVID with inflammation and mitochondrial dysfunction being the two leading villains. Long COVID prevalence goes down with recent variants, COVID vaccination, early antiviral use, being fit, being young, and surprisingly being male. The most important action to reduce the chance of Long COVID is COVID vaccination. The impact of COVID vaccination on Long COVID prevalence is quite uncertain. Papers report 10% to 100% reduction in Long COVID rates from pre-disease vaccination. The average reported reduction is 50%. The impact of vaccination on people with no comorbidities is uncertain with wide ranges being reported. There are no guaranteed treatments for Long COVID; however, some treatments offer either broad or organ-specific relief for many. This paper reviews 179 different Long COVID treatments described in 249 papers. These papers came from the author's personal data base called The Mouse That Roared of 24,000+ papers that have been accumulated over the last five and a half years. The Mouse That Roared papers cover all aspects COVID including the SARS-CoV-2 virus, the COVID disease, therapeutics, vaccines, behavior, testing, herd immunity, Long COVID, Long COVID Treatment, Politics and National COVID responses, etc. Unlike COVID, there are no excellent treatments, which I call silver bullets, for Long COVID Fortunately, there are some treatments that help some a bit. I will call those "bronze bb's." Even with them, healing is very slow. The recovery time with Long COVID is longer than the body's normal times because COVID's damage is widespread and because COVID damages our body's healing process.

Keywords: long COVID; COVID

1. Setting the Stage

Before discussing Long COVID treatment, a review of Long COVID is appropriate. Long COVID is very different than COVID as summarized in the next table:



Table 1. COVID as Compared to Long COVID.

	COVID	Long COVID
Date of First Paper	February 3, 2020 Nature – 19,000+ citations Lancet – 12,000+ citations	November 3, 2020 JAMA – 446 citations
What is it?	A disease caused by a virus	The multiple, diverse consequences of a disease
Contagious	Yes, very	No
Test	Yes – PCR and rapid antigen	No
% of US afflicted population	~90%	~7% of those who had COVID
Length of illness	Typically, 5-10 days	Months to years or perhaps permanent
Sex prevalence	Male	Female
Vaccination Impact	Significant reduction	No Long COVID vaccine and none is likely. However, pre-COVID vaccination helps. Post-COVID vaccination does not help.
Therapeutic objective	Avoid severe disease	Repair COVID damage
Therapeutic effectiveness tests	Biochemical tests based on the therapeutic type, i.e., antiviral, anti-inflammatory, oxygenation, and blood clots.	Human trials and highly qualita—tive studies
Therapeutic placebo effect	Some	Can be significant

Long COVID is similar to the long-term impact from other viral, bacterial and parasite diseases, e.g., Long Ebola, Long Lyme, and influenza. The following table summarizes some of the aspects of various diseases' post recovery conditions.

Table 2. Disease Post Recovery Impacts.

Disease / Virus	Common Long-Term Symptoms	Organs/Systems Affected	Duration	Percent Affected
COVID-19	Fatigue, brain fog, postural orthostatic tachycardia syndrome, heart palpitation gastrointestinal issues	Brain, nerves, lungs, heart, s,kidney, liver, pancreas, genitals, musculoskeletal, immune syster	•	~5 –15% higher after severe cases
Epstein-Barr	Chronic fatigue, memory issues, muscle pain	Brain, immune system, liver	Months to years	~10–15% chronic fatigue syndrome
Influenza	Fatigue, weakness, rare Guillain-Barré syndrome or encephalitis	Nervous system, lungs	Weeks to months	~1–2% mostly severe cases
Coxsackievirus B	Myocarditis, fatigue, chronic inflammation	Heart, muscles	Weeks to lifelong	~5–10%
Zika Virus	Guillain-Barré syndrome, neuropathy, fetal defects if pregnant	Nerves, brain (fetal/adult)	Weeks to lifelong	<1% Guillain-Barré syndrome, neuropathy ~5–10% mild neurological symptoms
SARS / MERS	Lung damage, post-traumatic stress disorder, fatigue	Lungs, nervous system	Months to years	~25–40%
RSV	Wheezing, asthma in kids, chronic cough Lungs, airway Months to years		~30–50% of children with severe RSV	
Measles	subacute sclerosing panencephalitis (ver rare), immune suppression	y Brain, immune system	Years later	Rare
Chickenpox	Shingles, nerve pain (post therpetic neuralgia)	Nerves, skin	Weeks to years	20–30% get shingles; ~10–15% of those get postherpetic neuralgia

COVID and Long COVID comorbidities, other than sex, are very similar. Sadly, just like COVID, socioeconomic and political context is a Long COVID comorbidity. A particularly surprising one, as reported by Nature [1] in July 2025, is viral rebound. It increases the odds of Long COVID by about 50% whether one has taken an antiviral or not. However, just as there are more COVID papers than

Long COVID papers, PubMed lists more COVID comorbidity papers than Long COVID comorbidity papers as shown by Figure 1 which was prepared by the author. Interestingly PubMed listed a Long COVID paper in 2019 though it was not discovered until 2020!

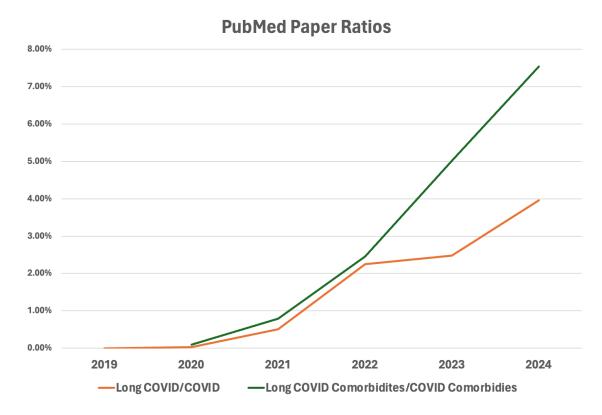


Figure 1. Ratios of COVID/Long COVID papers in the PubMed Paper Database.

2. Long COVID

Figure 2 from a National Academies of Sciences, Engineering, and Medicine [2] highlights Long COVID's major symptoms. Over two hundred different symptoms have been reported in journal papers.

Symptoms tend to fade with time as described by the paper *Persistence of Symptoms 15 Months since COVID-19 Diagnosis: Prevalence, Risk Factors and Residual Work Ability,* Life, December 2022 [3]. However, 1-2% of people with Long COVID in the US are disabled. Getting Social Security Disability benefits is difficult because of the lack of a diagnostic test. Cardiopulmonary testing, however, could give some insight into the degree of disability. Consequently, Social Security doesn't and can't report how many people with Long COVID are getting Social Security Disability benefits.

Figure 3 summarizes the slow course of recovery. While several papers [4-8] discussed recovery times, it is from ref. [4]. Notice the normal recover time of a few weeks to a few months for surgeries, bone breaks, etc. Notice the difference in recovery times for hospitalized and nonhospitalized patients which is another clue on the role of COVID severity in Long COVID. Long COVID recovery time is similar to inflammatory illness such as rheumatoid arthritis, lupus, Sjogren's syndrome, Inflammatory Bowel Disease, etc. As will become clear, Long COVID is also related to inflammatory dysfunction.

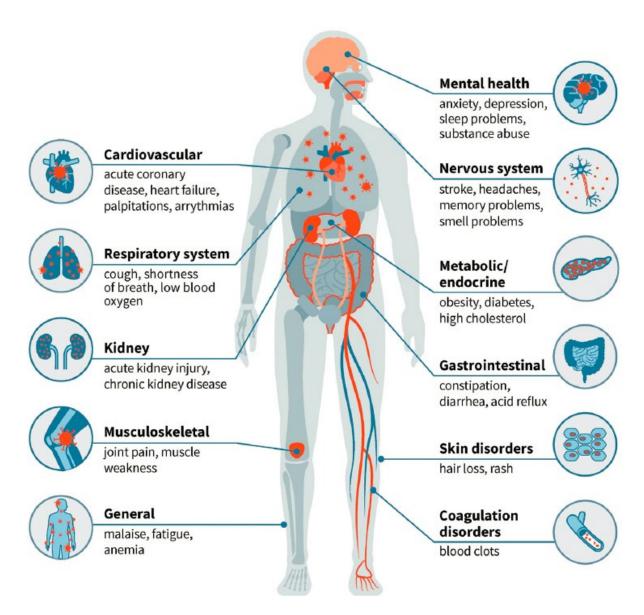


Figure 2. Long COVID's Major Symptoms.

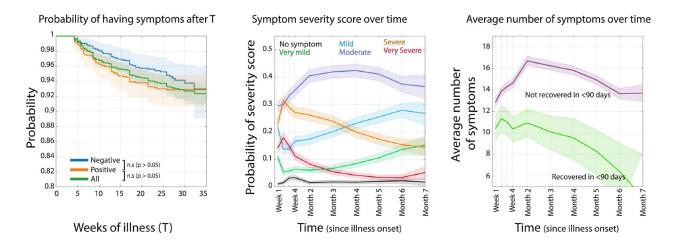


Figure 3. Long COVID Symptom Prevalence Over Time.

Even after a mild COVD case, recovery can take a long time. A Clinical Infectious Disease paper reported the recovery of smell or taste after mild COVID cases. Figure 4 summarizes the paper's results.

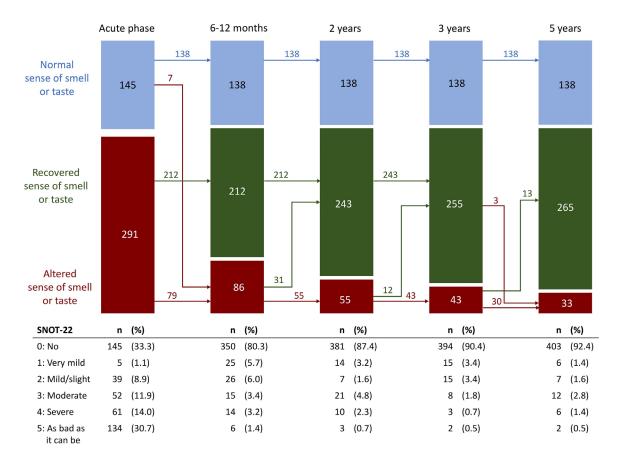


Figure 4. Smell or Taste Recovery Time After a Mild COVID Case. SNOT-22 is a Sino-Nasal Outcome Test.

One of the reasons the recovery time with Long COVID is longer than the body's normal times is that Long COVID damages our body's healing process [10].

There were 502 papers in *The Mouse that Roared* that addressed specific Long COVID impacts. Figure 5, which was prepared by the author, is the distribution of those papers into various categories.

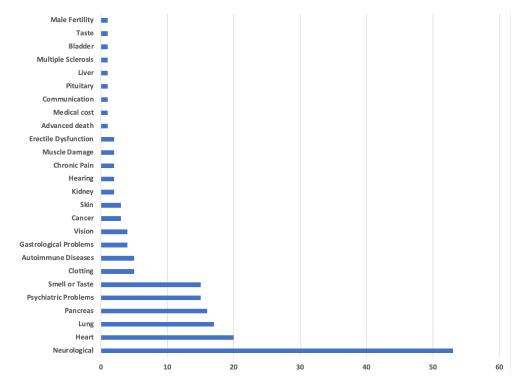


Figure 5. Long COVID Organ Disruption Papers in The Mouse That Roared.

Not surprisingly, neurological and cardiovascular disruptions were at the top of the list as disruptions in these symptoms can lead to the two top Long COVID symptoms which are fatigue and brain fog.

3. Long COVID Prevalence

The following summary of CDC Pulse study 11 prepared by the author provides one view of Long COVID prevalence in the US.

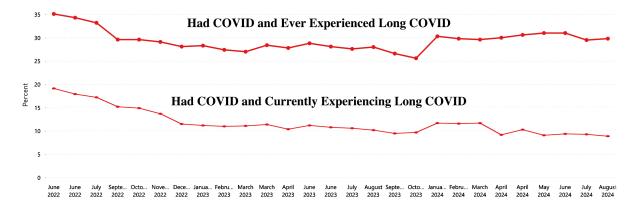


Figure 6. US Long COVID Prevalence.

The wide range of prevalence reported in *The Mouse that Roared* Long COVID papers is summarized in Figure 7.

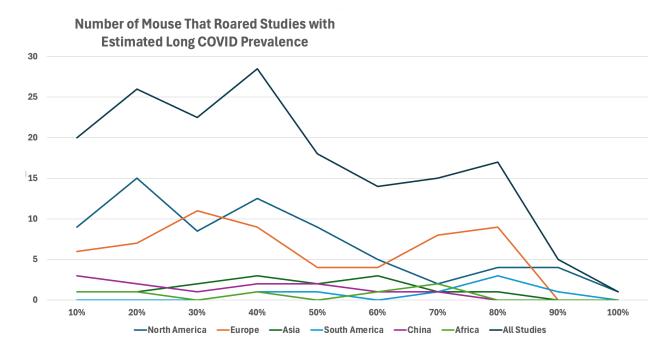


Figure 7. Number of Papers Reporting Differing Long COVID Prevalence.

(The x-axis in the number of papers in each geographical region for each prevalence rate) Finally, this chart from JAMA in 2021 [12], gives another view of the uncertainty in Long COVID (PASC) prevalence. Notice the huge range in prevalence (Y axis) regardless of when the prevalence was tested after infection (X axis). The chart is a random scatter plot.

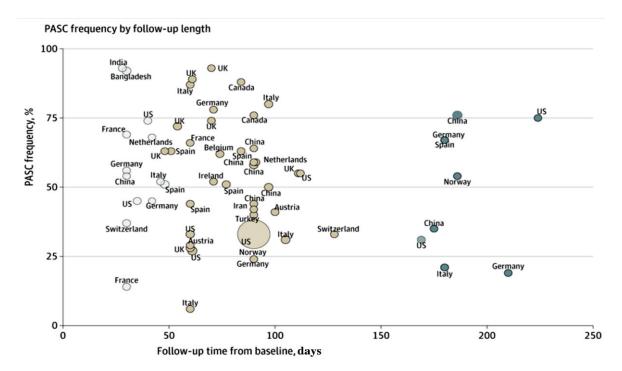


Figure 8. Long COVID (PASC) Prevalence Versus Time.

Scatterplot representing each study's PASC frequency (%) plotted according to length of follow-up from baseline (in days), represented by a circle proportional to the study's sample size and annotated according to country.

Prevalence by age isn't as one might expect. A 2021 Office of National Statics¹³ report included this figure.

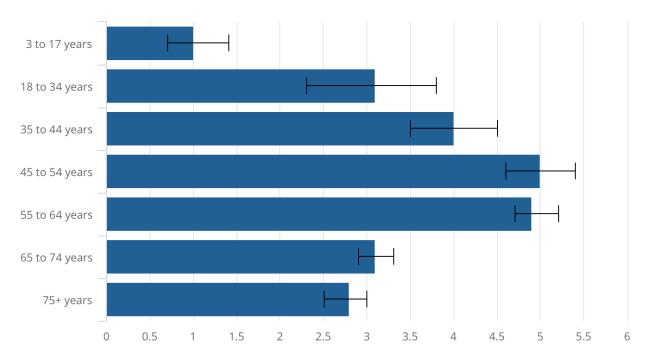


Figure 9. Percent of People with Long COVID-March 2024.

In a similar vein, prevalence differs by variant and vaccination status as shown by Figure 9 from a New England Journal of Medicine paper [14].

In Figure 10A, the numbers at the bottom are additional DALY's as days post-infection increase. There are many reasons for this high uncertainty in prevalence.

- 1. First, and most importantly, there is no diagnostic test for Long COVID. Thus, assessment techniques are qualitative. For example,
 - i. There are self-assessments with different criteria, e.g., walk test or how are you feeling?
 - ii. Frequently there are not controls who also could have Long COVID symptoms, e.g., fatigue or depression.
 - iii. There are mail surveys, on-line forms, phone calls, all of which have low response rates. Someone who doesn't feel well is more likely to respond than someone who feels great which bias results.
 - iv. There are different measures such as rate, risk ratios, and fully recovered.
 - v. While there is a large symptom base, only a few symptoms are usually measured, usually fatigue or brain fog.

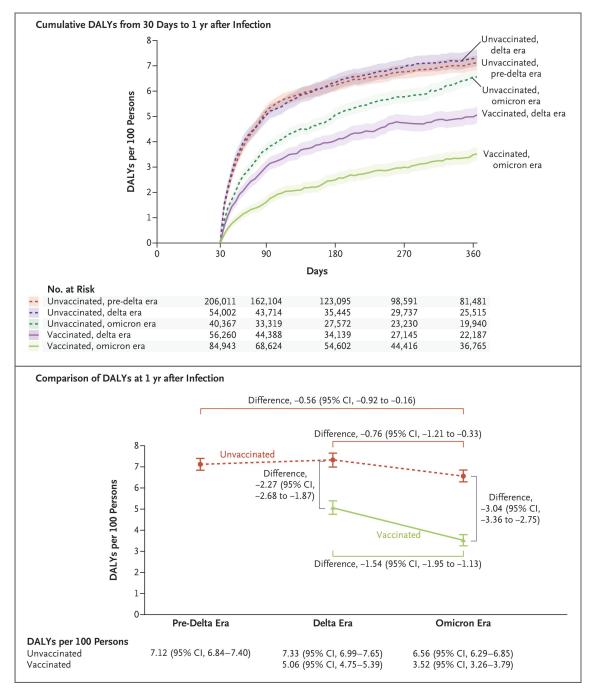


Figure 10. Long COVID Rates by Variant and Vaccination Status. DALYs—Disability-Adjusted Life Years.

- 2. The pandemic changed behaviors, e.g., less exercise and sleep, which can result in one having "Long COVID" symptoms.
- 3. Comorbidities affect the results. The comorbidities include:
 - i. Pandemic medical impacts, e.g., depression which can overlap with and can exacerbate Long COVID symptoms.
 - ii. Age, sex, BMI, diseases, frailty, genetics
 - iii. Variants
 - iv. Therapeutics
 - v. COVID Vaccination
- 4. There are different Long COVID definitions.

Reinfection has an interesting impact on Long COVID prevalence. A May 2025, medRxiv preprint [15] reported that Estimated long COVID risk following any COVID-19 infection was similar among 22 496 online survey participants (17.0% [95%CI, 16.3%–17.6%] and 3 978 telephone survey participants (15.9% [14.6%–17.2%]. The cumulative risk increased with the number of infections, but reinfections were associated with three times lower risk of long COVID than first infections.

Of course, just like prevalence, there is great variation on reported reinfection risk. An October 2023, Open Forum Infectious Disease¹⁶ paper reported Long COVID was reported by those \geq 16 years at a rate of 4.0% of first and 2.4% of second infection, respectively. The corresponding estimates among those aged <16 years were 1.0% and 0.6%. The adjusted odds ratio for Long COVID after second compared to first infections was 0.72 for those \geq 16 years and 0.93 for those <16 years. Thus, again, prevalence is complex.

4. Long COVID Root Causes

Long COVID has many root causes which are at the heart of Long COVID and the slow recovery from it. The major ones are:

- 1. **Inflammation**: Inflammation is probably Long COVID's major root cause. Inflammation includes recruiting white blood cells and the release of cytokines that initiate tissue swelling and injury.
- 2. **Persistent viral infection**: viral antigens, RNA, and SARS-CoV-2 proteins remain present and active in the body's tissues following acute infection and continue to damage it.
- 3. **Viral particle damage to organs**. A COVID case results in 1-30 trillion viral particles in the body. Some proteins, particularly the spike, the nucleocapsid, and the nonstructural protein 1 (nsp1) directly damage organs.
- 4. **Autoantibodies**: Infection with the SARS-CoV-2 virus can trigger autoimmune diseases.
- 5. **Biological processes and organs** are damaged.
 - a. All our organs are damaged.
 - b. Mitochondria, our energy workhorses, are greatly damaged by COVID. This results in fewer oxygen carrying molecules called ATP being generated for our bodies. This is a significant contributor to fatigue and brain fog.
 - c. The proteins that are involved in healing are dysregulated.

The following figure which was prepared by the author summaries the number of *The Mouse that Roared* papers that addressed these root cause damages.



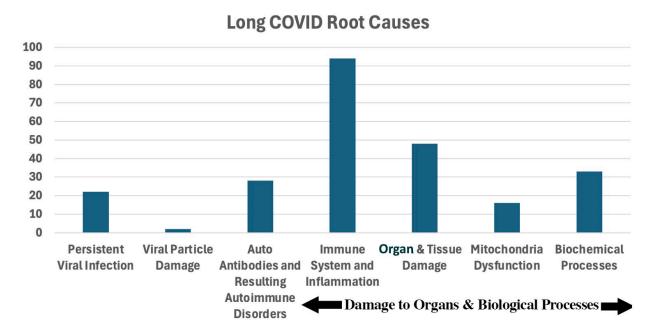


Figure 11. Long COVID Root Causes.

Thus, Long COVID is not a disease; rather, it is the multifaceted consequences of a disease.

5. Long COVID Biochemical Markers

Though there is no diagnostic test for Long COVID, there are many medical, biochemical and lifestyle markers that provide clues that Long COVID is present. They include but are not limited to biochemical markers for the following long list of symptoms, organs, and body characteristics. This long list is another indication of Long COVID's broad impact to the body:

- Pain
- Blood System
- Vascular System
- Retinal Microcirculation
- Musculoskeletal Changes
- Orthostatic Dysfunction
- Cardiac Changes
- Olfactory Bulb Changes
- Lung
- Diaphragm Weakness
- Gut Permeability
- Proteins
- Metabolites
- Bacteria Change
- Brain Changes
- Bacteria
- Autonomic Disfunction
- Connectivity
- Microglial And Macrophage Activation
- Brain Entropy
- Kinesiophobia



- Reaction Time
- Chemosensory Impairment
- Neurotransmitters
- Serotonin
- Protein Markers
- Plasma Changes
- Changes In Gene Expression
- Viral Proteins
- Spike Protein
- N Protein Anti-Nucleocapsid Igg
- Antibodies, Autoantibodies
- Antibody Levels
- Nasal
- Autoantibodies
- Coronavirus Imprinting
- Immune System
- Immune System Dysregulation
- Previous Coronavirus Infection
- Metabolic Changes
- T Cells dysregulation
- Monocytes
- Tryptophan & Kynurenine
- Myeloid Cells
- Mitochondria, Oxidative Stress
- Genetics
- Genes
- Epigenetic Changes

6. Reducing the Chances of Long COVID

As previously noted, the chance of Long COVID increases with COVID severity. Thus, the most important action to reduce the chance of Long COVID is pre-disease COVID vaccination. The assessments of vaccine impact are further complicated by vaccine type, age, variant, whether the person is immunocompromised, etc. The following chart shows the number of COVID vaccination impact on Long COVID papers in *The Mouse that Roared*.

Notice that even something as simple as the impact of vaccination on Long COVID rates has a wide range of answers. The average is 50%, but studies reported as little as 10% and as much as 100%!



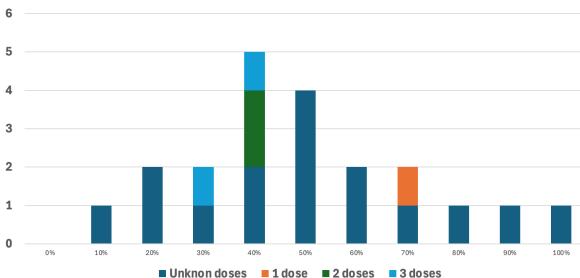


Figure 12. Papers Reporting Impact of COVID Vaccination on Long COVID.

The X-Axis is the number of papers for the reported reduction in Long COVID rates.

6.1. Long COVID Treatments

Vaccines and antivirals were COVID has *silver bullets*. They dramatically reduce COVID prevalence and severity. Long COVID has scattered, specialized therapeutics. None are as effective as COVID vaccines or approved antivirals.

The number of Long COVID versus COVID studies in June 2025 provides some insight into the research base associated with each malady.

Table 3. Long COVID and COVID Studies.

	COVID	Long COVID
	Treatments	Treatments
FDA clinical treatment trials	6,000	545
PubMed published papers ^a	198,000	17,000b
The Mouse the Roared papers ^a	3,800°	269 ^d

a. Procedures, drugs and nutrition. b. The number of papers is likely much smaller than 17,000, as many were just COVID. 14 drugs were approved by the FDA for US use. c. None was discovered during the pandemic. 179 unique Long COVID treatments. d. None have been FDA approved for US use.

One can get further insight into the relative progress of Long COVID treatment by analyzing the FDA Long COVID clinical trials using the <u>FDA Clinical Trial Tracker</u>. As of June 2025, 176 of the 545 trials are in the US. While one trial can address multiple issues, these are the symptoms addressed by the FDA trials:

Table 4. Long COVID Symptoms Assessed by FDA Clinical Trials.

Symptom	FDA Clinical Trial
Fatigue	279
Mental Health	138
Persistent Infection	106
Inflammation	66

Brain Fog	63
Antiviral	51
Gut Micro biodome	16
Microclotting	14
Cognitive Behavioral Therapy to Treat It	12
SSRI Antidepressants to Treat It	12
Auto Immune Diseases	12
Mitochondrial	11
Dementia	10

As of June 2025, no Long COVID clinical trial had posted clinical results. However, it is important to note that many Long COVID symptoms such as blood clots have approved therapeutics. Sadly, the Long COVID FDA trial rate decreased in 2024 and 2025.

Table 5. FDA Clinical Trials.

Year	Long COVID Trials Started
Pre 2020	2ª
2020	43
2021	120
2022	142
2023	155
2024	83
2025—through 8/31	57

This number demonstrates the frailty of the FDA clinical trial search program. One of the two studies was 2018. The other study said Long COVID, though Long COVID didn't appear until mid 2020.

Nonetheless, there is good reason to hope that progress will be made on Long COVID treatment.

- 1. The scientific community is early in focusing on Long COVID, so clearly other treatments will be discovered.
- 2. The huge, order of \$2.3 billion, US Long COVID project called <u>Recover Project</u> is just gathering momentum. This will be a long term, well-funded project if for no other reason than the order of 20 million Americans suffer from Long COVID. This website lists its published papers <u>Recover Project Published Papers</u>.
- 3. Though not as large as the US Recover Project, many countries have large Long COVID projects including, but not limited to the UK, Canada, Australia, China, Japan, South Korea, the European Union, and the Word Health Organization.
- 4. That is, the number of Long COVID treatment papers in *The Mouse That Roared* dropped precipitously in July and august 2025.

6.2. Treatment Strategy

This section will outline the approach one might wish to follow if one believes he/she has Long COVID.

I. Get the Right Set of Doctors

If the impact is focused, e.g., arrythmias, orthostatic hypotension, or loss of smell, then seeing an expert in that illness, who is also expert in Long COVID, is the right approach. If the impact is broad, one should pursue broad, Long COVID care.

II. Go to a Long COVID Clinic

A May 2024, BMC Health Services Research [17] paper noted that the economic and health burden of COVID-19 has transformed the healthcare system in the US. Hospitals have adapted to the



heterogeneity in Long COVID symptoms and the sheer number of people affected by this condition by building Long COVID centers and programs.

43 out of 50 of the top hospitals in the US offer Long COVID treatment services. The most common specialties were psychology (n = 25; 58%), neurology (n = 25; 58%), and pulmonary (n = 24; 56%). Sixty-three trials of the 134 Long COVID clinical trials had at least one top hospital listed as a study site.

Thus, if the impact is broad-based, e.g., brain fog and fatigue, one will likely need to see multiple doctors, e.g., a pulmonologist and a rheumatologist (for the inflammatory nature of the condition) at a **Long COVID clinic** depending on where you live. Johns Hopkins would be a great place to go if you live near Baltimore. It has a well-established Long COVID program. <u>Johns Hopkins Long COVID Program</u>

The <u>Long COVID Clinics</u> website lists 412 Long COVID Clinics. Be sure to go to one associated with one of the top hospitals. Some of the Long COVID Clinics listed on the website only provide specialized treatments such an oxygen chamber.

Starting in 2020, the Veterans Health Administration (VHA), established a national network of Long COVID Clinics (LCCs). A Health Affairs Scholar paper¹⁸ reported a retrospective cohort study of 494,547 veterans with documented SARS-CoV-2 infection from March 2020 to April 2022. Researchers examined trends in the U09.9 ICD-10 diagnosis code used for Long COVID in the VHA up to May 2024. Overall, 5.9% (n=29,195) of patients in the cohort had a documented U09.9 code and 2% had at least one LCC visit. Among Veterans with a U09.9 code, 17.4% used LCCs. LCC use rates were low across all patient subgroups. LCCs were more available to Veterans residing in the South Census region than Veterans in other regions.

In June 2025 the World Health Organization issued guidelines for COVID and Post COVID⁹ World Health Organization COVID and Post COVID Guidelines

U.S. Department of Health and Human Services Actions

In September 2023, the U.S. Department of Health and Human Services allocated major funding to 12 Long COVID clinics across the country.

The <u>Long COVID Alliance</u> is another good LONG COVID resource for understanding LONG COVID research and patience support

III. Consider Having Assessments for Root Causes

As previously discussed, there are several root causes for Long COVID. It could be worth getting tested for them to help guide treatment.

- Persistent Inflammation The main test for inflammation is for the IL-6 cytokine. <u>Persistent Inflammation Test</u> describes the test. Inflammation is probably the most important test as hyperinflammation is a leading cause of severe COVID which leads to the most severe cases of Long COVID.
- 2. **Mitochondrial Dysfunction** This is probably the second most important test. Initial laboratory tests such as lactate, pyruvate, urine organic acids, and plasma amino acids can inform the clinician about possible mitochondrial dysfunction.
- 3. **Persistent Infection** The main tests are:
 - i. Antibody Testing: Persistence of IgM or high IgG titers might indicate ongoing antigen exposure.
 - ii. T-cell Activation Profiles: Specialized tests can assess T-cell responses to SARS-CoV-2 antigens, indicating ongoing immune activity against the virus.
 - 4. **Autoantibodies** Testing for autoantibodies triggered by COVID-19 involves specialized laboratory assays that detect the presence of antibodies targeting the body's own tissues. They are several types.
 - i. Blood Tests to Detect Specific Autoantibodies



- Enzyme-Linked Immunosorbent Assay (ELISA): It is used to detect autoantibodies such as anti-nuclear antibodies (ANA), antiphospholipid antibodies, and others.
- b. Indirect Immunofluorescence: It is often used for detecting ANA or antineutrophil cytoplasmic antibodies (ANCA).
- Multiplex Autoantibody Panels: These are comprehensive tests that simultaneously evaluate multiple autoantibodies associated with autoimmune diseases.

ii. Functional Assays

- a. Neutralization Assays: These check for autoantibodies interfering with normal immune pathways, such as those targeting type I interferons which is linked to severe COVID-19.
- b. Complement Activity Assays: These evaluate the activity of autoantibodies against the complement system.

iii. Tissue-Specific Tests

- a. Thyroid Function Tests: If autoimmune thyroiditis is suspected, specific antibodies like TPOAb (thyroid peroxidase) can be tested.
- b. Liver Function-Related Autoantibodies: For autoimmune hepatitis, testing for anti-LKM1 or ANA might be necessary.
- iv. Specialized Tests for COVID-19-Triggered Autoimmunity
 - a. Anti-Interferon Autoantibody Testing: This is relevant for severe COVID-19 cases as these autoantibodies may impair the immune response to the virus.
 - b. Anti-Phospholipid Antibodies (aPL): Increased risk of blood clots in some COVID-19 cases can be linked to these autoantibodies.
 - c. Cytokine Autoantibodies: These assess disruption in immune signaling pathways, especially in post-COVID syndromes.
- 5. **Gut microdome dysfunction**—there are many tests.

IV. Summarize Relevant Personal Medical Data

Prepare a summary of your relevant health data. Include:

- 1. Pre-existing health issues being sure to include any autoimmune disease and other COVID comorbidities such as diabetes, active cancer treatment, etc.
- 2. COVID case data, including COVID dates, tests, severity, and therapeutics.
- 3. COVID vaccination history.
- 4. Long COVID history—start date, symptom trends, and treatments. The Cleveland Clinic's table is an excellent way to summarize Long COVID symptom data.



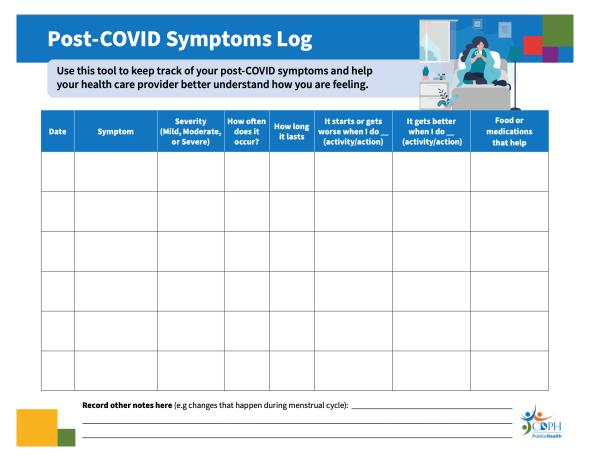


Figure 13. Post COVID Symptom Table.

V. Discuss Candidate Treatments

In going to the Long COVID Clinic, it is worthwhile having an idea of potential treatments. You might wish to discuss them with the doctors at the Long COVID Clinic.

Figure 14, which was prepared by the author, graphs the types of Long COVID treatment papers from *The Mouse That Roared* versus time.

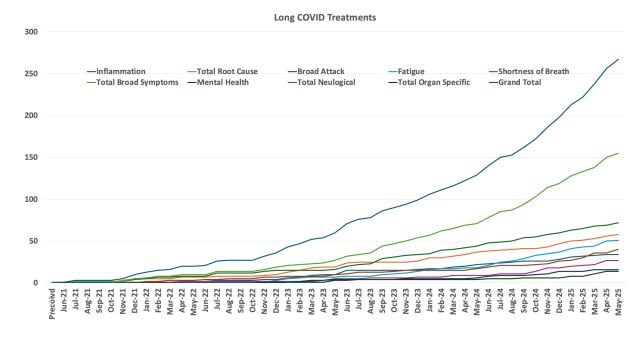


Figure 14. Types of Long COVID Treatments.

Three points regarding the chart:

- 1. Most of the root cause papers address inflammation.
- 2. The choice of assigning a paper to Broad Symptoms or Root Cause/Inflammation was a bit arbitrary and was often based on the way the paper's data was presented.
- 3. Notice how few organ-specific papers were written. This is not surprising as treating arrythmia, for example, induced by Long COVID is likely little different than treating non-COVID arrythmias.

The tables in appendix 1 summarizes the distinct treatments and the total number of papers, including the number of cases reported in the papers as of June 2025. Other more recent papers are included in the later discussion. As of the June 2025 analysis, there were 269 papers covering 168 distinct treatments.

Of them:

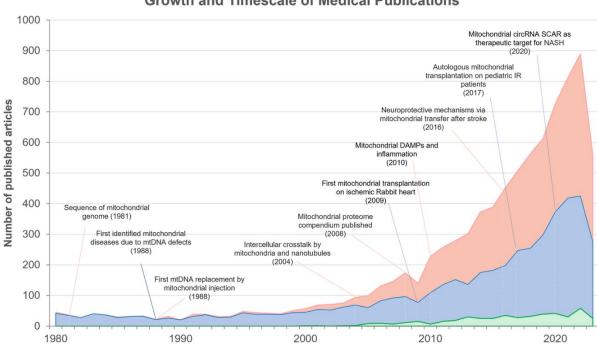
- Only 70 papers reported total human trial sizes of 100 or more. This would be the
 minimum size for an FDA phase 2 trial which determines a treatment's effectiveness. Only
 27 papers reported studies of 300 or more humans in their trials.
- 2. If one combines trials into the group that had the largest number of people in one trial, then exercise studies accounted for more than 10% of the papers.

Control groups are always important in assessing treatment effectiveness. For Long COVID treatment, this is particularly important given the natural wanning of symptoms, the lack of a diagnostic test, and the subjectiveness of Long COVID assessment. Nonetheless, as shown by a table in Appendix B, 69% of the trials had no control group.

Astoundingly, the papers that explicitly addressed root causes didn't have trials. However, other papers which had trials discussed therapies that addressed the root causes including

- 1. Corticosteroids—prednisone or dexamethasone
- 2. Colchicine
- 3. Low-Dose Naltrexone
- 4. Antihistamines and Mast Cell Stabilizers
- 5. Statins—atorvastatin, rosuvastatin
- 6. Omega-3 fatty acids
- 7. Palmitoylethanolamide
- 8. Curcumin
- 9. Resveratrol
- 10. Q10

Mitochondrial dysfunction is a major root cause. It is associated with sleepiness which can be related to fatigue [20]. A July 2025, Nature paper [21] reported that mitochondria were important for T cell functioning. A May 2024, Nature paper [22] discussed mechanisms and advances in therapies for mitochondrial dysfunction. As can been seen from Figure 15 from the paper, interest in mitochondrial dysfunction has dramatically grown in the last two decades.



Growth and Timescale of Medical Publications

Figure 15. Medical Papers on Mitochondrial Dysfunction.

The paper reported that notable interventions included: exercise protocols to promote the expression of peroxisome proliferator-activated receptor-gamma coactivator-1 alpha (PGC- 1α), dietary supplements to target primary nutrient deficiency, nicotinamide riboside (NR) to augment nicotinamide adenine dinucleotide (NAD) biosynthesis MitoQ for neutralizing mitochondria-derived reactive oxygen species (ROS) the global antioxidant Coenzyme Q10 (CoQ10) N-acetyl cysteine (NAC) and the mitochondrial inhibitor ME-344 (known for its anti-tumor properties). As you will see, many of these treatments were included in Long COVID Treatment Trials.

Years

Trial Sizes for FDA Drug Assessment

In assessing the trials, this is what the FDA considers appropriate for trial sizes:

Phase 1: Safety and dosage

Size: Small, typically 20 to 100 participants who are healthy volunteers or individuals with the disease being studied, depending on the drug.

Purpose: To determine if the drug is safe and well-tolerated, establish the best way to administer the drug, and identify initial dosage range and potential side effects.

Key points: Researchers start with low doses and gradually increase them, carefully monitoring for side effects and drug interactions.

Phase 2: Efficacy and side effects

Size: Typically, from 100 to several hundred participants with the specific disease or condition the drug is intended to treat.

Purpose: To evaluate the drug's effectiveness against the target disease or condition, continue monitoring for safety, and identify any short-term adverse reactions or risks associated with the treatment.

Key points: May involve comparisons with placebo or existing standard treatments, according to the American Cancer Society.

Phase 3: Confirming efficacy and safety

Size: Typically involving hundreds to thousands of participants with the disease or condition across multiple locations, potentially worldwide. While no minimum is specified, the trials normal range from 300 to 3,000 participants. Control groups are always included.

Purpose: To confirm the drug's effectiveness and safety in a larger population, compare it to standard treatments, and collect more data on long-term effects and rare side effects.

Key Points: They are very expensive. A phase 3 vaccine trial costs about \$100 million.

Thus, we shall summarize the treatments in four buckets based on the number of people in the treatment trial—300+, 100-299, 1-99 and none. While these were formal FDA drug trials, one has a qualitative sense of confidence in the trial's result based on its size.

Only two treatments—exercise and oxygenation—had a significant number of papers—exercise 27 and oxygenation 18. After that it dropped off quickly to:

Table 6. Number of Papers Describing a Treatment.

Number of papers describing a treatment	Number of treatments
6	1
5	1
4	1
3	6
2	18
1	107

I shall now discuss each of treatments. Treatments that lead to broad improvements generally attacked the underlying causes for Long COVID such as inflammation and/or microconidia damage. Those that address specific symptoms such as smell typically addressed a specific organ. A treatment could be a procedure (e.g., exercise), a drug (e.g., aspirin), or nutrition (e.g., probiotics).

Procedures

At Least One 300+ Trial

Broad Improvements

Exercise [23-60]

Exercise can reduce Long COVID symptoms by:

- 1. Reducing inflammation.
- 2. Stimulating mitochondrial biogenesis and improve ATP production, which can reduce fatigue.
- 3. Improving vascular tone, oxygen delivery, and tissue perfusion, potentially easing symptoms like brain fog or muscle aches.
- 4. Rebalancing the autonomic nervous system through designed recumbent or supine exercise (e.g., rowing, swimming, recumbent cycling) which may help recondition the cardiovascular system and reduce orthostatic symptoms.
- 5. Promoting neuroplasticity, potentially helping with cognitive symptoms (e.g., brain fog).
- 6. Promoting lymphatic flow and helping clear cellular debris and immune complexes.
- 7. Support fluid and waste clearance in the brain, helping with cognitive symptoms and sleep quality.

The trick is not to over exercise which can exacerbate symptoms.

Oxygenation [61-79]

There were many ways to increase oxygen in the body, either through direct oxygen or specialized breathing programs. Oxygenation helps reduce Long COVID symptoms by:

- 1. Significantly increasing the amount of oxygen dissolved in the blood plasma, allowing more oxygen to reach tissues that may be oxygen-deprived or poorly cleared of fluids.
- 2. Helping to reduce inflammation immune response.
- 3. Promoting a more balanced immune function.
- 4. Improving mitochondrial function, potentially increasing ATP production, reducing mitochondrial apoptosis signaling, and reducing oxidative stress. This leads to a boost in energy production and reduced fatigue.
- 5. Stimulating the growth of new neurons and improved neuroplasticity thereby potentially improving cognitive function.

Improving Mental Health [80-82]

Therapy and drugs improved mental health. Other therapies like exercise and oxygenation also improved mental health. Improving mental health reduces Long COVID symptoms by:

- 1. Reducing chronic stress which increases inflammatory cytokines which are already elevated in Long COVID.
- 2. Improving mood and symptom perception which may help people feel better, even if the underlying pathology remains.
- 3. Improving sleep quality which can significantly reduce daily symptom burden and improve mitochondrial function.
- 4. Regulating the autonomic nervous system which is linked to fatigue, and breathlessness.
- 5. Improving cognitive function which can help cope with brain fog and develop compensatory strategies, even if they don't reverse the cause.

SPA & Hot Spring Bathing [83-84]

There were broad improvements since hot water can reduce inflammation and sooth pain.

Speleotherapy [85]

There was no improvement in sense of smell

Dual Antiplatelet Therapy [86-88]

There was major improvement in fatigue, cognitive dysfunction, shortness of breath, and joint and muscle pains.

Drugs

Broad Improvements

SSRI Inhibitors [89-91]

2/3 reported improved overall symptoms.

Brexpiprazole + sertraline [92]

2/3 reported reduced PTSD symptoms

Rivaroxaban [93-94]

It reduced new atrial fibrillation as well as incidence of sudden cardiac death.

P2Y12 Inhibitor [95]

There was improved quality of life at 90 days.

Prospekta [96]

It led to significant, broad improvement.

Ensitrelvir [97]

It improved smell and taste by 39%.

Electrolyte Supplementation [98-99]



It improved biochemicals and heart parameters.

Oral Zinc [100]

It interfered with improvement

Traditional Chinese Medicine [101-102]

It improved chest tightness and insomnia

Cyclobenzaprine Hydrochloride [103]

It improved fatigue and sleep

SIM01—Gut Microbiota-Derived Formula [104]

Fatigue, memory loss, difficulty in concentration, gastrointestinal upset and general unwellness were all alleviated.

Transcutaneous Nicotine [105]

73.5% of patients reported a significant improvement in the symptoms.

COVID Vaccination Post Long COVID [106]

A discussed earlier, COVID vaccination reduces the chances of Long COVID and even if Long COVID emerges, it reduces its severity. However, the results from the post COVID vaccination papers were uneven and contradictory.

Nutrition

Broad Improvement

Salmon Oil [107-108]

It provided broad inflammation-resolving effects

Mediterranean Diet [109]

It led to better health markers linked to significant improvements in inflammatory and oxidative stress markers.

Homeopathy [110-111]

There was a decrease in symptoms

Trials with 100-299 patients

Weight Loss [112]

There were broad improvements.

Yoga [113-114]

There were significant reductions in levels of perceived stress, anxiety, and insomnia

Pressing Needle Therapy [115]

It improved mental health and sleep quality.

Speech Language Hearing Therapy [116]

It improved swallowing but less so in in those who were frail.

Olfactory Training [117-122]

There were mixed results on whether it helped improve sense of smell and taste.

Drugs

Corticosteroids [123-127]

Patients who received oral dexamethasone for hospitalized COVID-19 were less likely to experience persistent symptoms at 8-month follow-up.

Vortioxetine [128]

There were broad improvements.



Donepezil [129]

There were broad improvements.

Coenzyme Q10 [130-133]

There was little improvement

RSLV-132—catalytically active human RNase1 fused to human IgG1 Fc [134]

There was no long term improvement.

Deupirfenidone [135]

It improved the 6-min walk times.

Organ Specific Improvement

Mesenchymal Stem Cell [136-137]

17.9% in treatment group had normal lung CT images at month 12, but none in the placebo group.

Fuzheng Huayu [138]

The traditional Chinese medicine led to minor improvement in some measures.

Temelimab [139]

It showed no improvement.

Nutrition

Broad Improvement

Bufei Huoxue [140]

It reduced fatigue.

Ficus pumila L. extract [141]

It reduced insulin in diabetic patients.

Apportal [142]

There was broad improvement.

Vitamin K/D3 [142]

There was some improvement, particularly in inflammation.

Pycnogenol [144]

It did not improve health status compared to placebo over 12 weeks.

Echinacea angustifolia, rosehip, propolis, royal jelly and zinc [145]

It reduced fatigue.

These are the treatments from the smaller human trials.

Table 7. Moderate Sized Trials.

·	Procedures	
Trial Size	Treatment	Improvement
		Sleep
	Fecal Transplant ¹⁴⁶	Broad
	Enhanced External Counter Pulsation ¹⁴⁷	Lung
	Spinal Cord Transcutaneous Stimulation & Respiratory Training ¹⁴⁸	
	Digital Cognitive Training ¹⁴⁹	Fatigue And Concentration
50-99	Unified Phycological Protocol ¹⁵⁰	Broad
	Wearable Brain Activity Sensing Device ¹⁵¹	Broad
	Trained With Orange, Lavender, Clove And Peppermint Oils	152-3
	Contracting And Relaxing Pneumatic Cuffs 0n The Calves, Tl	nighs, Broad Impact
	And Lower Hip ¹⁵⁴	
		Broad Impact

	Immunoadsorption ¹⁵⁵	Broad
	Vagus Nerve Stimulation ¹⁵⁶⁻¹⁵⁸	Broad Neurological
	Transcutaneous Electrical Nerve Stimulation ¹⁵⁹⁻¹⁶¹	e
		Pain And Fatigue
	Tragus Nerve Stimulation 162-163	Broad
25-49	Matt Pilates ¹⁶⁴	Fatigue
	Photobiomodulation ¹⁶⁵⁻¹⁶⁶	Pain And Fatigue
	Stellate Ganglion Block ¹⁶⁷⁻¹⁷¹	Smell And Broad
	Ropinirole ¹⁷²	Restless Leg Syndrome
	Acupuncture ¹⁷³	Well Tolerated, No Measures On
		Outcomes
	Expectation Management ¹⁷⁴	Minor Broad
	Dance ¹⁷⁵	Broad
	Aripiprazole ¹⁷⁶	Reduced sleep duration
	Continuous Positive Airway Pressure ¹⁷⁷	Cognition
10-24	Olfactory Training With Vitamin A ¹⁷⁸	No Impact
	Functional Septorhinoplasty ¹⁷⁹	Smell
	Virtual Reality Training ¹⁸⁰	No Impact
	Neuromodulation ¹⁸¹	No Apparent Impact
	Oronasal Drainage ¹⁸²	Broad
	Plasmapheresis ¹⁸³⁻¹⁸⁴	Cognition
1-9	Light To Restore Circadian Rhythm ¹⁸⁵	Sleep
	Neural Feedback ¹⁸⁶	More Alert
	Plasma Exchange Therapy ¹⁸⁷	No Impact
rugs	0 17	1
Trial Size	Treatment	Improvement
	Leronlimab ¹⁸⁸	Inflammation
	Sea Urchin Eggs ¹⁸⁹	Pain
	Co-UltraPEALut ¹⁹⁰	Memory & Fatigue
	Naltrexone ¹⁹¹⁻¹⁹³	Broad & Tremors
	Antihistamines ¹⁹⁴⁻¹⁹⁵	Broad But Uneven
50-99	Amantadine ¹⁹⁶	Fatigue
	Propranolol ¹⁹⁷	Orthostatic Hypotension
	Lithium ¹⁹⁸	No Improvement
	Metoprolol ¹⁹⁹	Cardiovascular
	Rintatolimod ²⁰⁰	No Impact
	Gabapentin ²⁰¹	No Impact
	Gabapentin	Broad
	Valtrex + Celecoxib ²⁰²	
	AXA1125 ²⁰³	Fatigue
	TN - 201 207	Smell Improved
	Plasma ²⁰⁴⁻²⁰⁵	T C '1 T 1
27.40	Plasma ²⁰⁴⁻²⁰⁵ Treamid ²⁰⁶	Lung Capacity Improved
25-49	Treamid ²⁰⁶	Lung Capacity Improved Smell Improved
25-49	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸	Smell Improved
25-49	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹	Smell Improved Inconclusive
25-49	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰	Smell Improved Inconclusive Reduced Sleep Needs
25-49	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹	Smell Improved Inconclusive
25-49	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹²	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue
	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue Complete Remission
	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³ Nicotine Patch ²¹⁴	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue
	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue Complete Remission
	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³ Nicotine Patch ²¹⁴	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue Complete Remission Broad And Major
10-24	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³ Nicotine Patch ²¹⁴ Bupropion ²¹⁵	Smell Improved Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue Complete Remission Broad And Major Broad
10-24	Treamid ²⁰⁶ Palmitoylethanolamide Co-Ultramicronized With Luteolin ²⁰⁷⁻²⁰⁸ Phosphatidylcholine ²⁰⁹ Aripiprazole ²¹⁰ Hochuekkito ²¹¹ Creatine ²¹² Casirivimab/Imdevimab ²¹³ Nicotine Patch ²¹⁴ Bupropion ²¹⁵ Methylphenidate ²¹⁶	Inconclusive Reduced Sleep Needs Reduced Fatigue Fatigue Complete Remission Broad And Major Broad Broad

	Minocycline ²²⁰	Orthostatic Hypotension
	Epipharyngeal Abrasive Therapy ²²¹	Cleared Viral RNA
Nutrients		
Trial Size	Treatment	Improvement
	Nutritional Supplements Plus Exercise222	Broad
	Ayurveda System Of Medicine ²²³	Diarrhea And Broad
50-99	Astragalus Root Extract ²²⁴	Fatigue
30-99	Marine Oils ²²⁵	Fatigue
	Endocalyx ²²⁶	Cardiovascular
	Glycocalyx Dietary Supplement ²²⁷	Cardiovascular
	Beet Juice ²²⁸⁻²²⁹	Fatigue And Sleep
25-49	Probiotics ²³⁰⁻²³¹	Inflammation
	Maraviroc And Pravastatin ²³²	Broad
10-24	Salmon Oil ²³³	Inflammation
10-24	Tinospora Cordifolia ²³⁴	Inflammation

Naltrexone is of unusual interest. Several review papers highlighted it as an important treatment though there were no large studies justifying their recommendations. Naltrexone is approved by the Food and Drug Administration (FDA) to treat both opioid use disorder (OUD) and alcohol use disorder (AUD).

These are treatments that had no human trials.

Table 8. No Human Trials.

Procedures		
Infrared light ²³⁵	Cell cultures	Two ten minute exposures led to 80% IL-6 reduction in gene assay.
Hyperthermia ²³⁶	Review/ hypothosis	Modulates necroinflammation.
Drugs		
Tocilizumab ²³⁷	Trial underway	Reduce inflammation
Baricitinib ²³⁸	Trial underway	Reduce inflammation
Peptide LTI-2355 ²³⁹	Cell cultures	Mitigated inflammation in the respiratory tract.
CB2R agonists ²⁴⁰	Hypothosis	Reduce inflammation
Ginkgolide B-loaded lubosomes And vesicular LNPS ²	41 Human cell cultures	May protect against cell death
SPIKENET, SPK ²⁴²	Mice	Reversed the development of severe inflammation, oxidative stress, tissue edema, and animal death. Recall, vaccines in humans didn't help.
Fermentable fiber ²⁴³	Hypothesis	Reduce autoantibodies
Polyphenols ²⁴⁴	Hypothesis	Reduce autoantibodies
Resveratrol ²⁴⁵	Hypothesis	Reduce gut microdome dysfunction
Boost nicotinamide adenine dinucleotide (NAD+) ²⁴⁶	Hypothesis	Reduce gut microdome dysfunction
Gamunex-C ²⁴⁷	Proposed trial	Broad relief
Paracetamol and Dexketoprofen Trometamol ²⁴⁸	Analytic technique	Broad relief when administered with rivaroxaban
Modafinil ²⁴⁹	Literature search	Broad relief
Kyungok-go ²⁵⁰	Proposed trial	Broad relief
Cyclobenzapring Hydochloride ²⁵¹	Company annoucement	Reduce pain and improved sleep
Ivabradine and midodrine ²⁵²	Review of 32 studies	Reduced brain fog
Omega-3 fatty acids ²⁵²	Review	Improve mental health
Aspartate or Asparagine ²⁵³⁻²⁵⁴	Hypothosis	Improve vision
Macitentan ²⁵⁵	Hamsters	Restored bone loss
Tanshinone IIA ²⁵⁶	Chemical evaluation	Inflammation
Epigallocatechin-3-gallate-palmitate ²⁵⁷	Cell culture	Neurological

Tuning Organelle Balance In Human Mesenchymal Stem Cell ²⁵⁸	Cell Study	Major mitochondrial production
L-carnitine ²⁵⁹	Theory	Fatigue
Niclosamide ²⁶⁰	Review	Broad
Larazotide ²⁶¹	Proposed trial	Broad
Ecstasy ²⁶²	FDA Vote	Too risky
Sodium Pyruvate Nasal Spray ²⁶³	Proposed trial of drug useful in flu	Broad
Nutrients		
Korean Herbs ²⁶⁴	Mice cell cultures	Decreased nitrous oxide levels in
Rolean Herbs-	viice cen cultures	some cell types.
Melatonin ²⁶⁵⁻²⁶⁸	Hypothesis -3, Literature search	Reduce inflammation
Flavonoids Nobiletin & Eriodictyol ²⁶⁹	Human cells	Reduced pathogen-stimulated
Flavonoids Nobiletin & Eriodictyoi-	ruman cens	release of inflammatory mediators.
Herbs ²⁷⁰	Safety test	Broad improvements
Vitamin B12 ²⁷¹	Hypothesis	Improve vision

7. What Should I Consider If I Don't Want to or Can't Go to a Long COVID Clinic?

Let's assume:

- 1. I believe I have Long COVID.
- 2. I have the typical broad symptoms such as brain fog and fatigue.
- 3. I have a fine GP who is not expert in Long COVID.
- 4. I can't get root cause diagnostic tests.

Then I would try Pascal Wager Long COVID broad treatments, that is those with a potential upside but no downside. These are the ones I would review with my GP.

- 1. Exercise—I would get a script to get physical therapy or use the Pace Me application
- 2. Oxygenation—I would try to get to a hyperbaric chamber but if I couldn't, I would do home oxygenation.
- 3. Improve Mental Health—I would get Cognitive Behavioral therapy
- 4. Spa & Hot Spring Bathing—Sure, why not! Fun and relaxing
- 5. Mediterranean Diet—It has been shown to be good for one's health, so why not?
- 6. Fasting diet, no sugar—I would try it as it would be good for my general health
- 7. Weight Loss—If I was overweight, definitely as it is good for one's health
- 8. Yoga—if I am healthy, I would pursue as part of my exercise program
- 9. Contracting and Relaxing Pneumatic Cuffs on The Calves, Thighs, and Lower Hip—I would consider it even though it was a small trial

I would check with my GP on the following therapeutics.

- 1. SSRI Inhibitors
- 2. Traditional Chinese Medicine
- 3. SIM01—Gut Microbiota-Derived Formula
- 4. Transcutaneous Nicotine
- 5. P2Y12 Inhibitor
- 6. Prospekta
- 7. Cyclobenzaprine Hydrochloride
- 8. Vortioxetine
- 9. Donepezil
- 10. Bufei Huoxue
- 11. Apportal
- 12. L-carnitine—mitochondrial dysfunction though not reported in the papers discussed here.
- 13. Q10—though the trials were uneven, it has been shown to be good for mitochondrial dysfunction.



Finally, I would discuss possible treatments for inflammation that have yet to have Long COVID treatment trials such as COVID hyperinflammatory treatments, e.g., baricitinib, anakinra, and tocilizumab; and rheumatoid arthritis treatments, e.g., NSAIDS and steroids.

8. Conclusions

Long COVID is nasty. It is the post disease consequence of COVID. COVID is not alone in having severe post pathogen infection consequences. Influenza, Ebola, Marburg, Dengue, and Lyme Disease are other infections with severe post infection consequences.

Long COVID symptoms lessen with time, but much slower than other human non-viral illness or surgeries. While there are no magic bullet treatments, there are treatments that offer relief for many people. With time, more should become available.

There are several treatments that were assessed by 300+ trials that had control groups, e.g., exercise and oxygenation. Interestingly, many papers did not have a control group and there were no trials of the 100+ treatments that directly addressed Long COVID's root causes such as inflammation and mitochondrial dysfunction.

If one has Long COVID's broad symptoms, it is best to go to a Long COVID Clinic at a large national hospital.

Given the huge role that inflammation and mitochondrial dysfunction play in Long COVID, I think research into how to treat them should be Long COVID treatment top research priority.

Acknowledgments: I would like to acknowledge the careful and thoughtful comments by Mitch Ericson, Neal Friedberg, Ann Martin and Dan Sanzione.

Appendix A. Summary of Long COVID Treatment Papers, Including Trial Sizes

		Procedures		Drugs		Nutrition			
		Distinct	Total	Distinct	Total	Distinct	Total	Distinct	Total Papers
		Treatments	Papers	Treatments	Papers	Treatments	Papers	Treatments	and Trials
Root cause	Inflammation	2	. 2	20	39	2		24	43
	Persistent								
	Infection			7	8			7	8
	Microclotting			2	3			2	3
	Autoantibodies	1	2					1	2
	Gut Microdome								
	Dysfunction	1	1	6	9	3	3	10	13
Broad		23	62	8	13	7	9	28	84
Treatment	Exercise	1	32		13	,		1	32
	Oxygenation	4	12					4	12
Post COVID,	onygonia iron	,							
COVID									
Treatments				8	13			8	13
Fatigue		6	9	8	8	2	4	16	21
Shortness of									
Breath		3	19	2	2			5	21
Sleep		1	1					1	1
Pain		2	3	1	1			3	4
Neurological								0	0
	Brain Fog	2	2	4	4			6	6
	Orthostatic								
	Hypotension			5	5			5	5
	Mental Health	6	7	9	10			15	17
	Loss of Smell								
	and/or Taste	6	10	3	3			9	13
	Impaired Vision					1	1	1	1
Gastro-									
intestinal				2	2			2	2
Diabetes				1	1			1	1
Cardiovascular		4	4	2	2	2	2	8	8
Musculo-									
skeletal		1	1	2	2			3	3
	Totals	58	123	90	125	17	21	155	269

		Trial Size							
			100-					Distinct	Total Papers
		300+	299	50-99	10-49	1-9	none	Treatments	and Trials
		Total	Total	Total	Total	Total	Total		
Root Cause	Inflammation	0	8	3	14	0	18	24	43
	Persistent								
	Infection	0	1	0	2	2	3	7	8
[Microclotting	0	0	1	1	1	0	2	3
	Autoantibodies	0	0	0	2	0	0	1	2
	Gut Microdome	0					40	10	40
	Dysfunction	0	0	1	2	0	10		13
Broad		12	19	13	27	7	6	28	84
Treatment	Exercise							1	
	Oxygenation							4	
Post COVID, COVID									
Treatments		5	1	0	5	0	2		13
Fatigue		1	3	7	6	2	2	16	21
Shortness of									
Breath		0	5	5	9	2	0	5	21
Sleep						1	0	1	1
Pain		0	1	0	1	1	1	3	4
Neurological								0	0
	Brain Fog	0	0	0	2	4	0	6	6
	Orthostatic								
	Hypotension	0	0	1	0	2	2	5	5
	Mental Health	4	4	5	1	0	3	15	17
	Loss of Smell and/or Taste	3	2	1	5	2	0	9	13
	Impaired Vision					1		1	1
Gastro-									
intestinal					1	o	1	2	2
Diabetes							1	1	1
Cardiovascular		1	1	5	1	0	0	8	8
Musculo-									
skeletal		1	0	0	1	0	1	3	3
	Totals	27	43	43	81	26	48	155	269

Appendix B. Summary of Long COVID Treatments and Control Groups

	Root Causes					
		Persistent			Gut Microdome	
Trial Size	Inflammation	Infection	Microclotting	Autoantibodies	Dysfunction	
300+	0	0	0	0	0	
Control group	0	0	0	0	0	
No Control Group	0	0	0	0	0	
100-299	8	1	0	0	0	
Control group	8	0	0	0	0	
No Control Group	0	1	0	0	0	
50-99	3	0	1	0	1	
Control group	2	0	0	0	1	
No Control Group	1	0	1	0	0	
10-49	14	2	1	2	2	
Control group	9	1	0	0	1	
No Control Group	5	1	1	2	1	
1-9	0	2	1	0	0	
Control group	0	1	0	0	0	
No Control Group	0	1	1	0	0	
none	18	3	0	0	10	
Control group	0	0	0	0	0	
No Control Group	18	3	0	0	10	

	Broad		
Trial Size	Treatment	Exercise*	Oxygenation*
300+	12	8	1
Control group	3	1	0
No Control Group	9	7	1
100-299	19	7	4
Control group	8	4	3
No Control Group	11	3	1
50-99	13	5	4
Control group	7	3	2
No Control Group	6	2	2
10-49	27	12	2
Control group	8	3	1
No Control Group	19	9	1
1-9	7	1	1
Control group	0	0	0
No Control Group	7	1	1
none	6	0	0
Control group	0	0	0
No Control Group	6	0	0
Total trial	84	33	12

^{*}Excluded from totals as included in Broad Treatment

	Post COVID, COVID		Shortness of		
Trial Size	Treatments	Fatigue	Breath	Sleep	Pain
300+	5	1	0		0
Control	3	1			0
No Control	2	0	0	0	0
100-299	1	2	5		1
Control	0	2	4		1
No Control	1	0	1	0	0
50-99	0	8	5		0
Control	0	7	3		0
No Control	0	1	2	0	0
10-49	5	6	9		1
Control	4	2	6		1
No Control	1	4	3	0	0
1-9	0	2	2	1	1
Control	0	0	0	0	0
No Control	0	2	2	1	1
none	2	2	0	0	1
Control	0	0	0	0	0
No Control	2	2	0	0	1
Total trial	13	21	21	1	4

	Neurological						
Trial Size	Brain Fog	Orthostatic Hypotension	Mental Health	Loss of Smell and/or Taste	Impaired Vision		
300+	0	0	4	3			
Control	0	0	3	2			
No Control	0	0	1	1	0		
100-299	0	0	4	2			
Control	0	0	2	1			
No Control	0	0	2	1	0		
50-99	0	1	5	1			
Control	0	1	3	1			
No Control	0	0	2	0	0		
10-49	2	0	1	5			
Control	0	0	0	0			
No Control	2	0	1	5	0		
1-9	4	2	0	2	1		
Control	0	0	0	0			
No Control	4	2	0	2	1		
none	0	2	3	0			
Control	0	0	0	0	0		
No Control	0	2	3	0	0		
Total trial	6	5	17	13	1		

	Post COVID, COVID		Shortness of		
Trial Size	Treatments	Fatigue	Breath	Sleep	Pain
300+	5	1	0		0
Control	3	1			0
No Control	2	0	0	0	0
100-299	1	2	5		1
Control	0	2	4		1
No Control	1	0	1	0	0
50-99	0	8	5		0
Control	0	7	3		0
No Control	0	1	2	0	0
10-49	5	6	9		1
Control	4	2	6		1
No Control	1	4	3	0	0
1-9	0	2	2	1	1
Control	0	0	0	0	0
No Control	0	2	2	1	1
none	2	2	0	0	1
Control	0	0	0	0	0
No Control	2	2	0	0	1
Total trial	13	21	21	1	4

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