LONG COVID

Epidemiology Educational Guide

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What We Know

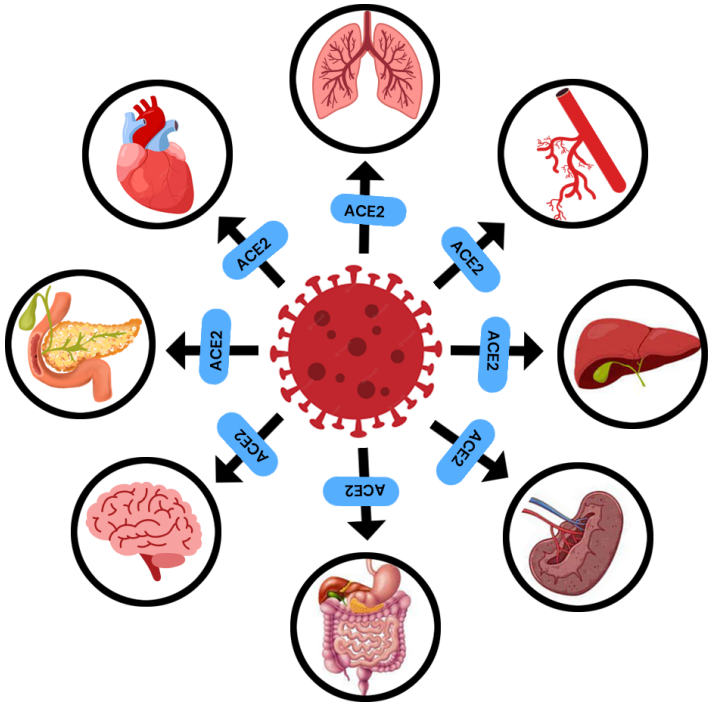
Current research shows that long COVID involves a multitude of new, returning, or ongoing symptoms that people experience more than six weeks after getting COVID-19. In some individuals, long COVID can last months or years and can ultimately lead to disability.

Additionally, the symptomology of long COVID can span the entire body. The symptoms that have been distinguished for long COVID include impairment to biological systems of the lungs, heart, brain, musculature, and reproductive or digestive tracts.

There are currently no laboratory testing methods for diagnosing long COVID. The primary measures for determining long COVID diagnosis, is time lapsed since COVID-19 infection and prevalence of disease symptomology.

Introduction:

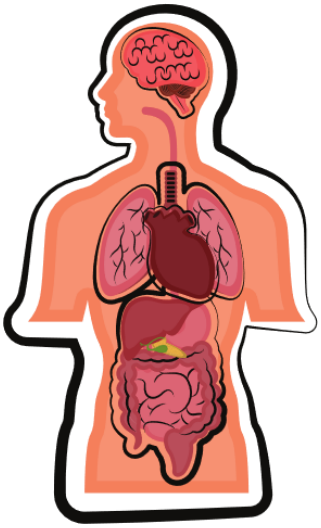
The severity of COVID-19 (SARS-CoV-2) can range from an asymptomatic infection to a fatal outcome. The virus can enter cells inside the body through angiotensin-converting enzyme 2 (ACE2) receptors. The ACE2 receptor is present in many cell types throughout the body including the oral and nasal mucosa, lungs, heart, gastrointestinal tract, kidney, liver, spleen, brain, and arterial and venous endothelial cells. Therefore, COVID-19 infection can cause damage to multiple organs simultaneously. The impact of COVID-19 infection has been damaging, however, the long term impact may be even more severe.



What is Long COVID:

Some individuals may have symptoms that last for four weeks or more after the initial infection, including those who had mild versions of the disease. The ongoing health concerns associated with COVID-19 are most frequently referred to as long COVID. However, it may additionally be referenced as long-haul COVID, post-acute COVID, post-acute sequelae of SARS CoV-2 infection (PASC), post COVID conditions, or chronic COVID.[1, 2]

Symptoms Associated with Long COVID:



There are a variety of symptoms associated with long COVID, which can impact a broad range of systems throughout the human body.

Respiratory: Most commonly reported respiratory symptoms include those of persisting shortness of breath, lingering cough, and difficulty breathing. Individuals may experience decreased respiratory muscle strength and decreased lung diffusion capacity for carbon monoxide (DLCO). Decreased DLCO, meaning decreased ability of the lungs to transfer gas from inhaled air to red blood cells. [21]

Digestive: Symptoms correlated to gastrointestinal disfunction include loss of appetite, acid reflux, dyspepsia (indigestion), irritable bowl syndrome, constipation, diarrhea, nausea, vomiting, and abdominal pain.[4,5]

Cardiac: Common symptoms related to cardiac health include palpitations (feeling heart beat rapidly), arrhythmia, and chest pain. Due to the impact of COVID-19 infection on the inner surface of veins and arteries, blood vessel inflammation can occur. This can lead to the damaging of small vessels and blood clots– which ultimately compromises blood flow to the heart or other parts of the body.

- **Type 1 Heart Attack:** typically caused by blood clots blocking hearts arteries, rare during or after COVID-19 infection.
- **Type 2 Heart Attack:** typically caused by increased stress on the heart, can be due to fast heartbeat, low blood oxygen levels or anemia– because heart muscles are not receiving adequate supply of oxygen in the blood to do the extra work. (Can be seen in elevated troponin levels in the blood). Type 2 heart attacks are seen more frequently after COVID-19 infection. [9, 10]

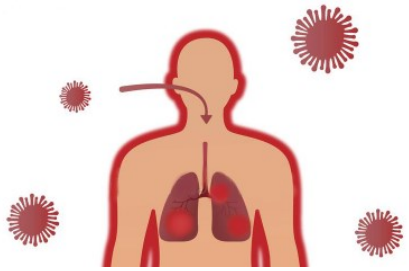
Neurological: Symptoms include difficulty thinking or concentrating (brain fog), headaches, sleep problems (insomnia), feeling of pins and needles, changes in smell or taste, depression and anxiety, and tiredness or fatigue that interferes with daily life. Symptoms that tend to get worse after physical or mental effort (post-exertional malaise). Cognitive difficulties include impaired ability to concentrate, speak, and remember. [8, 9]

Additional impacts include:

- Episodic disorders: epilepsy, seizures, etc.
- Movement disorders: abnormal involuntary movements, tremor, sudden jerks, contractions, Parkinson-like disease.
- Mental health disorders: Major depressive disorders, stress disorder, anxiety and psychotic disorders.
- Sensory disorder: hearing abnormality, vision abnormalities, loss of smell and taste, dizziness.

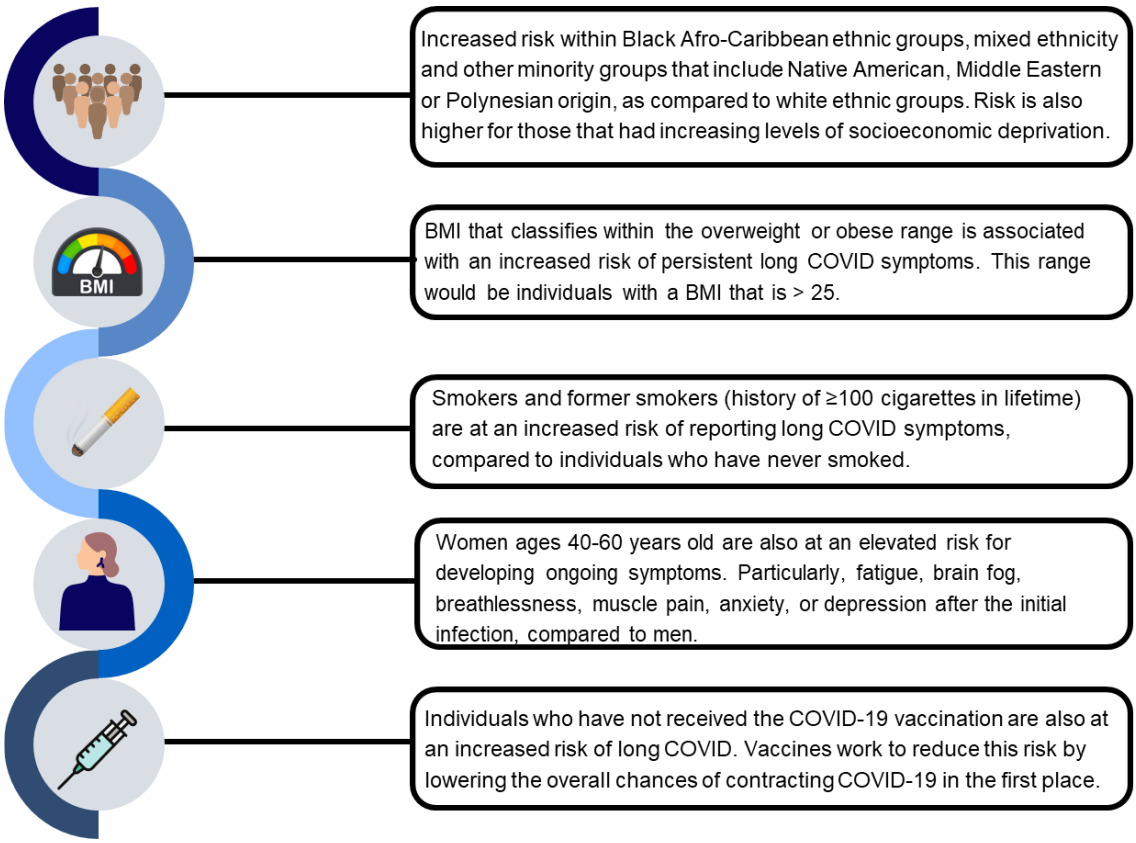
Other Symptoms: Joint or muscle pain, rash, hair loss, skin breakouts, changes in menstrual cycle, or autoimmune conditions with symptoms that last weeks or months after COVID-19 illness.

Biological Pathways Involved in Long COVID Symptoms: (4, 5, 8, 9, 10, 11, 12, 14)

System	Mechanism	Outcome
Neurological:	• Inflammation in multiple regions of the brain • Activation of coagulation: blood clots disrupting tissue blood flow and nerve communication	• Stroke, myelitis (nerve inflammation), Guillain-Barré syndrome (neurological disorder where immune system mistakenly attacks the body's own nerves)
Metabolic:	• Environmental factors: social isolation, temperature, humidity • Lymphatic system: vessels that drain toxins and waste from the tissues in the body may become congested	• Mitochondrial dysfunction (bioenergetic disorders); overall weakness • Fatigue
Sensory:	• The virus can invade the cells that play a major part in sense of smell and taste. This invasion will disrupt cell function	• Anosmia (loss of taste and smell)
Cardiovascular and Coagulation:	• The cells that make up the heart can become infected and coagulation (blood clotting) can occur, which resultingly can impair blood flow in the heart • Damages of the autonomic nervous system (which controls how fast and hard the heart pumps and the width of blood vessels)	• Heart attack and prolonged periods of chest pain • Increased resting heart rate
Respiratory:	• Lung fibrosis; thickening or scarring of organ tissue • The blood vessels of the lungs can become damaged. These vessels are necessary for the exchange of gases, adding oxygen, and removing CO2. Damage to these vessels puts increased stress on the lungs • Damages to the autonomic nervous system; impairs the mechanical reflex of the lung's ability to expand and contract	• Shortness of breath, coughing, wheezing, and dizziness 
Immune System:	• Mast cell activation syndrome (MCAS); Mast cells are part of the body's immune system. A type of white blood cell found in connective tissues in the body, such as under the skin, in nerves, and near blood vessels. In MCAS, mast cells release an inappropriate amount of histamine into the body	• Multi-system inflammatory syndrome (MIS-C) in children • Increased susceptibility to other infections and longer duration of illness and adverse health symptoms • Continuous cell-to-cell infection at a low level

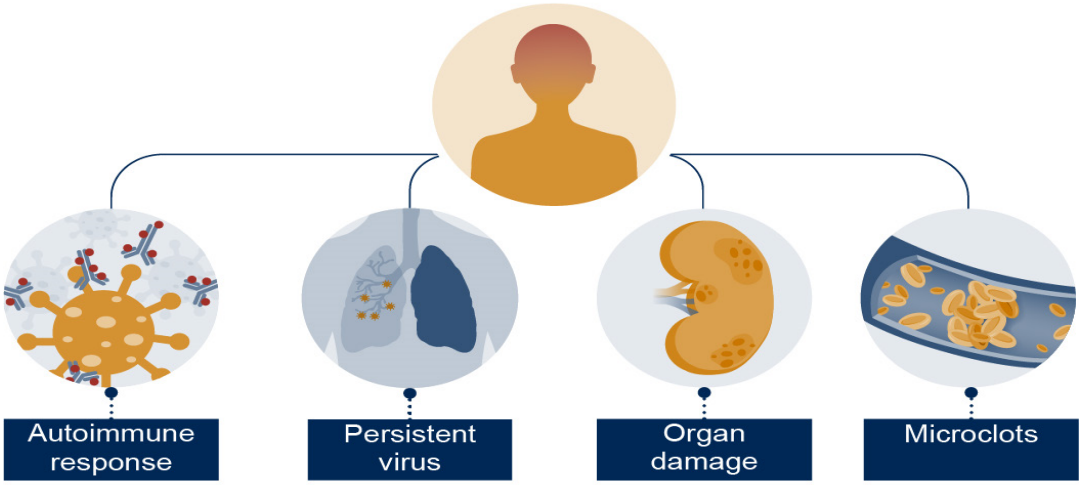
System	Mechanism	Outcome
Gastrointestinal:	• Cells along the intestinal lining become invaded by the virus, which leads to weakened or altered gut microbiome	• Overall GI dysfunction • Poor digestion, constipation, nausea, diarrhea, and bloating
Renal:	• Virus invades the cells that make up the kidney. This infection impacts the body's ability to filter excess water, salt, and waste products from the body • Microangiopathy; damage of the blood vessels within the kidney	• Kidney failure • Fluid and toxin build up in tissues (swelling)
Endocrine:	• Direct damage on the thyroid gland, leading to low thyroid levels • Viral invasion of cells that make up the pancreas, this impacts level of glucose and insulin in the blood • Lower levels of B12 and overall blood count (anemia).	• Irregular menstrual cycles associated with long COVID • Increased risk of developing diabetes
Musculoskeletal:	• Disruption of cells that make up muscle and connective tissue • Impact on circulation of oxygen and nutrients in bones. Inflammation of nerves and vessels within joints	• Reduced bone density/strength • Extended periods of joint pain and arthritis

Who is Most Susceptible to Long Covid: (3, 11)



How is Diagnosis Conducted:

Healthcare providers may use COVID-19 antibody tests in order to confirm previous infections, then rule out other conditions that may have similar symptomology. The primary distinguishing factors of long COVID include, increased autoimmune response, persistent viral load and symptomology, signs of organ damage, and chronic microclots [6,7].



Source: GAO analysis of medical literature. | GAO-22-105666

What Does Treatment Look Like:

Current treatment strategies are tailored to the **specific symptoms** patients are exhibiting. This may include existing approaches such as steroids or anti-inflammatory medications. There are multiple medicinal trials underway testing for therapeutics targeting long COVID.

Additionally, the University of Cincinnati Health Center has an active long COVID clinic that is working to best diagnose, treat, and educate patients in Cincinnati on how to best manage their long COVID related health concerns. The clinic utilizes a multidisciplinary team of health specialists that are collaborating to assess the broad range of symptoms associated with long COVID.

What are the Knowledge Gaps:

Individuals who are fully vaccinated and recovered from COVID-19 infection may still be at risk for long COVID. Despite symptoms being more mild for some individuals due to vaccination status, overtime the impact can become significant. There are no direct diagnostic tests for long COVID, however, current research efforts are looking into blood testing options. Additionally, long COVID is being researched as a potential autoimmune disease (AD). Due to the infection coinciding with disease onset and the appearance of autoantibodies.[20] Research efforts are still actively investigating this claim.

What Are Current Initiatives and Next Steps:

In April 2022, President Joe Biden issued a *Memorandum on Addressing the Long-Term Effects of COVID-19*, that called for two reports that address long COVID and the conditions that are associated with it. The first report that was released in August 2022, is The *National Research Action Plan on Long COVID*. This report provides information on the advances in current research and outlines a course for future study to better understand prevention and treatment of Long COVID. The second report also released in August 2022, was The *Services and Supports for Longer-Term Impacts of COVID-19*. This report provides resources for health care workers, and those effected by broader effects of COVID-19. The range of effects include mental health and substance use, and loss of caregivers and loved ones.

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This report is intended to provide more information about Long Covid and is not intended to be individual medical advice. If you have questions specific to your situation, contact your healthcare provider.