

**Testimony
of
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Before

**United States Senate Committee on Health,
Education, Labor and Pensions**

Hearing

**Addressing Long COVID: Advancing Research
and Improving Patient Care**

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Chairman Sanders, Ranking Member Dr. Cassidy, and members of the United States Senate Committee on Health, Education, Labor and Pensions:

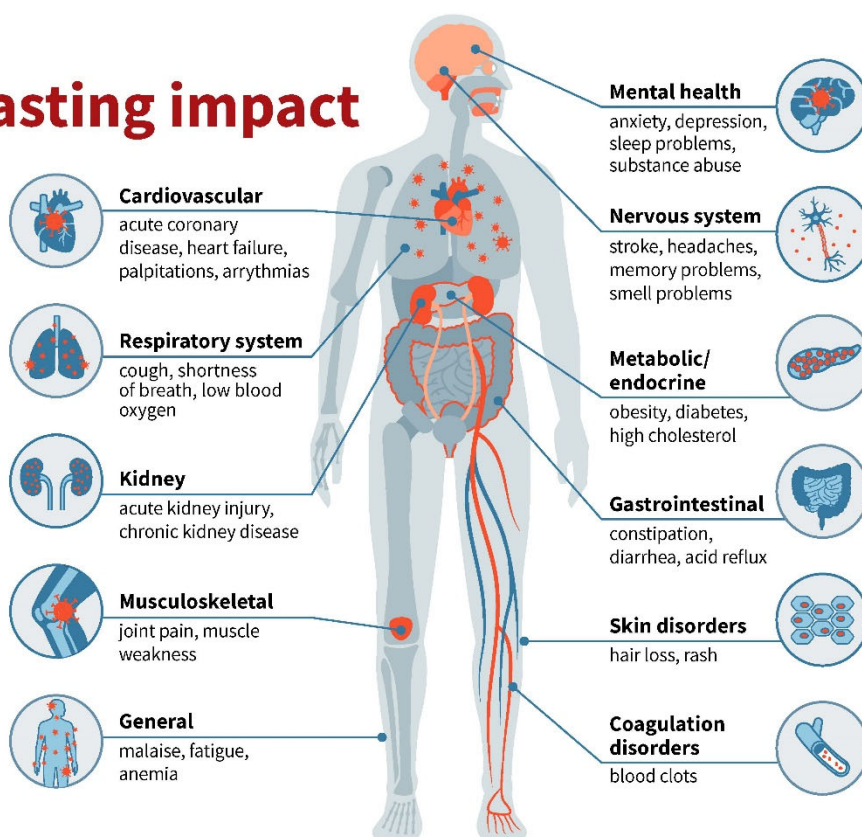
Thank you for the opportunity to testify today on the importance of addressing the needs of people with Long Covid.

I am a physician-scientist at Washington University in St. Louis. My team and I produced the first systematic characterization of Long Covid and the most widely cited research on Long Covid. We have been at the forefront of Long Covid research since the early days of the pandemic when patients started telling us that they are not fully recovering from COVID-19.

Long Covid represents the constellation of long-term health effects of COVID-19^{1,2}. Long Covid is a multisystem disorder that affects nearly every organ system including the heart³, the brain^{4,5}, the endocrine system⁶⁻⁸, the immune system⁹ and the gastrointestinal system¹⁰.

COVID-19: Lasting impact

WashU researchers link many diseases with COVID-19, signaling long-term complications for patients and a massive health burden for years to come.



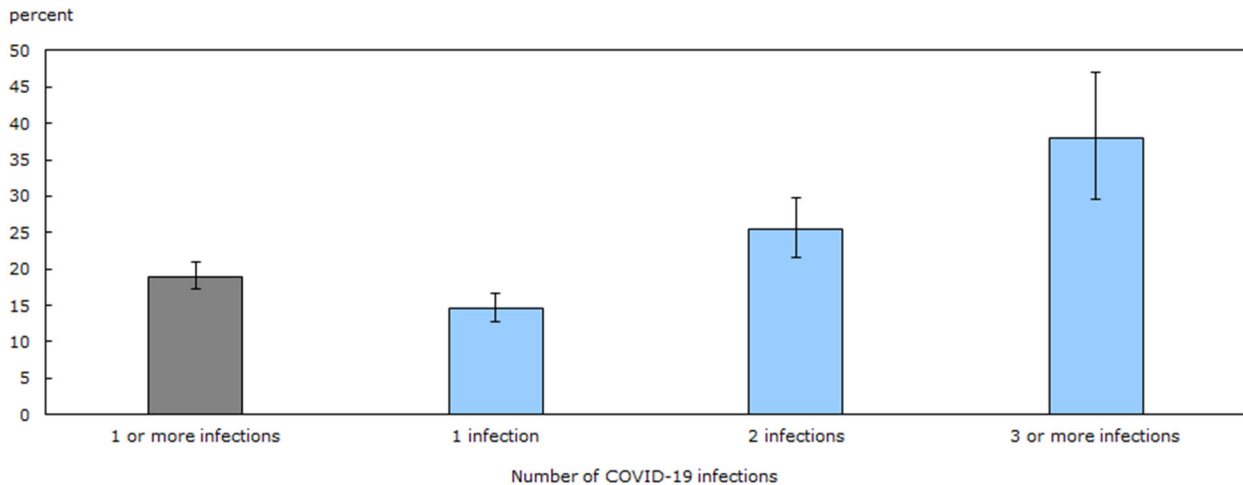
Long Covid affects at least 20 million Americans. It affects people across the lifespan – from children to older adults. It affects people across race, ethnicity and sex¹¹. The burden of disease and disability in Long Covid is on par with heart disease and cancer^{12,13}. Long Covid has wide and deep ramifications on the labor market and the economy^{14,15} – some estimates suggest that the toll of Long Covid on the U.S. economy is \$3.7 trillion^{14,15} – on par with the 2008 recession.

People can get Long Covid after reinfection^{16,17}. Research from the US and Canada is clear. Even if people managed to emerge unscathed after the first infection, they may get Long Covid

after reinfection^{16,17}. The national RECOVER program found 10% of people with one infection had Long Covid, compared to 20% of those with 2 or more infections.

The risks of getting Long Covid after reinfection are not known to the general public.

Percentage of Canadian adults with long-term symptoms, by number of self-reported COVID-19 infections, June 2023



Source: Statistics Canada, Canadian COVID-19 Antibody and Health Survey - Follow-up Questionnaire, 2023.

Likely because of viral persistence and other mechanisms, people can still develop problems related to the infection many months or even 2 years after the initial infection^{13,18,19}.

Recovery rates for many of the components of Long Covid are low. Some conditions that develop after COVID (e.g. heart disease, diabetes, etc.) are chronic conditions that last a lifetime. Some conditions including fatigue and brain fog seem to improve in a small fraction of people with Long Covid.

Between low rate of recovery and new cases from reinfection and breakthrough infection, Long Covid will continue to increase until we find better ways to prevent it and treat it.

The epidemiologic analyses demonstrating the wide-ranging multisystemic effects of Long Covid are complemented by careful imaging and autopsy studies showing structural abnormalities, prolonged inflammation and accelerated aging in human brains of people with even mild to moderate SARS-CoV-2 infection^{18,20-22} and persistence of the virus in brain and heart tissue of people with severe COVID-19¹⁸. Gut dysbiosis, dysfunctional hypothalamic-pituitary response (leading to inappropriately low levels of cortisol) and low serotonin induced dysfunction in vagal signaling have been suggested to play a role in the development of Long Covid^{23,24}. Immune dysfunction and mitochondrial failure (the energy generators that power each cell in the human body) have also been implicated in the mechanisms of Long Covid^{9,25}.

Prevention of Long Covid

The best way to prevent Long Covid is to prevent COVID in the first place. This requires a multilayered/multipronged approach. We must develop sustainable solutions to prevent repeated infections with SARS-CoV-2 and Long Covid that would be embraced by the public. This requires acceleration of development of oral or intranasal vaccines that induce strong mucosal immunity to block infection with the virus²⁶.

Ventilation and air filtration systems can also play a major role in reducing the risk of infection with airborne pathogens. We did an amazing job proofing our buildings against earthquakes that happen once every few decades or few centuries. Why don't we proof our buildings against the hazards of airborne pathogens. We can and should do this.

Vaccines partially reduce the risk of Long Covid in adults by 15-70% (~ mean 40%)²⁷; they partially reduce the risk of Long Covid in kids^{28,29}. The low rates of vaccine uptake in 2023-2024 winter season suggests that the public's appetite for boosters has declined dramatically. We need variant-proof vaccines that offer durable immunity (e.g. vaccine that lasts 5 years). People can then get their Covid-19 vaccines once every 5 years and be done with it.

Vaccines are safe and effective, but they are not free of side effects. The benefit of COVID-19 vaccines in reducing risk of severe COVID-19 illness, death and Long Covid outweighs the small risk³⁰⁻³². That does not mean vaccine side effects do not exist³³. We must recognize vaccine injury³³. We must understand how it happens and how to mitigate it. Understanding vaccine injury will not only help us produce safer vaccines, but it can also offer insights into the mechanisms of Long Covid.

Currently available antivirals may reduce the risk of Long Covid³⁴⁻³⁶, but their effectiveness seems to be weak. Also, we now are reliant almost exclusively on one antiviral (Paxlovid). Should the virus become resistant to Paxlovid³⁷⁻⁴⁰, it will become ineffective (we are putting our eggs in one basket). We must broaden the pipeline of antivirals and develop new ones that are more effective in preventing Long Covid.

Treatment of Long Covid

There are zero FDA approved medications for the treatment of Long Covid. This must change. People suffering from Long Covid need treatment yesterday. The ongoing and planned trials for Long Covid are too slow and too small (i.e. underpowered) to provide definitive answers.

We developed vaccines at warp speed. We are doing trials for Long Covid at snail speed.

We urgently need large scale trials to test a broad array of repurposed drugs and development of novel drugs to treat Long Covid.

This must be an all-hands-on-deck situation. This is not solely a U.S. Government problem.

We must identify and address the barriers that are preventing the private sector (pharmaceutical industry) from investing in trials for Long Covid (for example, build consensus around clinical trial endpoints that are acceptable to regulators).

Is COVID-19 unique in causing chronic illness (Long Covid)?

No.

SARS-CoV-2 is novel (was novel in 2019/2020) and the scale of the pandemic is certainly large. But the idea that a virus that produces acute infections can also cause chronic disease is not new. We just ignored it for 100 years.

Historical accounts of both the 1889-1892 (Russian flu) and 1918 Spanish flu pandemic show that many people suffered from long-term health effects including cognitive decline, debilitating fatigue and Parkinson's disease in the convalescent phase of the infection⁴¹⁻⁴⁶. Other viruses

including polio lead to chronic disease decades later; Epstein Barr virus (EBV) is known to lead to multiple sclerosis^{41,42,44,47}.

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a chronic debilitating multisystemic illness that is thought to be initially triggered by a flu-like illness^{2,48}. ME/CFS affects 4.3 million people in the U.S. (1.3% of the U.S. population)⁴⁹. These patients have been ignored and marginalized for decades.

Had we connected these dots (between acute infections and chronic disease) before the COVID-19 pandemic, we would have been in a much better place to address the challenge of Long Covid.

What do we learn from this?

If we learn one thing from this pandemic, we must recognize that “pandemics disable people”^{41,42} — that is acute infections can lead to chronic disabling disease. We call these Infection-Associated Chronic Conditions (IACC). These include Long Covid, ME/CFS and many other acute infections that lead to chronic disease.

Urgent and commensurate (proportional) response is needed

We don't go through an earthquake without dealing with its aftermath. We cannot live through the biggest pandemic of our lives without dealing with the aftermath. That aftermath is Long Covid. We must address the challenge of Long Covid.

The current research effort on Long Covid does not match the scale and the urgency of the problem. Research effort must be commensurate with the burden of disease caused by these infections. And it should be executed with a sense of urgency.

The U.S. should consider the establishment within the National Institutes of Health of an Institute for Infection-Associated Chronic Illnesses with a budget of at least \$1 billion per year to address the complexity and multisystemic nature of Long Covid, ME/CFS and other IACC. Because pandemics will continue to happen (and their frequency will likely be higher in the 21st century than in the 20th century), and because pandemics will likely produce in their wake droves of people with chronic disease and disability, understanding how infections cause chronic illnesses should also be a cornerstone of pandemic preparedness and resilience.

An NIH institute for the study of Infection-Associated Chronic Conditions will help us address the needs of Long Covid, other IACC and position us to be more optimally prepared for the next pandemic. I urge the U.S. Congress and the Executive Branch to work together to materialize this.

You have an historic opportunity to act. The lives of millions of Americans now and in the future depend on this.

Disclaimer: My employers had no role in developing this testimony. The contents of this testimony represent my views; they do not represent the views of my employers.

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