COLORADO
Lt. Gov. Dianne Primavera

2022

Report on Long COVID in Colorado

Office of Saving People Money on Health Care

Colorado's Office of Saving People Money on Health Care First Study Report on Long COVID and Post Viral Illnesses Caused by COVID-19, Pursuant to House Bill 22-1401

December 2022

> "
> I went from being a fit, active, successful and financially secure professional in the prime of life to a broken—and broke—person. COVID kills some people outright; many of us with Long COVID are dying, too—just very slowly and painfully.
> "
>
> - Chelsey B., 49 years old

January 3, 2023

The Honorable Governor Jared Polis
State Capitol
200 E. Colfax Ave., Rm. 136
Denver, CO 80203

CC:
Senator Kyle Mullica
Senator Dominick Moreno
Senator Rhonda Fields
Representative Lindsey Daugherty
Representative Dafna Michaelson Jenet
State Capitol
200 E. Colfax Ave.
Denver, CO 80203

Dear Governor Polis:

Please find enclosed the first annual report of the Office of Saving People Money on Healthcare ("The Office") on the impacts of Long COVID on the State of Colorado. C.R.S. §25-3-129 (1) requires an annual report be delivered to you each year, on or before January 1.

The Office was pleased to hire Dr. Mirwais Baheej as the Senior Policy Advisor on Long COVID and Post Viral Illness. Dr. Baheej began work on November 1, 2022, and has concentrated his attention on collecting data and developing recommendations on Colorado's response to and preparedness for the short and long term impacts of Long COVID.

As you are well aware, this is new territory and public health experts, scientists, providers and epidemiologists are all working to define Long COVID and understand its effects. Thus far, Dr. Baheej has been gathering information and building networks that will further his efforts by helping to develop baseline data and monitor the impacts of COVID-19 on Colorado's economy, workforce and medical and long term care needs. He also will work to assess the effect of Long COVID on healthcare affordability and other long term impacts, for example on educational attainment.

As far as we know, there are no other states undertaking similar work at this time although the White House has published two reports on Long COVID. We do hope to partner with the federal government as we move forward.

We appreciate the legislature's establishment of this position and look forward to establishing a framework for future work that will further the state's interest in developing infrastructure that will support and protect Coloradans impacted by Long COVID and other post viral illnesses.

Please do not hesitate to contact me should you wish to discuss this report.

Sincerely,

Dianne Primavera
Lt. Governor of Colorado

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Introduction:

This report is prepared pursuant to C.R.S. §25-3-129 (1), which charges the Office of Saving People Money on Health Care with exploring post viral illnesses caused by Post-Acute Sequelae of SARS-CoV-2 (PASC) or "Long COVID"', and its impact on health facility and public health system preparedness as well as on the mental, behavioral, physical, and financial health of Coloradoans. As the first annual report on this topic, this publication introduces the causes, symptoms, and impacts of long COVID based on currently available information. Using national and Colorado-specific data, the analysis includes a discussion of the prevalence of Long COVID in the United States and Colorado and its impacts on health and socioeconomic conditions of patients and communities. Finally, the report highlights federal initiatives to address Long COVID and outlines suggested areas for future study and exploration to save Coloradans money on health care. In time, this report will be followed by more in-depth analyses and policy recommendations that will aim to prepare the state to respond to the impacts of Long COVID on Coloradans.

Long COVID remains largely unknown, and it is too early to reach definitive conclusions about its impacts. However, initial data referenced in this report describes trends in order to inform future work. Patients with COVID-19 may experience long-term complications beyond four weeks from the onset of their first symptoms, including fatigue, post-exertional malaise, respiratory and cardiovascular symptoms, gastrointestinal symptoms, neurological symptoms, myalgias, cognitive impairment and difficulty concentrating, headache, rash, dysmenorrhea, anxiety, depression, and others. Risk factors may include severity of initial COVID 19 infection, hospitalization for COVID-19, women gender, older age, presence of underlying health conditions, and vaccination status, among others. Preliminary research suggests Long COVID may cause reduced exercise capacity and some forms of cognitive impairment. The burden of these experiences are estimated to already impact almost 7% of American adults, or 23 million people in the U.S, but more data is needed to understand whether there is a disproportionate impact by demographic factors. The data suggest that approximately 229,000 - 652,000 Coloradans may have been affected by Long COVID. Persistent symptoms can negatively impact quality of life and limit the ability to perform daily activities, including work. This can result in loss of employment and related benefits,increasing the risk of financial insecurity..

Research is underway to explore Long COVID's etiology, health and socioeconomic impacts, treatment, and disease management. A broad range of stakeholders, including the Federal Government, academic institutions and patient advocacy groups, are working to understand and plan for the impacts of this new phenomenon. Additional exploration of Long COVID's effects on health, disability status, workforce, healthcare costs, and affordability is needed. In order to leverage growing interest in Long COVID, Colorado should lead in developing comprehensive disease surveillance and data sharing systems to enable stakeholders to collaborate on further analysis to inform

prevention, treatment, and disease management. This is especially important in primary care contexts to ease access to care for patients and save people money on health care.

The Office of Saving People Money on Health Care is committed to contributing to the growing pool of knowledge that will inform future policies, programs, and strategies to benefit Coloradans. Moving forwards, the Office plans to develop multi-disciplinary partnerships with diverse stakeholders in order to further propel momentum towards understanding and coping with the impacts of Long COVID. This work will include expanding Colorado-specific, disaggregated data collection regarding disease prevalence, burden, and impact on affordability, long term care, behavioral health, labor and employment, education, and other post-viral illness experiences.

1.   What is Long COVID?
1.1.   Introduction

Coronavirus disease 2019 (COVID-19), the highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in significant morbidity and mortality around the world. With more than 6 million deaths worldwide, COVID-19 emerged as the most consequential global health crisis since the influenza pandemic of 1918 and has strained global health resources. The World Health Organization (WHO) officially declared the COVID-19 disease a global pandemic on March 11, 2020 warning the world of the alarming level of spread and its severity as well as its potential for catastrophic impacts. The WHO Secretary General called on countries to activate and scale up their emergency response mechanisms as well as build strategies to minimize its impacts through preventing infection and saving lives.

Since being declared a global pandemic, the COVID-19 virus has spread rapidly across the world given its highly infectious, unconventional, and ever-evolving nature. As per the WHO, as of December 15, 2022, there have been over 646.7 million confirmed cases of COVID-19 and 6.6 million deaths globally. As of December 13, 2022, over 13 billion vaccine doses have been administered worldwide. The U.S. has had a total of 99,826,698 confirmed cases and 1,087,013 deaths as of December 15, 2022, and is currently reporting more than 2,000 deaths each week, according to the CDC. The U.S. has experienced the highest total number of COVID-19 infections and related deaths, followed by Brazil and India. The U.S. reported COVID-19 cases surpassed 100 million on December 20, 2022; however, experts say this number is far less than the actual number of infections. This represents 15% of the nearly 655 million cases documented worldwide. With 1.09 million reported COVID-19 deaths, the United States also leads the world in the number of fatalities comprising about 16% of the total 6.7 million global COVID-19 deaths. The global case fatality rate for COVID-19 (defined as number of deaths due to COVID-19 divided by the total number of confirmed cases) has declined over time from nearly 5% at the beginning of the pandemic to 1.1% now. The case fatality rate in the U.S. is also 1.1%. Having around 330 deaths per 100,000 population, the United States is 16th in terms of COVID-19 deaths per 100, 000 population worldwide, while it is third among the 20 countries currently most affected by COVID-19 worldwide as per JHU CRC data. Colorado ranks 29th in the per-capita number of cases in the nation with 30,161 reported cases per 100,000 population which ranges from over 40,000 to 26,000 per 100,000 population in other states.

In Colorado, the first case of COVID-19 was detected on March 5, 2020. Currently as of December 15, 2022 there have been 1,719,778 cases and 14,444 deaths due to COVID-19 in Colorado as per the Colorado Department of Public Health and Environment's COVID-19 Dashboard. Colorado ranks 29th in per-capita number of cases in the nation with 30,161 reported cases per 100,000 population which ranges from over 40,000 to 26,000 per 100,000 population in other states.

Colorado has had a lower cumulative death rate compared to the national rate since the beginning of the pandemic and ranks tenth lowest in the nation in February 2022. The response to the pandemic became the primary focus of Colorado's governmental public health system, which scaled up quickly in terms of personnel, supplies, systems, and new technology. The advent of vaccines has offered a path to a more normal way of life as the safest and best protection against severe illness and hospitalizations. However, given the nature of the virus to evolve and create new variants, it is difficult to predict the level to which the population will gain and maintain immunity.

Different studies suggest that no one is entirely immune and individuals of all ages are at risk of contracting COVID-19 infection and developing mild to severe illness. However, patients older than 60 years and those with underlying comorbidities are at higher risk of acute COVID-19 and subsequent illnesses. COVID-19 patients have had a wide range of symptoms from mild symptoms to severe illness which may appear 2-14 days after exposure to the virus. According to the Centers for Disease Control and Prevention (CDC), common symptoms include fever, cough, shortness of breath or difficulty breathing, sore throat, fatigue, muscle or body pain, headache, loss of taste or smell, runny nose or congestion, nausea or vomiting, and diarrhea. Although the majority of COVID-19 patients are asymptomatic or experience mild to moderate symptoms, about five to eight percent of infected patients develop hypoxia, bilateral lung infiltrates, decreased lung compliance requiring non-invasive ventilation (NIV), or mechanical ventilatory support. COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations.

1.2. Long COVID Terminology and Definitions

Public discourse on COVID-19 has largely centered on those with severe symptoms or fatal illness. However, studies show that a growing number of patients with initially mild COVID-19 will experience prolonged symptoms, the profile and timeline of which remains uncertain. There are increasing reports of persistent and prolonged effects after acute COVID-19 similar to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics. A significant number of patients with COVID-19 experience prolonged symptoms, known as Long COVID. Patient advocacy groups, many members of which identify themselves as 'long haulers', have helped contribute to the recognition of post-acute COVID-19, a syndrome characterized by persistent symptoms and long-term complications beyond 4 weeks from the onset of symptoms. People call post-COVID conditions by many names, including: Long COVID, long-haul COVID, post-acute COVID-19, post-acute sequelae of SARS CoV-2 infection (PASC), long-term effects of COVID, and chronic COVID.

Few systematic studies have investigated the COVID-19 population to determine its burden and the symptoms or conditions that patients develop in different time frames after initial infection of COVID-19. The Lancet describes Long COVID as symptoms affecting multiple organs which range from cough and shortness of breath to palpitations, chest pain, joint pain, physical limitations, fatigue, depression, headache, and insomnia

which affect people of different age groups after COVID-19. Other researchers have defined it as a syndrome characterized by persistent symptoms or long-term complications of COVID-19 beyond 4 weeks from the onset of symptoms. Raveendran et al. classify Long COVID into two stages based on the duration of symptoms—post acute COVID where symptoms extend more than 3 weeks, but less than 12 weeks, and chronic COVID where symptoms extend beyond 12 weeks.

Long COVID: An Overview https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8056514/
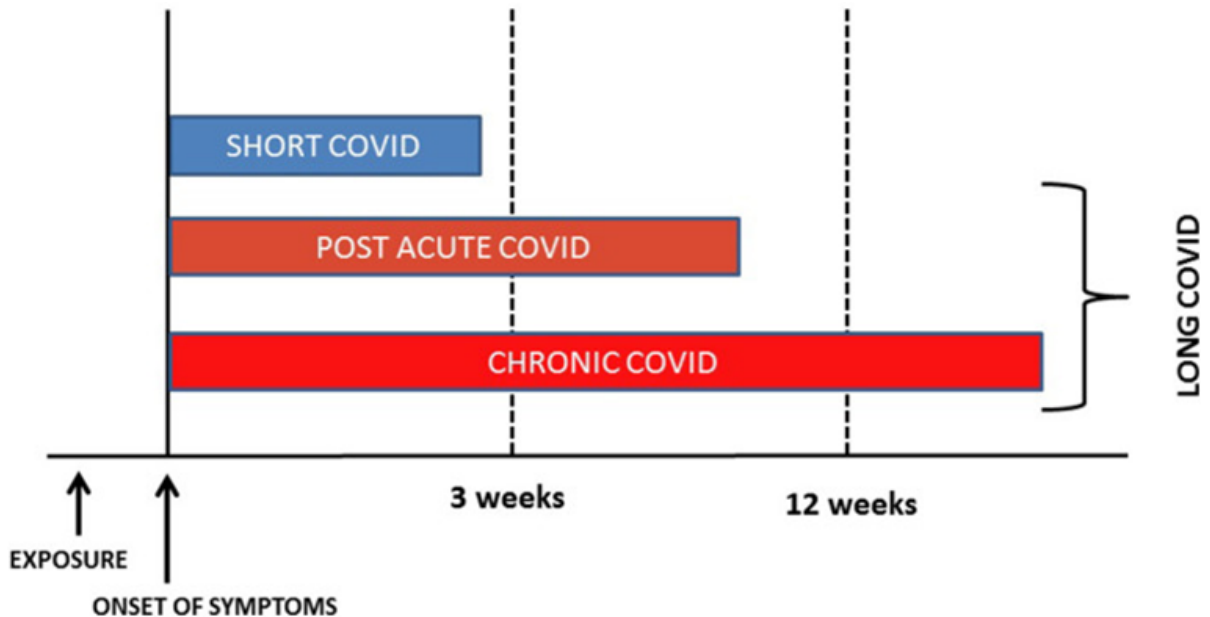
Below are definitions of Long COVID proposed by leading research institutions:
- The US Department of Health and Human Services broadly defines Long COVID as "signs, symptoms, and conditions that continue or develop after initial COVID-19 or SARS-CoV-2 infection. The signs, symptoms, and conditions are present four weeks or more after the initial phase of infection; may be multi-systemic; and may present with a relapsing– remitting pattern and progression or worsening over time, with the possibility of severe and life-threatening events even months or years after infection. Long COVID is not one condition. It represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes."
- The National Institute of Health (NIH) defines post-acute sequelae of SARS COV-2 infection as "ongoing, relapsing, or new symptoms, or other health effects occurring after the acute phase of SARS-CoV-2 infection present four or more weeks after the acute infection."
- The Centers for Disease Control and Prevention defines "Post-COVID Conditions" (PCC) as "a wide range of new, returning, or ongoing health problems people can experience four or more weeks after first being infected with the virus that causes COVID-19".
- The United Kingdom's National Institute for Health and Care Excellence (NICE) describes Long COVID as "signs and symptoms that develop during or after an

infection consistent with COVID-19, continuing for more than 12 weeks and are not explained by an alternative diagnosis".

- American Academy of Physical Medicine and Rehabilitation (AAPMR) defines Post-Acute Sequelae of SARS-CoV-2 infection (PASC) or Long COVID as "a condition that occurs in individuals who have had COVID-19 and report at least one persistent symptom after acute illness. AAPMR adds that Long COVID encompasses a constellation of varied and ongoing symptoms – even in the same patient across time – and may include neurological challenges, cognitive symptoms such as brain fog, cardiovascular and respiratory issues, fatigue, pain and mobility issues, among others."
- The World Health Organization, through the Delphi Consensus, has proposed a clinical case definition of Long COVID: "Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually three months from the onset of COVID-19 with symptoms and that last for at least two months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time."

All of these definitions conceptually coalesce around a definition of Long COVID as a set of persistent conditions or symptoms that develop after contracting COVID-19, indicating that it is a real disease and not merely a psychological effect of a viral illness. However, the precise medical definition and diagnosis of Long COVID is yet to be decided on by the medical community. Rather, at this time, Long COVID is a broad set of symptoms self-described by patients that last for a few weeks or months following COVID-19 infection.

International and national academics continue to contribute to the body of research surrounding Long COVID. Among articles reviewed, researchers are supporting the measurement and characterization, estimation of prevalence and incidence, understanding of the disease's mechanisms, and development of approaches in care and treatment of Long COVID. Furthermore, some research points to linkages between Long COVID and other post-viral illnesses.

Key Points

Long COVID or post-COVID conditions refer to a wide range of new, returning, or ongoing health problems people can experience more than four weeks after first being infected with the COVID 19 virus. A common feature of Long COVID is its relapsing nature, where individuals feel they have recovered from COVID-19 only to find symptoms return.

1.3. Risk Factors

Researchers are working to understand which groups of people are more likely to develop Long COVID, and why. A few factors are commonly associated with development of Long COVID based on the follow up of patients recovered from COVID-19. Presence of more than five symptoms as well as severity in the acute stage of illness, especially hospitalization or need for intensive care are associated with increased risk of developing Long COVID while study suggests that even individuals with mild symptoms at initial phase were noted to develop Long COVID. Women are twice as likely to develop Long COVID compared to men. Increasing age is another risk factor as study suggests that Long COVID patients are around four years older than those who have COVID-19 but do not exhibit symptoms of Long COVID. The presence of underlying health conditions also increases the risk of developing post COVID conditions. Experiencing multisystem inflammatory syndrome (MIS) during or after COVID-19 illness is another risk factor.

Researchers have studied whether vaccination and subsequent breakthrough infections affect risk for developing Long COVID. In one study using data from the Department of Veterans Affairs' national healthcare database, researchers found that vaccination partially reduces the risk of Long COVID compared to unvaccinated individuals. Another study using clinical data from the NIH Researching COVID to Enhance Recovery (RECOVER) Initiative, also found vaccination to have protective associations with Long COVID onset. These studies suggest that vaccination may remain a strategy for the prevention of Long COVID. Using data from the Department of Veterans Affairs again, researchers found an association between reinfection of COVID-19 and additional risks of death, hospitalization, and Long COVID, regardless of vaccination. Together, these studies suggest that vaccination may remain a strategy for the prevention of Long

COVID and strategies for reinfection prevention are required in reducing the overall burden of disease and death from Long COVID.

In April 2021, researchers from Harvard University and Columbia University published a literature review of persistent and prolonged effects after acute COVID-19 infection and proposed a framework for the identification of those at high risk for post-acute COVID-19 and their coordinated management through dedicated, interdisciplinary COVID-19 clinics.

In a Scottish population cohort study, six percent of people with lab-confirmed COVID-19 had not recovered and 42% had only recovered partially. The study showed symptomatic infection was associated with impairment across daily activities and poorer quality of life, and vaccination was associated with reduced risk of 7 of the 24 identified Long COVID symptoms.

Key Points

Studies show that Long COVID affects individuals of all health conditions, vaccination statuses, genders, races, and ethnicities. This includes individuals with and without disabilities and underlying health conditions and is regardless of the severity of the initial infection.

1.4. Pathophysiology and the Mechanism of Disease

The pathophysiology and mechanism of disease of Long COVID is not yet well understood. However, there are different theories based on preliminary findings. A number of mechanistic changes may underlie symptoms, including disruption to cellular energy production due to mitochondrial dysfunction, decreased oxygen supply due to coagulopathy and endothelial damage, ongoing viral activity associated with viral reservoirs, and immune dysregulation. Chansavath et al. found that Long COVID patients have increased concentrations of cytokines in serum at 8 months after infection, which indicates up-regulation of immune and inflammatory mediators. Akiko Iwasaki, Sterling Professor of Immunology at Yale University suggests some hypothesis such as persistent virus remnants in tissues, autoimmunity, dysregulated Gut Biome, and latent viral reactivation like Epstien Barr Virus while she believes "currently we are at the hypothesis stages and do not have concrete answers as to what causes Long COVID".

She argues that Long COVID is likely composed of multiple diseases under one umbrella but needs to be disentangled.

A study from University of California, San Francisco suggests that individuals with Long COVID symptoms tended to have reduced exercise capacity compared to individuals without Long COVID. This study recommends that reduced exercise capacity may not only be an objective measure that can be useful in potential therapeutic trials but also provide insight into the mechanisms of Long COVID. The value of exercise testing in understanding Long COVID is corroborated by a review by Astin et al. These researchers suggest that studies that utilize cardiopulmonary exercise testing can help identify the physiological mechanisms of Long COVID that cause exercise dysfunction. They also note that there may be other processes in play, such as ventilatory inefficiency, microclots and endothelial dysfunction, autonomic dysfunction, and mitochondrial dysfunction.

As for the cognitive symptoms of Long COVID, researchers are also attempting to understand the mechanism behind brain fog and other symptoms of cognitive impairment. In a systematic review, Monje and Iwasaki found at least six possible disease mechanisms such as neuroinflammation, autoimmunity, and direct brain infection. Much more research is needed to understand the underlying biological mechanisms of disease that causes Long COVID. Yet research is underway to characterize and differentiate the multiple possible etiologies.

1.5. Common Symptoms

A growing body of research exists describing that post-COVID conditions vary from mild symptoms to severe illnesses. Manifestation of post–COVID-19 can range from nonspecific symptoms such as fatigue, muscle weakness, and headache to specific conditions such as myocarditis, decreased glomerular filtration rate, and impaired lung function.

An online survey of people from 56 countries showed that the most frequent symptoms six months after viral contraction were fatigue, post-exertional malaise, and cognitive dysfunction. A Lancet study found that three-quarters of older patients still experienced debilitating effects six months after hospital discharge.

A cohort study which recruited patients from the Diagnostic and Severity markers of COVID-19 to Enable Rapid triage (DISCOVER) study in the UK showed that symptoms developed vary after COVID-19. 74% of the patients reported at least one ongoing symptom: 39% breathlessness, 39% fatigue and 24% insomnia. In terms of severity of COVID, 59% patients who had mild COVID-19 reported ongoing symptoms compared with 75% and 89% of patients with moderate and severe symptoms, respectively.
Another study showed that six months after acute infection, COVID-19 survivors had fatigue or muscle weakness, sleep difficulties, and anxiety or depression. A systematic review of 1.2 million individuals from 22 countries who had symptomatic COVID-19

infections estimated that 60% of them had cognitive problems, 51% had persistent fatigue with bodily pain or mood swings, and 35% had ongoing respiratory problems three months after symptomatic SARS-CoV-2 infection.

An earlier study, which included individuals with asymptomatic infections, suggested that Long COVID is specific to people with symptomatic infections. However, more research has been published suggesting that everyone has a risk of developing Long COVID. According to the WHO, Post COVID-19 conditions can arise irrespective of the person's age, the severity of the COVID-19 infection, or the circulating variant of the virus. Other studies show that Long COVID affects individuals of all health statuses, all vaccination statuses, all genders, all races and ethnicities, individuals with or without disabilities, individuals with or without underlying health conditions, and irrespective of severity of initial infection (i.e. symptomatic, asymptomatic, not hospitalized).

1.6. Potential Linkages Between Long COVID and Other Post Viral Illnesses

> **"**
> While COVID is new, post-viral illnesses are not. Long COVID patients are now finding themselves part of a larger community of chronic illness patients, many of whom have been seeking answers for years
>
> – Stephanie Whiteside, journalist
> Metropolitan Indianapolis Public Media **"**

Journalist Stephanie Whiteside covering COVID-19 for Metropolitan Indianapolis Public Media writes in article, "Long COVID Patients Join a Chronic Illness Community Seeking Answers"

Some researchers have found similarities or linkages between Long COVID and other post-viral illnesses. For example, the director of the National Institute of Neurological Disorders and Stroke (NINDS) stated that there is significant overlap between the symptoms of Long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

According to the CDC, ME/CFS is characterized by three core symptoms: greatly reduced ability to engage in usual activities, unrefreshing sleep, and post-exertional malaise. Additionally, diagnosis of ME/CFS requires the presence of one of the following symptoms: brain fog or worsening of symptoms while sitting or standing. Like Long COVID, the cause of ME/CFS is unknown and there is no known treatment. Studies suggest that up to 75% of ME/CFS cases are linked to viral infections.

"Many cases of Long COVID are effectively ME/CFS by another name", an article in the Atlantic claims. There are a limited number of physicians who specialize in ME/CFS in the U.S. whose knowledge could be vital to treatment and management of millions of similar patients — the long haulers.

Long COVID patients report prolonged symptoms with multisystem involvement and significant disability similar to patients with ME/CFS. A study found that more than 27% of survivors from another coronavirus, severe acute respiratory syndrome (SARS), had chronic fatigue syndrome four years after their initial infection. According to another study, many patients did not recover from systemic and neurological/cognitive symptoms after seven months of COVID-19 infection and have not returned to previous levels of work continuing to experience significant symptom burden.

The Office of Saving People Money on Health Care spoke with Coloradans suffering post viral illnesses including ME/CFS and Long COVID. Their experiences help us understand the immense human cost of these diseases that databases and statistics cannot convey.

Melissa, 54, describes her post COVID condition as follows:
"Four months after my initial symptoms in March 2020, my heart still raced even though I was resting. I could not stay in the sun for long periods; it zapped all of my energy. I had gastrointestinal problems, brain fog, extreme fatigue, ringing in my ears, and chest pain.

Today, it has been 33 months since I initially became sick and I am still not 100 percent. I experience slight progress each month, and I am not in the same debilitating condition that I was at six months. Now I have good days and bad days. I still get headaches, brain fog/memory issues, gastrointestinal problems, insomnia, and dizziness — to name a few — and am typically bedridden for at least two days a week."

Jane, who has been suffering from ME/CFS for 28 years, says:
"I have had chronic fatigue since 1994. At that time I was a single mom. I could no longer work, and after several months I ran out of money, became severely depressed, feeling my son would be better off without me, and attempted suicide. After that, my parents took myself and my son in, and we lived with them for four years. Miraculously, I went into remission, and was able to work 11 more years, until retirement. Then, the CFS came back. I no longer have to work, but the illness severely limits my participation in my grandchildren's lives, and my own daily life. I

can only be vertical for one to one and a half hours at a time, and then I have to rest for an extended period. I miss out on so much, and activities of daily living such as housekeeping, exercising, and socializing are severely limited".

Amanda, 35, describes her Long COVID experience as follows:

"*I tested positive for the 1st time on 11/11/20. Then again on 11/26/22. COVID has wrecked the person I thought I was before. I now have been forced to go back to full time work against my cardiologist recommendations. This was in fear of losing my job I've had for 7 years! I am 35 years old and have heart problems I've never had before. My cardiologist classified me as having severe POTS due to my heart rate raising 76 beats per minute when elevated from a laying down position to standing. I am newly engaged and scared to think about having children due to what COVID has done to my body. I am 100% a different person after COVID.*"

The [National Academies Institute of Medicine](#) has noted that once diagnosed with ME/CFS, patients can be treated with hostility, subjected to treatments that exacerbate their symptoms, and are "forgotten by society". This is attributed to skepticism that ME/CFS is a physiological, not a psychological illness rather than lack of treatment and disease management options. As a result, [Astin et al.](#) suggested that a better understanding of both ME/CFS and Long COVID and their linkage presents an opportunity to develop therapeutic interventions for both diseases. Nonetheless, better understanding of Long COVID, ME/CFS, and other post-viral illnesses is crucial to developing therapeutic approaches for individuals who are severely impacted by these conditions.

2. Prevalence of Long COVID in the US and Colorado

2.1. International context

The burden of Long COVID is difficult to ascertain. Because of the wide range of symptoms, the absence of a consistent case definition, and the lack of definitive diagnostic testing, there are a wide range of estimates of the burden of Long COVID among various populations. Although an ICD10 code[1] for Long COVID was introduced in [October 2021](#), researchers [suggest](#) that use of this code for research is limited until a standard definition is adopted. However, monitoring the use of the code can provide insight into how physicians are identifying Long COVID and the reliability of the diagnosis code as a measure of Long COVID burden.

British [population data](#) suggest that 22% to 38% of people with the infection will have at least one COVID-19 symptom 12 weeks after initial symptom onset, and 12% to 17% will have three or more symptoms. Similarly, 38% of individuals in the [UK REACT-2 Study](#) reported persistent symptoms at 12 weeks after contracting COVID-19 while 15% had three or more symptoms lasting more than 12 weeks. As a proportion of the UK population, the prevalence of self-reported Long COVID was greatest in people aged 35

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[1] International Classification of Diseases, Tenth Revision, Clinical Modification codes are commonly used in healthcare settings for disease tracking and insurance claim reporting

to 69 years, females, people living in more deprived areas, those working in social care, those aged 16 years or over who were not working and not looking for work, and those with another activity-limiting health condition or disability, UK Coronavirus Infection Survey data suggest.

In a study by Imperial College London, a random community sample of 508,707 people showed that all age groups were affected by Long COVID, including children, with an estimated 33,000 aged 2 to 16 years with Long COVID, of which 78% had symptoms for at least 12 weeks and 27% for at least one year. In a group of COVID-19 survivors discharged from a Rome hospital, 87% were still experiencing at least one symptom 60 days after their initial infection, a team of researchers reported. Further, results from an observational cohort study in the Netherlands suggests that Long COVID symptoms affect one in eight adults, some for two years. Around 10–20% of COVID-19 patients experience persistent symptoms following an acute SARS-CoV-2 infection according to WHO. As there have been approximately 650 million confirmed cases of COVID-19 worldwide, the burden is substantial.

A systematic review of 57 studies with 250,351 survivors of COVID-19 suggests that between 31% and 69% of COVID-19 patients suffer from post-acute sequelae of COVID-19 (PASC), The Institute for Health Metrics and Evaluation (IHME) at the University of Washington's School of Medicine conducted modeling which suggests that nearly 145 million people globally suffered from any of three symptom clusters of Long COVID during 2020 and 2021. Furthermore, modeling from IHME estimates that 6.2% of individuals who survived acute COVID-19 continued to experience at least one of three Long COVID symptom clusters: persistent fatigue with bodily pain or mood swings, cognitive problems, or ongoing respiratory problems.

2.2. US Context

The broader public health, social, and economic effects of Long COVID are unclear. Studies in the U.S. estimate that 10 to 30 percent of COVID-19 survivors develop Long COVID based on different definitions. If so, 10 to 30 million people in the U.S. may have developed Long COVID as of December 2022, which is a considerable number of Americans.

> 66
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> These are debilitating symptoms! Symptoms that are so far removed from the person I was before that I don't even know who I am anymore, and I mourn myself, my past life, and the future I thought I would have.
>
> - AnaKacia S., Colorado Long COVID Patient
>
> 99

According to the US Household Pulse Survey (HPS), 6.8% of all American adults are currently

experiencing Long COVID which accounts for 23 million Americans. 78.5% of adults who currently have Long COVID have an activity limitation from the condition while 23.1% of adults with Long COVID have significant activity limitations due to post COVID conditions. **An earlier version of** this survey shows that an estimated 7.5% of adults (1 in 13 adults in the U.S.) have Long COVID symptoms. Notably, the prevalence of Long COVID is greatest among younger, working-age adults.

According to a recent study published in the Journal of the American Medical Association by Perlis et. al., of the 16,091 individuals who had tested positive between February 2021 and July 2022, approximately 60% individuals who developed Long COVID were infected with the original virus strain that emerged in China, while over 17% infected by the delta variant and more than 10% caught omicron.

Long COVID is more common among women than men, studies suggest. According to Census Bureau Household Pulse Survey (HPS), 18% of women had Long COVID at some point during the pandemic, compared with 11% of men. Perlis et. al. also found that almost 18% of COVID-19 survivors who had symptoms for more than two months were women, while 10% were men. Further, a literature review of Long COVID shows that women are more likely than their male counterparts to experience both physical and psychological symptoms, including autoimmune rheumatic conditions, fatigue, and depression. Proportions of Long COVID in females and males among infected cohorts are estimated at 35% and 23% respectively as per HPS data from November 2022. Another study suggests that women have twice as much the risk of Long COVID as men. This has grabbed the attention of a growing number of media as well. All these and a growing number of research suggests that women make up a disproportionate share of Long COVID patients from almost 60% to two third.

Among children, those infected by COVID-19 have twice the rate of heart disorders and other systemic diseases compared to children without a history of COVID-19 infection. Researchers at the CDC evaluated nine persistent signs and symptoms and 15 conditions thought to be related to COVID-19 among nearly 800,000 children who were infected by COVID-19 and more than 2.3 million children who were uninfected. The data shows that previously infected children had higher rates of acute pulmonary embolism followed by myocarditis and cardiomyopathy (inflammation of the heart muscle and enlarged heart), venous blood clots, acute and unspecified kidney failure, type 1 diabetes, coagulation and hemorrhagic disorders, type 2 diabetes, and abnormal heart rhythms, compared with patients without previous history of COVID-19.

While the data on the disproportionate impact of Long COVID across different communities is incomplete, it is strongly believed that people of color are most likely to be affected by Long COVID as a result of their increased likelihood of contracting COVID-19, higher incidence of underlying health conditions, and reduced access to healthcare. Moreover, bisexual and transgender communities are believed to be mostly affected by Long COVID due to their lower access to healthcare and stigma associated

with [gender or sexuality](). Data also suggests that the highest rates of Long COVID are seen in the most economically deprived areas as social deprivation increases, the prevalence of LONG COVID increases. However, socioeconomic disparities of rates of Long COVID needs to be further explored as this is an area that warrants further research and intervention.

Key Points

Studies in the U.S. estimate that 10 to 30 percent of COVID-19 survivors develop Long COVID based on different definitions. If so, 10 to 30 million people in the U.S. may have developed Long COVID as of December 2022.

2.3. Prevalence of Long COVID in Colorado

Below is an estimate of the burden of Long COVID in Colorado which is provided by the Disease Control and Public Health Response Division within the Colorado Department of Public Health and Environment (CDPHE), with assistance from the Center for Health and Environmental Data. The purpose is to use published data about the rate and duration of Long COVID to provide an estimate of the likely burden of Long COVID in Colorado.

2.3.1. Methods

This analysis followed methods originally developed by [Chen et al.]() and published in the Journal of Infectious Disease in 2022. All data was obtained from publicly available sources and published literature. No proprietary data was used.

To estimate the burden of Long COVID in Colorado, first the total reported probable and confirmed cases of COVID-19, COVID-19 hospitalizations, and deaths among COVID-19 cases were extracted from CDPHE's [COVID-19 data website](). Data was accessed on December 7, 2022. The number of cases who were not hospitalized was obtained by subtracting the number of hospitalizations from the total number of cases; similarly, the number of hospitalizations which did not result in deaths was obtained by subtracting the number of deaths among cases from the number of COVID hospitalizations.

Next, the overall count for non-hospitalized cases and hospitalizations was divided into age and gender groups based on percentages on the CDPHE website. Non-hospitalized cases and hospitalizations were classified as pediatric (0-19 years), adult (20-59), and older adult (60 and older). Adult and older adult non-hospitalized cases (but not hospitalizations) were subdivided into male and female gender categories. Hospitalized cases were not subdivided by gender. Cases with unknown age or gender were not included.

Long COVID rates were derived from two sources:
- Rate estimates and ranges published in peer-reviewed meta-analyses. These included Chen et al. for adults and Lopez-Leon et al. for pediatric estimates.
- Published CDC rate estimates.

Rates among older adult cases and hospitalizations were extrapolated from rates among adult cases using a factor of 1.331, following data about the risk of Long COVID by age and assuming a median adult age of 40 and median older adult case age of 70.

Duration estimates were used to convert rate into person-days of Long COVID disease burden. Duration estimate methods differed between the two data sources (meta analyses and CDC rate estimates).

For the estimates provided using the meta analysis, different data sources were used for children and adults. For children, duration of symptoms was based on literature from Borch et al. For adults, duration estimates provided by Chen et al. were used. For both data sources, duration estimates were not broken out by hospitalized vs non-hospitalized.

The CDC does not provide estimates for duration of symptoms, but instead provides point rate estimates for non-hospitalized individuals at various time frames. A linear estimate was used to identify the time point when 50% of non-hospitalized individuals with symptoms at 30 days would have become asymptomatic. No such extrapolation was possible for hospitalized patients; the CDC only provided a single point rate estimate of 180 days, which was used as symptom duration.

Estimates of true case rates (using either modeling data or a fixed case ascertainment bias estimate) were not used. As published literature about Long COVID rates almost exclusively considers individuals with a positive diagnostic test, including individuals without a positive diagnostic test would reduce the applicability of published rate estimates to our denominator. Individuals who did not obtain testing may be more likely to have a milder initial infectious course than those who were tested, and thus less likely to develop Long COVID. On the other hand, some individuals who test positive using a home test may not seek confirmatory testing, regardless of how serious their illness may have been. These latter individuals would be classified as a "suspect case" and would not appear in the data used for this analysis if they were not hospitalized.

Burden of Long COVID
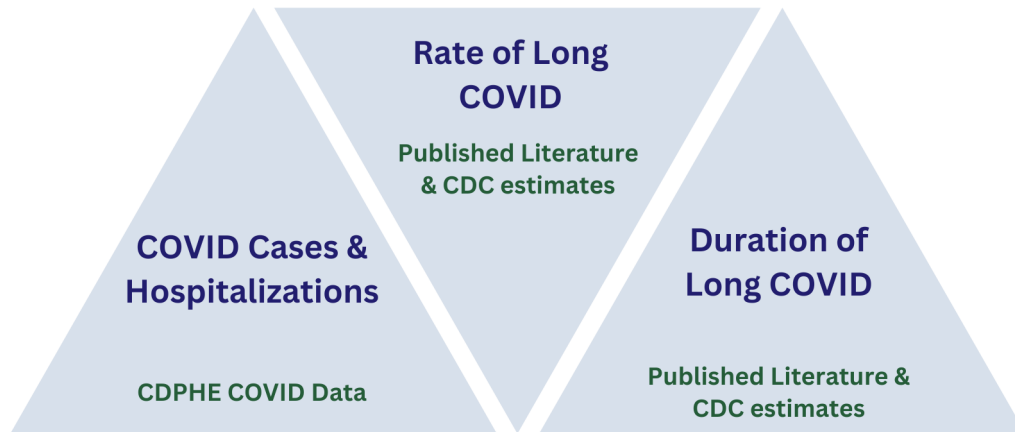
Summary of methods for burden estimation

2.3.2. Results

The following three tables show the total number of Coloradans that contracted COVID-19 segregated by age, gender and hospitalization, rate and total burden estimate of Coloradans affected by Long COVID per literature and CDC estimates respectively.

A total of 1,648,184 reported cases of COVID-19 were included in the analysis of total COVID burden. Age and gender breakdown is shown in below table:

Age Group	Gender and Hospitalization Status	Count
Pediatric (0-19 years)	Non-hospitalized	324,402
	Hospitalized	2,888
Adults (20-59 years)	Non-hospitalized Female	497,470
	Non-hospitalized Male	543,139
	Hospitalized	27,081
Older adults (60+)	Non hospitalized Female	107,436
	Non-hospitalized Male	117,910
	Hospitalized	27,859
Total		**1,648,184**

Rate estimates using data from published literature are shown below:

Age Group	Gender and Hospitalization Status	Proportion of COVID 19 case resulting in Long COVID (range)	Number of Persons Affected
Pediatric (0-19 years)	Non-hospitalized	25% (18% - 33%)	81,879 (58,944 - 107,117)
	Hospitalized	29% (18% - 81%)	843 (515 - 2335)
Adults (20-59 years)	Non-hospitalized Female	43% (35% - 63%)	213,912 (174,115 - 313,406)
	Non-hospitalized Male	37% (25% - 51%)	200,961 (135,785 - 277,001)
	Hospitalized	54% (44% - 63%)	14,624 (11,916 - 17,061)
Older adult (60+)	Non hospitalized Female	57% (47% - 84%)	61,489 (50,049 - 90,088)
	Non-hospitalized Male	49% (33% - 68%)	58,067 (39,235 - 80,038)
	Hospitalized	72% (59% - 84%)	20,023 (16,315 - 23,360)
Total			**651,798 (486,872 - 910,407)**

Rate estimates and total burden using CDC data are shown below:

Age Group	Gender and Hospitalization Status	Proportion of COVID 19 case resulting in Long COVID	Number of Persons Affected
Pediatric (0-19 years)	Non-hospitalized	13%	43,145
	Hospitalized	30%	866
Adults (20-59 years)	Non-hospitalized Female	13%	66,164
	Non-hospitalized Male	13%	72,237
	Hospitalized	30%	8,124
Older adult (60+)	Non hospitalized Female	13%	14,289
	Non-hospitalized Male	13%	15,682
	Hospitalized	30%	8,358
Total			**228,866**

Summary

Although direct measurement of Long COVID burden in Colorado is not currently possible, the best available estimates place the burden at between **228,000 and 651,000** affected Colorado residents through November 2022. The reasons for this range in estimates include

variable symptoms and duration, lack of consistent diagnostic criteria, and variability between different study populations.

Discussion

Rate calculations - based on publicly available data, published literature, and CDC estimates - provided a range for the burden of Long COVID in Colorado, ranging from 16.9 million to 39.4 million person-days, affecting as much as 15% of Colorado's population.

The existing literature suggests that the majority of those affected by Long COVID eventually recover without specific therapies. This is consistent with our findings, as Long COVID hospital encounters peaked following a peak in COVID cases and became less frequent as time passed, potentially reflecting recovery from the condition. This correlation is also seen in other published data based on national data sets. However, even a small proportion who never return to their prior state of health presents a tremendous burden of disability and poor health. The fraction of individuals who fall into this latter category is difficult to estimate with available data.

This problem of Long COVID-related disability has reached a national scale such that HHS issued "Guidance on 'Long COVID'" as a Disability under the ADA, Section 504, and Section 1557 as early as July 2021. The magnitude has likely only grown in magnitude in the subsequent years as more have been infected by COVID and developed Long COVID.

CO APCD data on Long COVID

In addition to the Long COVID burden estimates, we asked the Center for Improving Value in Health Care (CIVHC) to provide us with an overview of the number of Coloradans diagnosed with long COVID using the ICD 10 code U09.9 from the **Colorado All Payer Claims Database** (CO APCD) dataset. CIVHC provides public, HIPAA-compliant analyses and data sets using claims information submitted by payers to the CO APCD. ICD 10 code U09.9 which is a diagnostic code for Long COVID was introduced by the CDC on Oct 1, 2021.

Below is an overview of distinct insured Colorado residents diagnosed with a post-infectious condition after COVID-19 by CIVHC. These diagnoses are described by age, gender, race/ethnicity, and county of residence. This analysis includes members with a long COVID diagnosis on or after October 1, 2021 (when the ICD-10 long COVID code was implemented). Claims from October 1, 2021 through August 31, 2022 were included (see data limitations below for more details on claims runout and Medicare FFS claims). This analysis includes Colorado residents with Commercial, Medicaid or Medicare FFS or Medicare Advantage coverage. Claims with a diagnosis code (ICD-10) of U09.9 are included. Payer type (i.e. Commercial, Medicare Advantage, and Medicaid) is assigned based on the insurance product type submitted on the medical claim. Colorado County is assigned based on the member's county of residence at the time of first diagnosis.

Data Limitations: This analysis includes claims from October 1, 2021 (when the ICD-10 long COVID code was implemented) through August 31, 2022 for Medicaid, Medicare and commercial payers in the CO APCD. Due to claims submission run-out, however, not all claims paid through August are currently in the data warehouse, and therefore counts may be underrepresented. In addition, Medicare Fee-for-Service (FFS) claims are underrepresented with current submissions only available from 10/1/2021 to 12/31/2021. Finally, breakout categories (age groups, county of residence, etc.) may not add up to the total due to unknown or missing data in the data warehouse (i.e. no date of birth or sex assignment).

Total Unique Coloradans with a Long COVID Diagnosis, *All Payers, 10/1/2021-8/31/2022
16,072

By Age at time of first diagnosis	
0-9	253
10-20	529
20-29	1,130
30-39	2,184
40-49	2,624
50-59	2,858
60-69	3,110
70-79	2,233
80+	1,150

By Sex		
Female	10,182	63%
Male	5,888	37%

Data by race/ethnicity and by geography can be found in Appendix 2.

Colorado APCD data shows that a total of **16,072 individuals** were diagnosed with long COVID in Colorado from October 1, 2021 to August 31, 2022. Despite the data limitation discussed above and the time frame that only includes data for 11 months and misses the data from the onset of COVID 19 to Oct 1, 2021 (17 months), which indicates that the data is not representative, yet the count could be an indication that long COVID has hit a greater number of Coloradans.

Having reviewed the Long COVID patients data from different sources such as University of Colorado Anschutz Medical Center's Post-COVID 19 Clinic, the National Jewish Health's Center for Post-COVID Care and Recovery, the Kaiser Permanente Colorado EHR on Long COVID, and CIVHC's CO APCD to estimate the burden of Long COVID in Colorado, it is evident that women are disproportionately affected by long COVID in Colorado which

corresponds to the national ratios discussed earlier in this section. The proportion of women with Long COVID ranges from 62% to 67% of total Long COVID cases across different data sources in Colorado. This is an area that we plan to study in depth to inform future policies and ensure equity.

The future of the burden of Long COVID is uncertain. It may be that better awareness and understanding of the disease process leads to improved therapies and reduced burden of disease. Similarly, changes in COVID incidence and the protective effect of vaccination against Long COVID symptoms may cause Long COVID rates to decline. Alternatively, continued circulation of COVID-19 may continue to lead to new cases of Long COVID, including among individuals who may never recover completely. The risks associated with reinfection are also unknown, and may cause a recurrence of symptoms among previously affected individuals.

Key Points

Although direct measurement of Long COVID burden in Colorado is not currently possible, the best available estimates place the burden at between 228,000 and 651,000 affected Colorado residents through November 2022. The range in estimates is due to variable symptoms and duration, lack of consistent diagnostic criteria, and variability between different study populations. The rate of new Long COVID diagnosis varies over time with the overall rate of new COVID infections.

3.   Impacts of Long COVID
3.1.   Impacts on Physical, Mental, and Behavioral Health

Acute COVID-19 affects multiple organ systems, including the respiratory system, digestive system, kidneys, heart, and brain. The long-term clinical consequences of COVID-19 are still poorly understood and are collectively termed post-acute sequelae of SARS-CoV-2 infection (PASC), or Long COVID as discussed earlier. The symptoms associated with Long COVID vary widely, and include fatigue, post-exertional malaise (feeling worse after exercise or exertion), respiratory and cardiovascular symptoms, gastrointestinal symptoms, neurological symptoms, myalgias (muscle aches and pains), brain fog, cognitive impairment and difficulty concentrating, headache, rash, dysmenorrhea (painful menstruation), and others. Long COVID is more likely to occur among people who had more severe COVID-19, were

unvaccinated, or had underlying health conditions prior to COVID-19. Below is an illustration of Long COVID symptoms by Lopez-Leon et al.
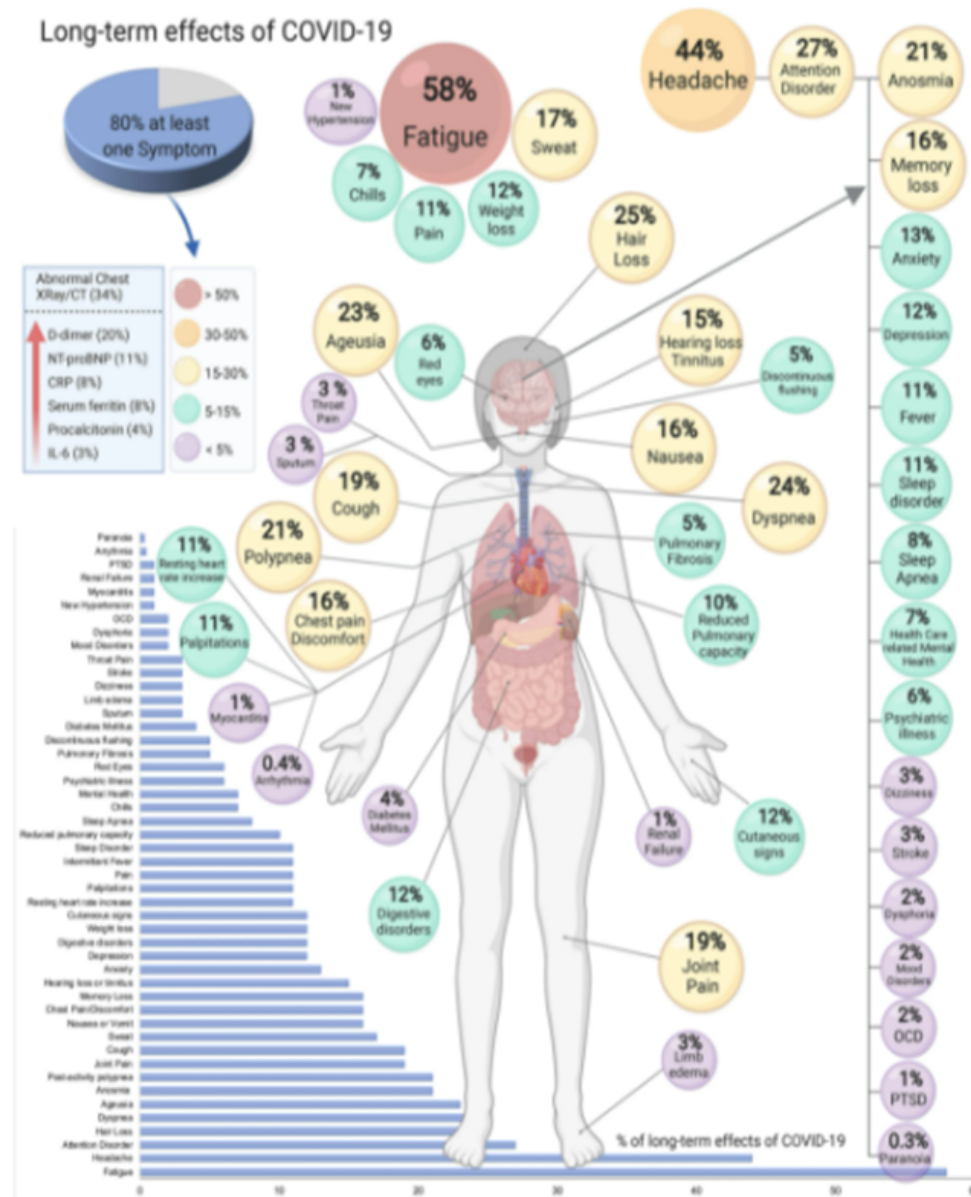
Long-term effects of coronavirus disease 2019 (COVID-19). The meta-analysis of the studies included an estimate for one symptom or more reported that 80% of the patients with COVID-19 have long term symptoms. CRP C reactive protein, CT computed tomography, IL-6 Interleukin-6, NT-proBNP (NT) pro hormone BNP, OCD Obsessive Compulsive Disorder, PTSD Post-traumatic stress disorder. This figure was created using Biorender.com.

Source: Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C. et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. Sci Rep 11, 16144 (2021). https://doi.org/10.1038/s41598-021-95565-8

Patients may have organ damage that can persist long after the acute phase of the infection has passed. A systematic review of 124 studies published earlier this year, found major organ damage is a common outcome in studies of COVID-19 patients after leaving the hospital. Prevalence of new-onset respiratory disease ranges between 2%

and 22% while prevalence of dyspnoea was higher at 64%. Some were at greater risk of new issues like stroke after being discharged. Compared to controls, COVID-19 patients were also at higher risk of new cardiovascular disease outcomes such as acute myocardial infarction, coronary disease and heart failure. Study showed that the prevalence of acute kidney injury, new-onset chronic kidney disease, new onset of diabetes, gastrointestinal diseases and new-onset chronic liver disease, among other organ systems, were higher in COVID-19 cohorts than in non-COVID control cohorts. In an editorial, the Lancet Diabetes & Endocrinology called for large, well-controlled epidemiological studies with follow-up periods of greater than 1 year in order to clarify any association between COVID-19 and metabolic complications, including new-onset diabetes.

Further, emerging data describe a potential for developing lingering symptoms following COVID-19 infection even among those who do not require hospitalization. As a result of the COVID-19 pandemic, there appears to be an increased number of people with disabilities. The link between Long COVID and disability is an emerging area and more study is necessary in order to explore the impact of Long COVID on short and long term disability.

A meta-analysis of 38 studies reported that exercise capacity was reduced among individuals with COVID-19 symptoms more than 3 months after infection. An earlier US study found that only 65% of COVID-19 patients had returned to their previous level of health 2-3 weeks after a positive test. Another study found that more than 80% of patients are not back at their baseline at least 2 weeks after their illness. It is evident that long-term complications of COVID-19 are increasingly being recognized and are associated with increased morbidity.

Nevertheless, Long COVID remains an area of ongoing research and investigation. The pathophysiologic mechanisms which lead to the condition are not well understood, and the best course of treatment is still being investigated. It is not known if Long COVID represents a single entity or is a combination of several distinct pathologies (see Appendix 1).

The symptoms associated with Long COVID vary widely, most commons include fatigue, post-exertional malaise (feeling worse after exercise or exertion), respiratory and cardiovascular symptoms, gastrointestinal symptoms, neurological symptoms, myalgias (muscle aches and pains), brain fog, cognitive impairment and difficulty concentrating, headache, rash, dysmenorrhea (painful menstruation). There are over 200 symptoms patients are reporting related to Long COVID.

3.2.   Socio Economic and Workforce Impacts

In addition to poor health, disability and morbidity, emerging studies confirm that Long Covid also has social and economic costs. While the magnitude of health and economic impacts is unknown, it is estimated to be significant.

British population data suggest that 12 weeks after initial symptom onset, 22% to 38% of people with the COVID-19 infection will have at least one symptom, and 12% to 17% will have 3 or more Long COVID symptoms. One in five Americans who survived COVID-19 still suffer from Long COVID and have to deal with the conditions according to a large study from the CDC published early this year. Another study found that among 200,000 COVID-19 survivors, one-third experienced neurological or psychological symptoms such as anxiety, depression, post-traumatic stress disorder, and psychosis within 6 months of initial infection. These persistent conditions impact the life of individuals and limits the ability to perform daily activities including work. Individuals have also said that Long Covid symptoms interfere with childcare, exercise, and social activities.

The UK Coronavirus Infection Survey published in December 1, 2022 (which contains data from 2.2 million self-reported Long COVID individuals), suggests that Long COVID symptoms adversely affected the daily activities of 75% of participants, while 17% reported very limited ability to undertake their day-to-day activities due to Long COVID symptoms. These figures correspond to US cohorts' data. According to the US Household Pulse Survey (HPS), 6.8% of all American adults are currently experiencing Long COVID. 78.5% of adults who currently have Long COVID have an activity limitation from the condition while 23.1% of adults with Long COVID have significant activity limitations due to Long COVID conditions.

People with the post COVID conditions work and earn less than they would have otherwise due to these limitations. Some individuals have reported a need to adjust their work hours or stop working altogether due to chronic fatigue or cognitive impairment which causes individuals to work and earn less than they would have otherwise. One survey found that 44% of people with Long COVID were out of the labor force and 51% worked fewer hours. Another study of nearly 4,000 Long COVID individuals found that 45% reduced their work hours.

Change in job status can have implications such as loss of health insurance and access to health care. In two separate studies, 23% and 28% of patients with symptoms of Long COVID were unemployed at the time of each study. This implies that approximately 1.1 million Americans may be unemployed due to Long COVID at any given time, accounting for approximately $50 billion in lost earnings annually. Excess healthcare costs, adds to this burden on individuals and on the government.

David Cutler, an economist at Harvard University, has estimated the total financial toll of Long COVID on the US economy to be $3.7 trillion, calling Long COVID the "next public health disaster". This roughly translates to an $11,000 cost per capita and accounts for 17% of pre-COVID US GDP. Cutler estimates the largest economic cost to be reduced quality of life at $2.2 trillion, followed by the cost of reduced or lost earnings at $997 billion. In addition, Cutler projects that the increased medical spending due to Long COVID will be $528 billion. According to the Health+ Long COVID report by HHS, Long COVID was estimated to affect as many as 23 million Americans since the beginning of the pandemic. Further, the Household Pulse Survey estimates 16 million of affected Americans are working-age (aged 18 to 65). Of those, two to four million are out of work due to Long COVID. The annual cost of those lost wages alone is around $170 to $230 billion a year. With 10.6 million unfilled jobs in January 2022, Long COVID potentially accounted for 15% of the labor shortage according to the Brookings Institute.

Due to the lack of data and published studies on the economic impacts of Long COVID in Colorado, we have attempted to extrapolate an estimate based on the national figures to highlight the economic costs and financial burden of Long COVID in Colorado. In June 2022, job hires in Colorado had decreased 21.7% relative to June 2020, while job openings increased by 117% compared to the same period. Part of this could be attributed to labor shortage due to Long COVID. In 2022, Colorado had twice as many job openings as the number of unemployed individuals. As per the Colorado Talent Pipeline Report released on December 16, 2022, there are 35,296 fewer women in the Colorado workforce than there were prior to the pandemic. Although there is no evidence of correlation or causation, this is concerning because the data shows higher rates of Long COVID among women compared to men. Long COVID may be one of many contributing factors to this disparity, among other factors such as lack of affordable child care. Further research is needed to validate these assertions. as the economic and social impacts of long COVID remain under-studied, particularly, there is a lack of data and published studies on the economic impacts of Long COVID in Colorado. Thus there

is dire need for in depth analysis of the economic and social impacts of long COVID specific to Colorado to guide policy decisions.

Key Points

In addition to health issues, Long COVID may cause a substantial financial burden for patients and social problems, including loss of employment, housing insecurity, social isolation, grief and overall increased stress, among other impacts which may contribute to patients' mental and behavioral health

3.3. Deaths from Long COVID

The number of deaths due to post-COVID conditions and the prevalence of disability due to long COVID are yet to be explored. However, research is progressing. A new study published in December 2022 by the CDC's National Center for Health Statistics counted at least 3,544 deaths involved Long COVID, according to death certificates between January 2020 and June 2022. The count was limited to death certificates that included the Long COVID diagnosis code, so researchers believe it is likely an underestimate of the true toll.

The study added that almost 80% of the reported Long COVID deaths occurred in seniors. The age group 75-84 years made up the largest percentage (28.8%) of Long COVID deaths, closely followed by the 85+ age group (28.1%) and the 65-74 age group (21.5%). Around 80% of the reported deaths occurred among White Americans, while fatalities were higher in men than women in almost every age group.

Due to the limited data and information about Long COVID mortality, no estimates of the number of Long COVID deaths in the U.S are available. As we understand more about the condition, long COVID diagnostic guidelines may improve, giving a better picture of mortality caused by Long COVID over time.

4.   The White House and Long COVID

On April 5, 2022, the White House issued a *Memorandum on Addressing the Long-Term Effects of COVID-19*, to organize a Government-wide response to the long-term effects of COVID-19. The Memorandum charged the U.S. Department of Health and Human Services (HHS) to lead a whole-of-government response on Long COVID and to create two reports within 120 days. In order to lead and coordinate the work on Long COVID, HHS established a U.S. government-wide **Long COVID Coordination Council (LCCC)**, chaired by the HHS Assistant Secretary for Health while serving as the "Long COVID Coordinator". HHS will establish a new **Office of Long COVID Research and Practice** to formalize the responsibility. In August 2022, the HSS published two reports that together, pave an actionable path forward to address Long COVID and associated conditions:

1. *The National Research Action Plan on Long COVID*, created in coordination with 14 government departments and agencies, introduces the first U.S. government–wide national research agenda focused on advancing prevention, diagnosis, treatment, and provision of services and supports for individuals and families experiencing Long COVID. It proposes an effective, comprehensive, and equitable research strategy to inform the US national response to Long COVID. The Plan was developed with four guiding principles, namely, orienting research towards improving patient care and outcomes, health equity, accelerating and expanding existing research, and partner engagement. The Federal Government Long COVID research portfolio is organized into the following 7 areas:
   a. Characterizing the Full Clinical Spectrum of Long COVID and Diagnostic Strategies;
   b. Pathophysiology;
   c. Surveillance and Epidemiology;
   d. Long COVID and Overall Well-Being;
   e. Therapeutics and Other Health Interventions;
   f. Human Services, Supports, and Interventions; and
   g. Health Services and Health Economics Research.

   The National Institutes of Health runs the largest national research initiative on Long COVID: the Researching COVID to Enhance Recovery (RECOVER) initiative. The project is a 4-year, $1.15 billion initiative to study Long COVID. It includes the ways the virus and its long-term symptoms interact with neurological and mental health, pathophysiology, diagnosis, possible treatment, and management by supporting a multidisciplinary consortium of investigators who collaborate and coordinate across studies.

2. *The Services and Supports for Longer-Term Impacts of COVID-19 Report* outlines federal services available to the American public to address longer-term effects of COVID-19, including Long COVID and its related conditions, as well as its other

impacts on individuals and families. It provides valuable information in three key areas:

    a. Federal Government supports and services available for people experiencing Long COVID, from how to navigate their rights to how to navigate health care coverage, community services, financial assistance, nutrition and educational questions and more;

    b. Resources for health care personnel treating patients with Long COVID, as well as support for healthcare personnel experiencing stress and trauma related to COVID-19; and

    c. Services for individuals confronting challenges related to mental health, substance use, and bereavement.

A recent Federal report on Long COVID, the *Health+ Long COVID* report is intended to complement the findings and recommendations of the two previous reports by "broadening the conversation and elevating what is often underrepresented in Long COVID statistics, scientific literature, and policy making—the narratives and expertise of people with Long COVID and what they want and need to live better, healthier lives." This report is based on human-centered design, a collaborative approach that includes the people affected by a problem as active participants to help craft solutions that address their most urgent concerns. The report explores how and why the effects of Long COVID differ from person to person. It also notes that various social determinants of health influence how profoundly Long COVID affects an individual's life. These determinants include place of living, access to healthcare and quality, economic stability, and insurance status, in addition to other factors such as disparities in quality of care associated with a patient's race, ethnicity, age, gender, or sexual orientation.

The last section of the report discusses opportunities and recommendations on how to deliver high-quality care, relevant and intentional resources and supports to individuals and families impacted by Long COVID to improve their quality of life. Nine opportunity areas, namely, general public awareness, personal support systems, school and workplace accommodations, access to assistance, structural capacity, system navigation, preparation for healthcare providers, Long COVID research, and advocacy led by people with Long COVID are identified with recommendations. Longer-term recommendations include creating social security credits for people with Long COVID and their caregivers, as well as consolidating—one stop shop—treatment and professional help for navigating and understanding existing support services.

Centers for Disease Control and Prevention is the leading agency in the provision of knowledge about Long COVID. Researchers at the CDC are pursuing a number of studies to explore different aspects of Long COVID from risk factors to pathophysiology, health impacts to social consequences, preventive measures to medical diagnosis and possible treatment and management. CDC, in partnership with several universities across the nation, initiated a CDC-funded study called the Innovative Support for Patients with SARS-CoV-2 Infections (INSPIRE). This study aims to describe the

long-term effects of COVID-19 infection. Participants will describe how they are feeling by completing online surveys and sharing their medical information through a secure, confidential, cloud-based personal health platform every 3 months over a total of 18 months. CDC provides updated knowledge and guidelines through its website to different audiences from general public to Long COVID patients, clinicians and healthcare providers to scientific community and researchers.

Links to useful websites and dashboards can be found in the Appendix 3.

5.   Findings and Recommendations

This section discusses the main findings from our work, focused on systemic shortcomings that, if addressed, would benefit Coloradans. The following section lays the foundation for future work.

5.1. Data Collection and Disease Surveillance

Current surveillance systems do not monitor ill health and long-term implications of COVID-19. What is required here is agreement and implementation of surveillance case definitions for post COVID conditions and recovery. Additionally, state data systems are fragmented. There is a need for a comprehensive and coherent data system to help estimate the burden of Long Covid, and enable different stakeholders to access relevant data. Research suggests that racial/ethnic disparities exist in Long COVID cohorts, however, there is not Colorado specific data which is an area that needs to be focused to guide social and health equity policies.

5.2. Interdisciplinary Collaboration

Multi-disciplinary centers, including University of Colorado Anschutz Medical Center's *Post-COVID Clinic* (UCHealth Post-COVID-19 Clinic), and National Jewish Health's *Center for Post-COVID Care and Recovery* are working on Long COVID, but there does not seem to be a collaboration between them. Meaningful collaboration is needed among different institutions to build knowledge, devise strategies, and gather resources to combat Long COVID and its consequences. Therefore, there is a need to call out for a partnership specific to gather data and define the course of the infection and Long COVID and how it could be treated and managed. Partnerships are vital to scientifically defining the problem through consensus and informing future work.

5.3. Access to Care

When it comes to treatment of Long COVID patients, the current health system is built around tertiary care which is more complex and requires specialty care (diagnosis, advanced procedures and treatments performed by medical specialists in state-of-the-art facilities). This is more costly for patients and delays care. The health system is unable to look after Long COVID patients in tertiary settings/centers. Thus, there is a need to expand access to Long COVID community-based support services, as well as, rehabilitative services.

6. Next Steps and a Path Forward

6.1. Develop Partnerships

Initiatives to better understand Long COVID are underway at federal, state, and local levels. There are multi-disciplinary Long COVID clinics operating in Colorado, including at UCHealth, National Jewish, and the University of Colorado Hospital. In addition, advocates who represent or are themselves impacted by Long COVID and other post viral illnesses, have a strong interest in ensuring Colorado is aware of and prepared for the long term impacts of COVID-19. Coordination of the work underway is vital and will enable Colorado to better define the problem and collect appropriate data to assess and address the short and longer term impacts of COVID-19. The Office of Saving People Money on Health Care will work to build effective partnerships with academic institutions, public health agencies, policy centers, advocates, health care providers, research organizations, tribal entities, and government agencies to cooperatively define problems and capture the data necessary to support the State in understanding and planning for the impacts of Long COVID.

6.2. Expand Data Collection

Ensuring Colorado is prepared to address the impacts of Long COVID will depend on the availability of good data. However, there is very little data yet that can help us understand the medical, economic and social costs associated with Long COVID. The Office of Saving People Money on Health Care will work to develop mechanisms for meaningful Colorado-specific data collection on the impacts of Long COVID on workforce, health insurance, health care affordability, educational attainment, disability needs, and other social and economic impacts of Long COVID. Multi-sector stakeholder participation is essential to creation of a shared data infrastructure, establishing the capability to serve current and future health and non-health analysis needs, and making the best use of data. In addition, as we move forward, we will work with stakeholders including local authorities to collect data on the disproportionate impact of Long COVID by race/ethnicity, geography and other demographic characteristics to inform equitable policy making in the future.

6.3. Explore Impact on Health Care Affordability

Preliminary data shows that Long COVID has associated costs to individuals and their families. No formal data exists yet that would help to assess whether Long COVID has had an impact on health insurance rates or measurably increased the number of people seeking long term care. In addition, most people with ongoing illness are faced with out of pocket costs whether co-pays, deductibles or to pay for needs that may not be covered by insurance. The Office of Saving People Money on Health Care will explore the impact of Long Covid on health care affordability over the coming year.

6.4. Understand Long Term Care Dynamics

Long COVID may impact the number of people enrolled in Colorado's long term care programs. The Office of Saving People Money on Health Care will work to track the development of short and long term disability attributable to Long COVID in Colorado in order to plan for increasing systemic needs. Additionally, these learnings will contribute to our understanding of the impact on Medicaid and how and whether long COVID may impact Medicaid enrollment and home health and other medical care workforce needs.

6.5. Behavioral Health

The Office of Saving People Money on Health Care will work with Colorado's newly established Behavioral Health Administration and the Health Cabinet to examine whether there are increased needs for behavioral health supports related to the prevalence of Long Covid.

6.6. Workforce, Education, and Employment

We intend to examine the extent to which post COVID conditions are taking people out of the labor market, what that means for employers and employees and whether there is an increased need for accommodations due to increases in short and long term disability. The prevalence of Long COVID may accelerate our broader examination of the nature of work and the workplace depending on what percent of the population is left with an illness debilitating enough to require modified work schedules.

6.7. Intersection between Long COVID and Other Post-Viral Illnesses

There appears to be a growing body of work suggesting that Long COVID may be similar to other post viral illnesses, such as Chronic Fatigue Syndrome or Myalgic Encephalomyelitis (ME/CFS). In addition, there is currently speculation that COVID may trigger dormant viral infections already present in the body. While we are not proposing to make scientific determinations, we believe it is important to understand the impacts of Long COVID in the context of other post viral illnesses. Proposals to address the impacts of Long COVID may have implications for others impacted by post viral illnesses.

Acknowledgements

Appendices
Appendix 1.

Proposed pathophysiological mechanisms for long COVID, reproduced from [Castanares-Zapatero et al](#), Annals of Medicine 2022:

System	Involved symptom(s)	Mechanisms
Neurology	Cognitive/mental health disorders Pain Headache Fatigue Anosmia/Ageusia Neuropathy	Functional brain disturbances Hypometabolic activity in various cerebral zones Reduced activity of the GABA inhibition Neuro-inflammation and brain microstructural modifications Micro-structural, volumetric and vascularization disorders
Smell and taste	Anosmia/Ageusia	Structural lesions in the olfactory and taste system at imaging and histology Injury in olfactory neuronal pathways Persistent inflammation of the neuroepithelium and with SARS-CoV-2 RNA identification Invasion and replication of SARS-CoV-2 in taste buds type II cells
Cardiovascular system	Fatigue Dyspnoea Chest pain	Persistent vascular inflammation Macrovascular vascular inflammation Microvascular inflammation: increased level of cytokines, circulating endothelial cells, coagulation activation microvascular retinal impairment (at autopsy, evidence of endothelial cells and cardiomyocytes viral invasion with signs of structural alterations) Auto-immunity: auto-antibodies able to modulate the cardiac frequency and vascular tone (acting as receptor agonists on the β2-adrenoceptor, the α1- adrenoceptor, angiotensin II AT1-receptor, angiotensin 1,7 and endothelin receptors) Persistent alteration of coagulation (sustained increased of D-dimer levels)

Respiratory	Dyspnoea Chest pain Cough	Persistent inflammation and dysregulated host response of lung repairIncreased plasma biomarkers of lung inflammation and fibrosis (Lipocalin 2, Matrix metalloproteinase-7, Hepatocyte growth factor) Persisting inflammation in lungs, mediastinal lymph nodes, spleen, and liver Involvement of iron homeostasis disturbances in end-organ damage Relationship between metabolic abnormalities and lung sequelae
Gastro-intestinal system	No specific symptom	Gut microbiota modifications after recovery Decreases gut commensals with known immunomodulatory potential Perturbed composition of microbiota correlated inflammation biomarkers
Immune system	Multi-system symptoms	Persistent immune inflammatory response impairing organ functioningRemaining inflammation in blood samples analysis, long-lasting phenotypic and functional disorders of lymphocytes, decreased amounts of dendritic cells and persisting alterations of activation markers Signs of mild organ impairment at magnetic resonance imaging and [18F] FDG PET/CT Autoimmunity: auto-antibodies against the nociceptive receptors, immunomodulatory proteins (including cytokines, chemokines, complement components, and cell-surface proteins) and tissue components Persistence of the SARS-CoV-2 nucleic acids in tissues Multisystem Inflammatory syndrome in children (MIS-C)
Dermatological system	Skin disorders	At biopsy, presence of lymphocytic or neutrophilic infiltrates, endothelitis, microangiopathy, and microthrombosis

Appendix 2.

Coloradans with Long COVID-19 by Race and Ethnicity. CO APCD data analyzed by CIVHC.

Race and Ethnicity	Distinct People
Non-Hispanic/Latino	
Asian	77
American Indian/Alaska Native	28
Black	153
White	4,939
Native Hawaiian or other Pacific Islander, Two or More Races or Other Race	764
Non-Hispanic/Latino, Unknown Race	8,739
Hispanic or Latino Any Race	849
Unknown Race and Ethnicity	523
Total	16,072

Data limitation: race and ethnicity data submitted to the CO APCD does not fully represent the race and ethnicity distribution in Colorado as all payers (public and private) are working on improving their data collection and submission. CIVHC continues to work with payers to improve race and ethnicity information. Additionally, This analysis includes claims from October 1, 2021 (when the ICD-10 long COVID code was implemented) through August 31, 2022 for Medicaid, Medicare and commercial payers in the CO APCD. Due to claims submissions run-out, however, not all claims paid through August are currently in the data warehouse, and therefore counts may be underrepresented. In addition, Medicare Fee-for-Service (FFS) claims are underrepresented with current submissions only available from 10/1/2021 to 12/31/2021.
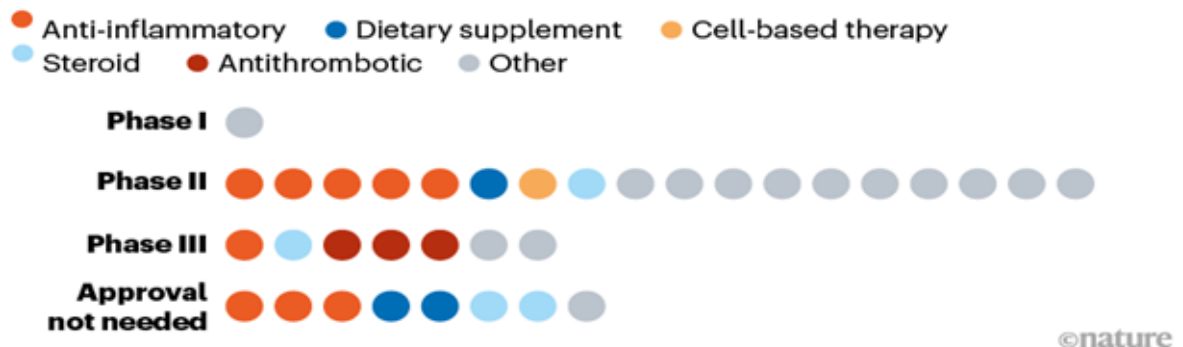
Appendix 3.

Following are links to dashboards providing useful information and updated data about Long COVID:

- [Long COVID | NIH COVID-19 Research](#)
- [Long COVID Terms and Definitions Development Explained](#)
- [Post-COVID Conditions: CDC Science | CDC](#)
- [Long COVID or Post-COVID Conditions | CDC](#)
- [Post-COVID Conditions: Information for Healthcare Providers | CDC](#)
- [CDC COVID Data Tracker](#)
- [Johns Hopkins Coronavirus Research Center](#)

For healthcare providers, there is a CDC funded program called the [Long COVID and Fatiguing Illness Recovery Program](#) quarterly courses which offer learning sessions by Family Health Centers of San Diego, the ECHO Institute, the University of Washington, the University of New Mexico and the University of Colorado. The training is intended to rapidly disseminate Post-COVID Conditions (PCC) and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) findings and emerging best practices.

TRIALS TAKE OFF

At least 26 randomized trials are under way to test therapies for long COVID. Many candidates target symptoms such as inflammation or clots. Some, such as the antidepressant fluvoxamine, act on different symptoms. Some researchers are repurposing drugs already approved for other conditions.

● Anti-inflammatory ● Dietary supplement ● Cell-based therapy
● Steroid ● Antithrombotic ● Other

Phase I
Phase II
Phase III
Approval not needed

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[**Long-COVID treatments: why the world is still waiting (nature.com)**](#)

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Systematic Reviews and Meta-analyses RCS Retrospective cohort study rt-PCR Real-time reverse transcription-polymerase chain reaction. Published online 123AD. doi:10.1038/s41598-022-13495-5

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