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RESEARCH ARTICLE

Consequences of U.S. COVID-19 Policy in 2024

Charles M. Lepkowsky, Ph.D.

Independent Practice
1143 Deer Trail Lane, Solvang, CA 93463-9519

*clepkowsky@gmail.com

ABSTRACT

COVID-19 is entering its fifth year as an active contagion. The evolution of the COVID-19 pandemic is explored with attention to epidemiology, virology, prevalence and prevalence variations based on geographic regionality, age, gender, political affiliation and other variables, policy, proliferation of variants, evidence-based methods for diagnosis, vaccination, testing and treatment, COVID complications, and long COVID. Current consequences of COVID-19 party politics are described including current vaccination and mortality rates, long COVID denialism, COVID exceptionalism, abandonment of safety protocols, adverse outcomes and fatalities, healthcare provider burnout, impact on access to healthcare, economic impact, impact on population-wide IQ, and likely contagion trajectory. Specific recommendations are made for COVID-19 pandemic management.

Keywords: COVID-19, policy, long COVID, variants, neurological impairments, burnout

Introduction

March 13, 2024 marked the fourth anniversary of the COVID-19 national lockdown in the United States (US).[1] Since 2020, the CDC estimates that 1,188,991 American deaths have been attributed to COVID-19.[2] That figure exceeds the number of American lives lost in all the wars since the beginning of the 20th century, including World War I, World War II, the Korean War, Vietnam, the Gulf War and Afghanistan.[3,4]

As alarming as those numbers are, the World Health Organization (WHO) states that American COVID-19 deaths have been significantly underestimated.[5] In 2023, the WHO estimated global COVID-19 excess deaths exceed the officially reported figure of 5.42 million by 14.83 million, or 2.74 times more deaths than reported for the period between 2020 and 2023.[6] These statistics do not include post-COVID infection deaths related to long COVID, or disease or events triggered by recent COVID infection. Although COVID-19 vaccinations and boosters and antiviral medications have significantly reduced acute COVID-19 deaths, COVID-19 remains the only virus among the top ten causes of death in the US, in fourth place following heart disease, cancer, and accidental death.[7]

Wide variations in COVID-19 vaccination and booster acceptance correlate with geographical region.[8] Due to a combination of COVID-19 home testing, people who elect not to test for COVID-19, and termination of public policy requiring local health agencies to report COVID-19 infections, SARS-CoV-2 infections are significantly undercounted in the United States. In March 2024, the WHO estimated about 110 million documented cumulative US COVID-19 cases.[11] However, seroprevalence testing for Sars-CoV-2 infection (including wastewater testing) suggests that there are currently at least twice the number of infections as what is officially counted.[12] Using seroprevalence rates in a longitudinal study of ~178,000 blood donors, the Centers for Disease Control and Prevention (CDC) estimates that by the end of 2023, 98.9% of American adults and older teens had antibodies from vaccination and/or at least one prior COVID-19 infection.[13] The data are potentially confounded by the unknown number of reinfections. While infection might provide increased resistance to infection by the same strain of COVID-19, the rapid rate of mutation and the proliferation of variants increases the risk of reinfection.[14] Moreover, repeated COVID-19 infection increases the risk of poor outcome, including long COVID, chronic health impairment, and mortality.[15]

Four years after the national COVID-19 lockdown, the SARS-CoV-2 virus continues to spread and mutate but is largely dismissed as a current concern, despite the startling statistics cited and ongoing warnings from the scientific community.[16,17] The purpose of this paper is to provide a comprehensive review of the impact of US COVID-19 policy on COVID-19 case and fatality rates, COVID-19 tracking, the proliferation of SARS-CoV-2 variants, evidence-based COVID-19 vaccines, treatment and testing, potential long-term consequences of COVID, long COVID, and current consequences of COVID-19 party politics including current vaccination and mortality rates, long COVID denialism, COVID exceptionalism, abandonment of safety protocols, adverse outcomes and fatalities, healthcare provider burnout, impact on access to healthcare, economic impact, impact on population-wide IQ, and likely contagion trajectory. Specific recommendations are made for more effective COVID-19 pandemic management.

US COVID-19 Policy Changes 2020-2024

Early phase COVID-19 pandemic safety protocols 2020-2021

The US Department of Health and Human Services (HHS) formally recognized COVID-19 as a serious threat to national public health and safety, declaring a Public Health Emergency (PHE) in January of 2020.[18] The US government quickly implemented policies to contain the spread of COVID-19, including shelter in place policies closing private and public businesses, schools and outpatient healthcare facilities, masking mandates and social distancing protocols.[19-23] Tensions rapidly developed between the Trump administration and the scientific community, state governors promoting the adoption of safety protocols, and U.S. government agencies including the Department of Health and Human Services (HHS), the Centers for Disease Control and Prevention (CDC) and the National Center for Immunization and Respiratory Diseases (NCRID).[24] Then-President Trump engaged social media to promote anti-scientific rhetoric, as part of a growing "infodemic."[25-29]

Trump's anti-scientific rhetoric galvanized the beliefs of Americans who characterized COVID-19 safety protocols as violations of their personal rights and openly opposed them.[30] Conservative governors refused to enforce COVID-19 safety protocols, leading to widespread COVID-19 outbreaks.[31] The United States Food and Drug Administration granted emergency authorization for the use of the first COVID vaccination on December 14, 2020,[32] and full authorization on August 23, 2021.[33] The public's initial adoption of COVID-19 vaccination was enthusiastic, with significant reductions in new case and fatality rates.[34]

Rejection of COVID-19 pandemic safety protocols 2022-2024

Heightened tensions over COVID-19 safety protocol enforcement undermined these advancements,[35] and beginning in June of 2021 the US government stopped enforcing COVID-19 safety protocols.[36] The CDC changed its use of language from COVID-19 "policies" to "recommendations" or "suggestions," citing the absence of authority to enforce a "policy."[37]

The US government terminated the Public Health Emergency on May 11, 2023.[38] Since that date, the CDC accepts COVID-19 new case rate and fatality data, but without authority to gather comprehensive or reliable data, no longer updates its COVID Data Tracker Weekly Review.[39-41] Research data gathered over four years clearly demonstrates the efficacy of face masks for containing the spread of COVID-19.[42,43] Nonetheless, policies regarding masking and social distancing have disappeared, and even states that once led the adoption of safety protocols for COVID-19 now offer meek "guidelines" for masking.[44]

Similarly, implementation of COVID-19 booster vaccinations has decreased over time. At present, only a small percentage, about 7%, of the American population is current on vaccination boosters.[45] In January 2022, the CDC abandoned the policy of quarantine after exposure or infection, instead recommending wearing a high-quality mask for ten days and getting tested on day five.[46] On March 1, 2024, the CDC further downgraded expressed concern about COVID-19 exposure or infection. It now recommends that people who test positive for COVID-19 stay at home 24 hours before returning to normal activity, and only wear a mask if they have an active fever and/or cough, characterizing COVID as similar to or a type of common influenza.[47]

Proliferation of SARS-CoV-2 Variants

The SARS-CoV-2 virus continues to mutate, and COVID-19 variants with enhanced immune-escape capabilities continue to produce spikes in the infection rate in the United States population.[48] Spikes in infection rates have been associated with specific variants since 2020. Notably, these include Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1),

Delta (B.1.617.2), Omicron (B.1.1.529) and its subvariants,BA.1 (B.1.1.529.1), BA.2 (B.1.1.529.2), BA.3 (B.1.1.529.3), BA.4, BA.5, and descendent lineages, more recently including BQ.1, BQ.1.1, BA.4.6, BF.7, BA.2.75.2, XBB.1, and BF.7.[49]

A variant of great concern in mid- to late-2023 was BA.2.86, credited with equal or greater immune-escape potential than XBB.1.5 from antibodies elicited by pre-Omicron and first-generation Omicron variants or vaccinations.[50-54] BA.2.86's more than 30 mutations in the spike part of the virus responsible for entering healthy cells caught the attention of scientists and public health officials, who feared BA.2.86 might produce a winter wave of COVID-19 infection.[55] Nicknamed "Pirola," BA.2.86 is more likely to escape existing immunity from prior COVID-19 infection and/or vaccination, prompting experts to encourage the public to remain current on updated booster vaccinations inducing a more robust immune response.[56]

Concern about BA.2.86 was soon replaced by the emergence of a new COVID variant labeled JN.1. Although JN.1 appeared susceptible to immune protection from the 2023-2024 COVID vaccination/booster, less than 16% of American adults had accepted that vaccination, creating concern in December 2023.[57,58] In fact, dire predictions regarding JN.1 were realized. In early November 2023, JN.1 accounted for less than 5% of COVID-19 cases in the U.S. By the beginning of January 2024, over 60% of new COVID-19 cases in the U.S. were attributed to JN.1.[59] By January 19, 2024, the CDC estimated that JN.1 was responsible for about 85.7% of cases in the United States.[60] The rapid spread of JN.1 is largely due to the very low percentage of Americans who remain current with COVID-19 vaccinations and boosters.

COVID-19 Vaccines

The biggest breakthrough in the management of the COVID-19 pandemic was the development of effective COVID-19 vaccines. As the FDA granted emergency use approval for COVID-19 vaccines, a growing number of Americans received vaccination.[61] The United States Food and Drug Administration granted emergency authorization for the use of the first COVID vaccination on December 14, 2020,[62] and full authorization on August 23, 2021.[63]

Since 2020, vaccination boosters have been developed, updated and reformulated to remain effective against the proliferation of new COVID-19 variant strains. Bivalent vaccinations initially proved most effective against COVID-19 and the earlier variants.[64] Following termination of the PHE on May 11, 2023, withdrawal of government funding increased consumer costs and led to shortages of vaccinations and boosters, frustrating the public and further contributing to lower vaccination rates.[65] In 2023, the FDA determined that bivalent vaccines were no longer effective against the extant variant strains of COVID-19, and no longer authorized their use in the United States.[66] Consequently, COVID vaccines and boosters have been reformulated to be effective against the most recent XBB mutant strains.[67]

COVID-19 Treatments

On October 22, 2020, the FDA approved the antiviral drug Veklury (remdesivir), the first medication for the treatment of COVID-19 infections in adult and pediatric patients 12 years of age and older.[68] A systematic review of research literature indicates that Remdesivir is potentially safe and effective, especially when used during the early course of the disease, but acknowledged that its safety in patients with complications of COVID-19 has yet to be established.[69] However, Remdesivir was only available as an injectable medication, which limited its availability.

On May 25, 2023, the FDA approved the first oral antiviral, Paxlovid (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) for the treatment of COVID-19. Paxlovid was intended to treat mild-to-moderate COVID-19 in adults with high risk for progression to severe COVID-19, including hospitalization or death. Paxlovid was the fourth drug approved by the FDA to treat COVID-19 in adults.[70] Paxlovid has some limitations, and is not recommended for patients with known or suspected severe hepatic impairment[71] and/or renal impairment.[72] Case studies indicated that some patients treated with Paxlovid experienced rebound COVID-19 infections and symptoms 2 to 8 days after completing a 5-day course of Paxlovid. In 2022, the CDC issued a Health Alert Network Health Advisory to update the public on the potential for COVID-19 rebound after Paxlovid treatments. Rebound rates are highest in patients who were not vaccinated.[73] However, the rates of COVID-19 rebound in a real-world population or whether rebound is unique to Paxlovid remains unknown.[74]

Antivirals including remdesivir and nirmatrelvir-ritonavir (Paxlovid) are most effective as outpatient treatments early in the course of COVID-19 and for less severe infection. Nirmatrelvir-ritonavir appears ineffective at reducing most post-COVID conditions.[75] For severe COVID-19 disease, immunomodulatory therapies including dexamethasone and interleukin-6 or Janus kinase inhibitors have proven more effective. As new COVID-19 variants emerge that appear less responsive to treatment with anti-SARS-CoV-2 monoclonal antibodies, use of those medications has been decreased.[76]

COVID-19 Health Complications

Numerous complications have been associated with even a single, mild SARS-CoV-2 infection. Among the better-known symptoms are enduring loss of taste and smell, which can last from days to months or even years. Of the 36 million Americans diagnosed with COVID in 2021, 60% reported losses in smell or taste. Some research indicates that most patients with mild COVID infections recover the senses of smell and taste within 3 years.[77] Although most people eventually recover, about 24%

do not fully recover their sense of smell and/or taste, and over 3% had no recovery.[78]

Cardiovascular complications

Cardiovascular complications are also frequent consequences of SARS-CoV-2 infection. These include increased risk for dysrhythmia, pericarditis, myocarditis, ischemic heart disease, heart failure, and thromboembolism. During the acute phase of infection, cardiovascular complications are associated with rates of high mortality rates. In chronic COVID, they are linked to high rates of morbidity that negatively impact the patient's quality of life and lead to an increased likelihood of poor health outcomes. Cardiovascular complications occur in a significant percentage of patients with COVID-19, those hospitalized with severe infection are most vulnerable and likely to experience enduring health impairments.[79]

Although the pathobiology underlying cardiovascular complications is not fully known, it appears that SARS-CoV-2 directly infects coronary vasculature and induces plaque inflammation, which might explain the increased risk of ischemic cardiovascular complications up to 1 year after infection.[80] Also among the more immediately dangerous cardiovascular complications are increased rates of venous thromboembolism. Because thromboembolism is not a universal COVID complication, the use of antithrombotic therapy for COVID patients is limited.[76] Although nirmatrelvir-ritonavir appears ineffective at reducing most post-COVID conditions, thromboembolic events are the exception.[75]

Long-term consequences of SARS-CoV-2 infection

Long-term consequences of SARS-CoV-2 infection also include iron dysregulation, inflammatory stress erythropoiesis[81] and almost twice the average risk of developing alopecia areata.[82] Even mild COVID infection bears significant risk of neurologic and psychiatric disorders.[83,84]

Neurologic COVID complications

Potential neurologic COVID complications include gliosis.[85] Gliosis is a "nonneoplastic reaction (hypertrophy and/or proliferation) of astrocytes and/or microglial cells, is a frequent finding in the central nervous system (CNS [brain and/or spinal cord]) in nonclinical safety studies."[86] Gliosis can be induced by trauma, injury or disease, and is described as the production of more or larger glial cells (cells that support nerve cells). Gliosis can induce symptoms including cognitive changes (memory loss or impairment, impaired cognitive functioning), personality changes, mood impairment (depression), psychiatric symptoms (hallucinations) and neurologic impairment (seizures).[87] Neurologic damage following acute viral infections may be attributed to an excessive immune response to the infection.[88]

Although rarely mentioned in the media, an alarming finding is that even mild SARS-CoV-2 infection can lead to enduring impairment in intellectual functioning. Patients tested a year after recovery from mild COVID infection demonstrate an average 3 point reduction in IQ test scores. A year after hospitalization in an intensive care unit for severe COVID infection, recovered patients demonstrated an average 9 points drop in IQ.[89]

Long COVID

The term "long COVID" came into use in the early part of 2020, coined by patients to describe their failure to recover.[90] In the most general sense, long COVID describes extended SARS-CoV-2 symptoms that persist for weeks, months, or years.[91] The definition of long COVID, or Post Acute Sequelae of COVID (PASC) is based on systematic reviews of large cohort studies.[92]

The CDC defines long COVID as symptoms persisting beyond the 4-week acute phase. Although recovery may occur after 12 weeks, the likelihood of the presence or emergence of persistent illness is greatly increased.[93]

Long COVID presentation

Long COVID presents in a variety of ways, including exacerbation of pre-existing symptoms or conditions; the persistence of persistent symptoms and conditions that begin at the time of acute COVID-19 illness; "new-onset signs, symptoms, or conditions following asymptomatic disease or a period of acute symptom relief or remission; an evolution of symptoms and conditions that include some persistent symptoms (e.g., shortness of breath) with the addition of new symptoms or conditions over time (e.g., cognitive difficulties)."

Epidemiology of long COVID

It is unclear why some people develop long COVID. Research suggests that there are at least six subcategories of long COVID patients, based on distinct profiles of phenotypic abnormalities. These subcategories may include pulmonary, neuropsychiatric, cardiovascular, and broad or severe symptom manifestations with increased risk of mortality. Pre-existing conditions and measures of severity during acute COVID-19 also correlate with phenotypic groupings.[94] Immune system abnormalities, including thromboinflammation, have been implicated as a potential cause of long COVID.[95]

Differential diagnosis of long COVID

Differential diagnosis of long COVID is complicated by pre-COVID medical conditions, physical deterioration due to inactivity during acute COVID, depression, anxiety and other mental or physical conditions consequent to any extended or complicated illness, loss of access to usual social, physical or vocational activities that might induce stress, and resemblance to other post-infectious syndromes, including but not limited to "myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), postural orthostatic tachycardia syndrome (POTS) and other forms of dysautonomia, or mast cell activation syndrome (MCAS). For example, several of these conditions have been observed in patients subsequent to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), two similarly potentially lethal coronavirus infections.[96,93]

Long COVID symptoms

According to the CDC, "a wide range of other new or persistent symptoms and clinical findings can occur in people with varying degrees of illness from acute SARS-CoV-2 infection, including patients who have had mild or asymptomatic SARS-CoV-2 infection. These effects can overlap with multiorgan complications, or with effects of treatment or hospitalization. This category is heterogeneous, as it can include patients who have clinically important but poorly understood symptoms (e.g., difficulty thinking or concentrating, post-exertional malaise) that can be persistent or intermittent after initial acute infection with SARS-CoV-2."[93]

Commonly reported long COVID symptoms include dyspnea or increased respiratory effort; fatigue; post-exertional malaise (PEM: worsening of symptoms following even minor physical or mental exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks) and/or poor endurance; cognitive impairment or "brain fog;" cough; chest pain; headache; palpitations and tachycardia; arthralgia; myalgia; paresthesia; abdominal pain; diarrhea; insomnia and other sleep difficulties; fever; lightheadedness; impaired daily function and mobility; pain, rash (e.g., urticaria); mood changes; anosmia (loss of smell) or dysgeusia (loss of sense of taste); menstrual cycle irregularities; and erectile dysfunction. Categorically, acute and long COVID are known to affect any of the following systems: cardiovascular, pulmonary, renal, psychologic, neurologic, cognitive, gastrointestinal, immunologic, endocrine, reproductive, genitourinary, and dermatologic.[93]

Long COVID and pre-existing health issues

A systemic review of prospective cohort studies on long COVID also found that patients with preexisting allergic conditions like asthma or rhinitis may be linked to a higher risk of developing long COVID.[97] Long COVID can also interfere with blood glucose regulation and exacerbate or induce type 2 diabetes.[98] The National Institute of Diabetes and Digestive and Kidney Diseases documents a 60% increase in risk for new-onset diabetes in people who had COVID-19, usually type 2, compared with people who never had COVID-19 In a study of over 181,000 U.S. veterans, after one year, those who had COVID-19 had a 40% higher risk of new diabetes, compared with controls.[99]

Persistent long COVID symptoms

In addition, physical health impairments known to persist after resolution of acute COVID-19 include pulmonary fibrosis,[100] myocarditis and pericarditis.[101] Patients who experienced multisystem inflammatory syndrome (MIS) during or after COVID-19 illness may be at higher risk for on-going multiorgan system effects and Post-COVID Conditions. It is unknown how long multiorgan system effects might last and whether the effects could lead to chronic health conditions.[102] In this context, COVID infections appear to trigger other autoimmune diseases such as human immunodeficiency virus (HIV),[103] rheumatoid arthritis and type 2 diabetes.[104-107] Patients with rheumatic autoimmune disease are twice as likely to develop long COVID.[108,109]

Gender differences in long COVID

Gender differences also appear to influence long COVID. Women are twice as likely as men to develop long COVID.[110] Long COVID disproportionately affects premenopausal women. A literature review of research documented female reproductive health impacts of long COVID including disruptions of the menstrual cycle, gonadal function, and ovarian sufficiency; menopause; infertility, menstrual symptom exacerbation and endometriosis. The review also documented reproductive health impacts of overlapping and associated illnesses including myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS), postural orthostatic tachycardia syndrome (POTS), connective tissue disorders such as Ehlers-Danlos syndrome (EDS). 70-80% of patients with these conditions are women, who have increased rates of dysmenorrhea, amenorrhea, oligomenorrhea, dyspareunia, endometriosis, infertility, vulvodynia, intermenstrual bleeding, ovarian cysts, uterine fibroids and bleeding, pelvic congestion syndrome, gynecological surgeries, and adverse pregnancy complications such as preeclampsia, maternal mortality, and premature birth. The menstrual cycle, pregnancy, and menopause are also affected by long COVID.[111] In perimenopausal women, specific, severe long COVID symptoms include brain fog, fatigue, new-onset dizziness, and dysregulated sleep.[112,113]

Long COVID and older adults

Long COVID poses special challenges to older adults. The CDC estimates that 25% of adults infected with COVID-19 over 65 years of age will experience Long COVID symptoms compared to 20% of adults under 65 years.[114] Older adults have less resilient immune systems, placing them at significantly higher risk for contracting COVID-19 and developing long COVID. Their immune systems can enter a state known as "immunosenescence," which can exacerbate "inflammaging" and the development of various comorbidities, increasing susceptibility to long COVID. The physical and mental effects of long COVID can significantly reduce older adults' quality of life.[115]

Long COVID and cognitive functioing

Even in the general population, long COVID is associated with declines in cognitive functioning. As mentioned previously, in a large-cohort study, patients tested a year after recovery from mild COVID infection demonstrate an average 3 point reduction in IQ test scores, and those who had been treated in an intensive care unit for severe COVID infection demonstrated an average 9 points drop in IQ.[89] Another large-cohort study assessed patients between March 2020 and April 2023. Participant-reported memory function was numerically worse at several time points up to 36 months after a positive SARS-CoV-2 test.[116] "Brain fog" including memory loss and difficulty concentrating affects as many as 46% of patients with long COVID. These symptoms may be the consequence of viral brain injury that can persist for years. Recent research suggests that long COVID brain deficits are equal to 20 years of brain aging.[117]

Prevalence of long COVID

Difficulties with differential diagnosis for long COVID have also made it difficult to accurately determine its prevalence. Estimates of COVID patients who develop long COVID range from 5% to 30%. About 9% of anyone who has had COVID-19, or at least 65 million individuals worldwide, are estimated to have long COVID.[118] A systematic review of research indicates that 16.2% of pediatric COVID-19 patients develop long COVID.[119]

Reasons for these wide-ranging estimates include differences between researchers in symptoms or conditions investigated, time frames employed (varying from weeks to months after acute infection), inpatient or outpatient settings, which speaks to the severity of each patient's acute COVID-19 symptoms, varying sample populations, and varying methods used to assess symptoms (e.g., self-report or medical evaluation).[93] Current data on long COVID can be found on the U.S. Census Bureau's Household Pulse Survey.[120] Best estimates are that 6.4% to 7% of Americans currently report symptoms of long COVID, many of whom have never fully recovered.[121,122]

Vaccinations and long COVID

COVID vaccination might reduce the likelihood of developing long COVID. Research data on this issue vary, due to differences between study methods, time since vaccination and definitions of long COVID. Only one study suggests that there is no significant difference in the development of long COVID between vaccinated individuals and unvaccinated individuals.[123]

Other studies suggest that vaccines provide partial protection, with a reduced risk of long COVID between 15% and 41%.[124]

Regional variation in rates of long COVID

There is wide regional variation in rates of long COVID.[125] Long COVID prevalence tends to be lower in New England and the Pacific and higher in the South, Midwest, and West.[126,127] Long COVID rates are higher for women than men, higher among whites compared with African Americans and Asians, and to correlate with lower levels of education and income. Long COVID rates are highest among people in midlife and strongly associate with negative affect (anxiety, depression, worry and a lack of interest in things), especially for people with long COVID and severe symptoms.[127]

Diagnosis and treatment of long COVID

A variety of new ways to diagnose and treat long COVID are undergoing clinical trials. Abnormally high levels of the neurotransmitter catecholamine are evidence of long COVID, so catecholamine testing is now used to diagnose long COVID, especially when presenting symptoms include dysautonomia, a manifestation of autonomic nervous system dysfunction characterized by dizziness, low blood pressure, nausea, and brain fog.[128]

Long COVID has also been identified by biomarkers including low serotonin levels, thought to be a consequence of SARS-CoV-2 virus remaining in the patient's system.[129] Complement dysregulation tests might also diagnose long COVID.[130] Phenotyping has been especially useful in identifying specific treatment(s) most likely to be effective for each long COVID patient. For example, treating long COVID fatigue requires a different approach than treating POTS or dysautonomia.[94]

There is an emerging body of strong data suggesting mitochondrial dysfunction as the cause of long COVID in some patients. Loss of mitochondrial membrane potential, possible dysfunctional mitochondrial metabolism and altered fatty acid metabolism, as seen in myalgic encephalomyelitis might be the mechanism involved in long COVID in patients who develop myalgic encephalomyelitis.[131]

Treatment of long COVID dysautonomia symptoms including brain fog, fatigue, and dizziness is being explored using stimulation of the vagus nerve, the main nerve of the parasympathetic nervous system that mediates a wide range of functions including digestion and mental health.[132,133] Long COVID fatigue is being successfully treated with low doses of naltrexone.[134] Beta-blockers are now being used to treat postural tachycardia syndrome (POTS), a symptom of long COVID that happens when the heart rate increases rapidly after someone stands up or lies down.[135,136]

Clinical trials are underway, exploring the repurposing of two HIV antiviral medications, Truvada and Maraviroc, to reduce levels of circulating SARS-CoV-2 virus in the body thought to cause long COVID.[137] Ongoing trials are also exploring the treatment potential of SARS-CoV-2 monoclonal antibodies, to determine whether antibodies might target SARS-CoV-2 viral "reservoirs" inducing persistent long COVID symptoms.[138]

Consequences of COVID-19 Party Politics

Vaccination and Mortality Rates

The influence of party politics on COVID case and mortality rates is notable. When vaccines were initially administered in December of 2020,[62] there was no partisan difference in COVID case or fatality rates. COVID-19 vaccination rates increased quickly during early 2021, but due in large part to the headwind of anti-vaccination misinformation, stalled in the middle of 2021. At the beginning of 2022, the US COVID-19 "fully vaccinated" rate (having received the initial two doses) was at 63.6%. By June 21, 2022, that number had increased to 66.9%.[139] A year later, the US COVID-19 vaccination rate for full vaccination (two initial doses) had increased to 69.3%, and for at least one updated booster dose to 17%.[140] Vaccinations lose potency over time, so the relevant number is the current booster vaccination rate.[141-143]

Perhaps as a legacy to former President Trump's anti-science rhetoric, a large percentage of the American population has declined vaccination and/or eschews booster vaccinations, apparently influenced more by partisan politics and/or regional attitudes than by scientific evidence. Vaccination avoidance correlates with lower educational attainment, rurality, and regions characterized by a relatively high Trump vote share.[144] Anti-vaccination populations (more than pro-vaccination populations) share conspiracy theories, engage more in discussions on Twitter, use emotional language, and largely followed the anti-vaccination Tweets of Donald Trump, highlighting the impact of the infodemic as employed by the former president.[145] The anti-vaccine movement has dovetailed with far-right political propaganda.[146]

Anti-science rhetoric continues to gain momentum and turn public opinion against vaccination, boosters and other COVID-19 safety protocols,[147] despite consistent demonstration of their effectiveness,[148] limited risk[149] and safety for most of the population, including children.[150] Predominantly Republican counties have had higher COVID-19 death rates than predominantly Democratic counties. Political party affiliation and attitudes regarding COVID-19 vaccination, social distancing, and other safety protocols have led to a growing partisan death rate gap,[151-155] especially in geographic regions that strongly identify as Republican.[156-158]

Additional factors contributing to reduced rates of booster vaccination include difficulty gathering accurate data about new COVID case rates,[159,160] reduced news coverage about COVID,[161] and consequent reduced public concern about contagion. In addition, members of marginalized communities are most likely to remain unvaccinated against SARS-CoV-2.[162]

In the summer and fall of 2020, more than two-thirds of the American population viewed COVID-19 as a major threat to the health of the U.S. population. A March 2024 survey by the Pew Research Center indicated that only one-fifth of Americans expressed the same concern.[163] This is likely much of the reason that by the end of 2023, only 7% of American adults had received the latest COVID booster vaccination, meaning that 93% of Americans remain unprotected from current strains of COVID-19.[45] JN.1's two-month rise from an obscure variant of interest to the predominant COVID-29 strain in the U.S.[60] is a potent illustration of how unprotected the American public is from emerging COVID-19 variants.

The CDC estimates that 1,188,991 American deaths have been attributed to COVID-19.[2] However, the World Health Organization (WHO) states that American COVID-19 deaths have been significantly underestimated.[5] The WHO estimated global COVID-19 excess deaths in 2023 exceeded the officially reported figure of 5.42 million by 14.83 million, or 2.74 times more deaths than reported for the period between 2020 and 2023, not including post-COVID infection deaths related to long COVID, or disease or events triggered by recent COVID infection.[6] In 2023, the CDC estimated that since the beginning of the COVID-19 pandemic, over 5,000 Americans had died from long COVID.[164] The chilling possibility, if not inevitable likelihood, is that an equally virulent strain will arise with much greater lethal potential.

Long COVID Denialism

Conservative anti-science and antivaccine rhetoric now includes long COVID denialism, which is on the rise. There is a vast, growing body of scientific data demonstrating that long COVID is a multisystemic disease with sequelae affecting almost all organ systems, whose effects can be life altering and permanent. Even a resolved episode of COVID-19 increases risk of numerous chronic diseases, which contribute to the rising economic healthcare burden of cardiovascular disease, diabetes, neurologic impairment, and autoimmune conditions.[93] COVID-driven increases in the rate and severity of such conditions will increase demand on healthcare systems, increasing healthcare costs, and eroding U.S. life expectancy, which has declined 2.2 years since the COVID-19 pandemic began.[165,166]

COVID Exceptionalism

Further obscuring COVID-19 and long COVID's potential for long-term, multi-systemic health impairments (and associated burdens, both financial and emotional on the healthcare system) is the movement afoot among some healthcare experts to end "COVID exceptionalism," which means treating COVID-19 differently than other respiratory infections. The CDC's most recent guidance on quarantine for COVID-19 reflects this sentiment, shortening isolation times. It states "COVID-19, flu, and RSV are very common respiratory viruses that cause significant amounts of disease, especially in the fall and winter season," characterizing COVID-19 as one of several common seasonal respiratory viruses. The CDC's prior guidance for those testing positive for COVID-19 was "a minimum isolation period of 5 days plus a period of post-isolation precautions." Their updated guidance, issued in March 2024, recommends that "people stay home and away from others until at least 24 hours after both their symptoms are getting better overall, and they have not had a fever (and are not using fever-reducing medication). Note that depending on the length of symptoms, this period could be shorter, the same, or longer than the previous guidance for COVID-19."[167] Notably, the CDC's current guidance is based on the patient's subjective observation of symptoms. Rapid COVID-19 testing is neither advised nor even mentioned.

Epidemiologists have been alarmed by the opposition to COVID exceptionalism, including the CDC's most recent guidance on quarantine for COVID-19. Dr. Ellie Murray, an assistant professor of epidemiology at Boston University's School of Public Health, states "It's not good science. It's not good public health. It doesn't provide people with accurate information… It's undermining the whole rest of the public health system, because what people are hearing is, 'Actually, diseases aren't as bad as we'd said they were, and we don't actually need to do anything. It's not actually that bad if some people die.'" Eric Topol, MD, founder and director of the Scripps Research Translational Institute, also states "I completely disagree with the idea there is no COVID exceptionalism. The overwhelmingly abundant evidence for this virus over the past 4 years tells us that it is a far more dangerous pathogen than flu, which lacks seasonality, is still evolving, has induced Long COVID in tens of millions of throughout the worlds, and cannot be 'FLU-ified.'"[168] In his own blog, Dr. Topol states: "I remain very disappointed and surprised by the recent change (1 March) of CDC policy towards isolation, without regard to using rapid antigen tests. Their own data shows that at least 1 in 3 people will still be infectious at 5 days after symptom onset! That's by culturable virus, the gold standard, which tracks very closely with the rapid tests. To reduce infecting others, especially high-risk vulnerable individuals, no less adding to the toll of Long Covid, rapid tests should be used before people circulate."[169]

Abandonment of Safety Protocols

Although mask mandates were lifted nationwide by the CDC and several states in the beginning of the year, the CDC's current guidance does encourage those with respiratory infection symptoms to "wear a high-quality, well-fitting mask, like an N95 mask, when you need to be around others…for the next five days, … practicing physical distancing, and testing yourself when you'll be around other people indoors."[170] In fact, a winter wave of COVID-19 and flu wave prompted some hospitals to reinstate mask mandates for patients, staff, and visitors.[171] However, this was a short-lived resurgence of masking policy, ended quickly due to the public's negative response and the increasingly political climate of the election year.

Politically-driven abandonment of safety protocols including vaccination, social distancing and masking has left the American population largely unprotected from COVID-19 and long COVID, which is on the rise.[139,172] In the absence of safety protocols, US COVID-19 case rates fluctuate, but on average have remained at about 30,000 a day. US COVID fatalities average about 200 per day, with over 1.2 million US deaths attributed to COVID-19 to date.[173] For perspective, the highest annual number of gun-related deaths in the US (including accidental shootings and suicides) was 48,830 in 2021.[174]

Funding necessary for research to develop effective diagnostic and treatment methods for COVID-19 and long COVID is imperiled by long COVID denialism, which obscures the widespread impact of long COVID and conflates its symptoms with adverse vaccination side effects. Long COVID's full impact has yet to be realized, and it may be years before its impact can be fully understood.[175]

Adverse Outcomes and Fatalities

There have also been significant practical complications consequent to COVID. Rates of adverse outcomes and death have been significantly higher consequent to COVID-19 pandemic-era disruptions in health care access, routine visits and follow through, including diabetic ketoacidosis (DKA) in children[176] and cancer.[177-180]

Healthcare Provider Burnout

The COVID-19 pandemic has also had a significant impact on healthcare workers. Research demonstrates that since the inception of the pandemic, this population has experienced increased risk not only for SARS-CoV-2 infection, but also for anxiety, depression, interpersonal difficulties, health issues, and other consequences of extended exposure to stress.[181-183] A Canadian study found that the risk of COVID infection for healthcare workers can be twice that for the general population.[184] Numerous studies going back to year 2020 indicate increasing rates of stress, depression & anxiety among healthcare workers.[185-187] Subsequent research has found that these effects have become cumulative over time,[188] leading to high rates of Burnout in healthcare providers[189,190] including physicians across specialties, nurses, physicians' assistants, hospitalists, mental health professionals and medical school students.[191-199] In 2023, more than 50% of physicians reported feeling burned out, and almost 25% reported feeling depressed, the highest percentages in 5 years.[200,201] 67% of physicians assistants report burnout, depression, or both[202]. Nurse practitioners report high rates of burnout, depression and suicidal thoughts tied to overwork and stress.[203]

There are also significant gender differences in burnout among healthcare professionals. In a study of more than 1300 clinicians, female physicians in their 30's practicing in primary care reported the highest rates of burnout.[204] Higher rates of burnout among younger female physicians has been an historical trend[205] that has not changed during the pandemic.[206] Similarly, female medical school students experience significantly higher rates of burnout than their male peers. Although more than half (54%) of medical students overall report symptoms of burnout, compared with male medical students, female medical students are more likely to experience symptoms of burnout (60% vs. 44%), emotional exhaustion (80% vs. 73%), and cynicism (62% vs. 49%).[207] Gay, lesbian, and bisexual medical students experience higher levels of stress and burnout than cisgendered peers.[208]

Perhaps ironically, but of significant concern, more than 25% of psychiatrists internationally meet the criteria for burnout on the Maslach Burnout Inventory (MBI), and more than 50% qualify on the Copenhagen Burnout Inventory (CBI).[209] If those providing mental health care and treatment for healthcare providers suffering from stress and burnout are themselves burned out, the long-term outlook for the quality of care appears bleak. In fact, primary care physicians in ten developed countries report severe burnout that they admit could compromise the quality of care they provide patients. Burnout and emotional distress among clinicians in Canada, the UK, and New Zealand is consistently worse than it is in the US.[210]

Healthcare professional burnout is among the factors leading to shortages in healthcare workers at every level.[211-213] In a 2021 study of COVID-related healthcare provider stress in the US, 23% of physicians and 40% of nurses stated that they planned to leave their practices within the next 2 years.[214] The US Surgeon General has expressed concern about healthcare provider burnout. He has stated that the nation's health depends on the well-being of our health workforce; that direct harm to health care workers can lead to anxiety, depression, insomnia, and interpersonal and relationship struggles; that health care workers experience exhaustion from providing overwhelming care and empathy; that health care workers spend less time with patients and too much time with EHRs; and that there are health workforce shortages. He specifically noted that one of the unreported stresses of open access for patients through EHR communications is the empathy drain on physicians. He observed that for every hour of direct patient care, physicians currently spend 2 hours on the EHR system. Most practices allow 10%-20% of time for catch up, although 50% is a more reasonable estimate of the time required, a concept is fully lost on, or ignored by administrators. He states that administrative burdens need to be reduced by 75% by 2025.[215] Achieving the goal of reducing medical documentation requirements by 2025 seems unlikely, because there has been no movement to do so, which would require Congress to change existing legislative requirements under the Affordable Care Act of 2010 (ACA)[216] and the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA).[217]

Impact on Access to Healthcare

As the COVID-19 pandemic continues in the absence of safety protocols, the burden on healthcare providers will continue to increase, exacerbated over time by the yet-realized impact of long COVID and the long-term sequalae of COVID.[175] Accordingly, the long-term outlook is that access to healthcare will continue to diminish, as the demand for healthcare increases.

Economic Impact

COVID-19 has had a significant economic impact on the US economy. At the beginning of the pandemic, real gross domestic product (GDP) fell sharply to 9 percent below its level at the start of the recession.[218] The overall economic burden of the COVID-19 pandemic on the US economy was estimated at $14 trillion by the end of 2023.[210] Estimates of COVID-19 healthcare costs vary from a 50% increase[220] to a net increase of 300%.[221] In July of 2022, David Cutler of Harvard University estimated that the total economic cost of long COVID to that date was $3.7 trillion, about $11,000 per capita or 17% of the 2019 gross domestic product (GDP).[222]

Impact on Population-wide IQ

A cost more difficult to assess is that of COVID's impact on the nation's ability to reason. Even a mild, short-term case of COVID-19 can induce an average 3 point reduction in IQ test scores, and severe infection can lead to a 9 point drop I IQ scores.[89] These deficits can persist for at least three years after a positive COVID-19 test.[116] Symptoms including memory loss and difficulty concentrating equal to 20 years of brain aging affect almost half of long COVID patients, apparent consequences of viral brain injury that can persist for years.[117] The CDC estimates that 98.9% of American adults and older teens have antibodies from vaccination and/or at least one prior COVID-19 infection.[13] Currently, only 7% of American adults have received the latest COVID booster vaccination. 93% of Americans remain unprotected from current strains of COVID-19.[45] Conservatively, these statistics suggest that the majority of the American population has experienced, or is at risk of experiencing, a loss of between 3 and 9 IQ points.

The implications of a "dumbing down" of the American population should not be dismissed. "Brain aging" is characterized by reduced neuroplasticity[223-225] Neuroplasticity is necessary for learning,[226-228] creativity[229] and cognitive flexibility,[230,231] which are necessary for the ability to reason,[232-234] accommodate to novel situations and make cognitive and behavioral compromises,[235] abilities that are known to be impaired in people with cognitive impairments.[236,237]

Reduced neuroplasticity on a national scale suggests reduced ability to reason or make compromises, which might explain in part the widening partisan schism in American politics and increased violence since the beginning of the pandemic,[238,239] as well as regressive legislation,[36] especially in politically conservative regional and politically affiliated populations with consistently higher rates of COVID-19.[145-147,152-159] It might also explain the same trends of extremism, fundamentalism, tribalism, inflexibility, refusal to compromise and increased violence on an international scale.[240-243]

Conclusion

The COVID-19 pandemic is not over and has never abated. In the absence of meaningful pandemic management policy, COVID and long COVID appear to be on an unrestricted trajectory. The consequent devastating impacts on the public's physical and mental health, the economy, the healthcare system and domestic and international politics are only now beginning to emerge. It is strongly suggested that legislators make health care policy based on attention to the data and guidance from the best-informed epidemiologists and virologists, in order to generate and enforce evidence-based COVID-19 pandemic management policies and protocols.

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