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A Comprehensive Narrative Review of Coronavirus Disease 2019 (COVID-19): From Pandemic to Endemic

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Background: Coronavirus disease 2019 (COVID-19) was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first identified in Wuhan, China, in December 2019 and became a global health crisis. More than 7 million deaths were officially reported, and the real mortality number is expected to be higher. in May 2023, the Public Health Emergency of International Concern ended. Since then, SARS-CoV-2 has become an endemic respiratory pathogen. Aim: This review critically assessed the evidence on COVID-19, starting from its beginning as an emergency crisis to the endemic stage. Methods: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, in addition to data from the World Health Organization (WHO) and other major public health agencies, were searched for literature related to COVID-19 and published between December 2019 and October 2026. The main priority was directed to systematic reviews and meta-analyses, randomised controlled trials, large cohort studies, and current guidelines. Results: The clinical presentation of COVID-19 ranges from asymptomatic cases to critical illness. Before administration of vaccination, about 80% of symptomatic cases were mild, 15% were severe, and 5% were critical. Severe disease represents an immune and vascular systemic response. RT-PCR remains the standard diagnostic method, and rapid antigen tests are also available with less sensitivity, especially in asymptomatic patients. Large trials reported that dexamethasone, interleukin-6 receptor inhibitors, and baricitinib could reduce mortality in hospitalized patients on oxygen. Hydroxychloroquine, ivermectin, and lopinavir-ritonavir have no therapeutic role. Early antivirals, including nirmatrelvir-ritonavir, remdesivir, and molnupiravir, could help the unvaccinated high-risk patients. Their role in vaccinated individuals is smaller and uncertain. Also, the evidence on convalescent plasma remains controversial. Vaccines resulted in a marked decline in the number of severe cases and deaths, although protection against the virus wanes within months. Notably, long COVID affects millions of people, but the prevalence varies widely, and no effective treatment has been determined. Conclusions: COVID-19 has become an endemic disease, characterized by continuous emergence of Omicron-derived lineages. Major concerns regarding vaccination strategy, the role of antivirals, the mechanisms and treatment of long COVID, and the risk of antigenically distant variants have appeared. Continuous surveillance and large clinical trials in current populations are recommended.

Keywords: *COVID-19, SARS-CoV-2, endemic, antivirals, vaccines, long COVID, narrative review*

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Introduction

On 31 December 2019, pneumonia cases of unknown cause were reported by health authorities in Wuhan, China. Within days, the sequence of a novel betacoronavirus was released (Huang et al. 2020, Zhu et al. 2020). On 30 January 2020, the World Health Organization (WHO) declared a Public Health Emergency of International Concern, and it announced the outbreak as a pandemic on 11 March 2020 (WHO 2020). The global crisis was overwhelming. It impacted health and economic systems. Billions of people lived under complete lockdowns and movement restrictions. The scientific community exerted a massive effort. Within weeks, the viral genome was sequenced. And effective vaccines were authorized within a year (Ball 2021).

On 5 May 2023, WHO canceled the Public Health Emergency of International Concern. Since then, COVID-19 has become an endemic respiratory infection that causes illness, death, and long-term disability, especially among older adults, unvaccinated populations, and immunocompromised individuals (WHO 2023).

The aim of this narrative review is to critically assess the evidence on COVID-19, including virology, epidemiology, pathophysiology, diagnosis, treatment, prevention, and long-term complications. The review addresses the following research questions:

- Which information on the virology, origin, transmission, clinical course, and diagnosis of COVID-19 is well established, and which remains controversial?
- How strong is the evidence for the preventive measures and therapies used during the pandemic, and how has their role changed after vaccination?
- How has SARS-CoV-2 evolved since the emergence of Omicron, and what are the implications for clinical management and vaccination?
- What is known and unknown about long COVID?
- What lessons and research gaps remain for future pandemic preparedness?

Methods

Study design: This is a narrative review. This design was selected because the research questions cover several disciplines. The review was prepared in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA) (Baethge et al. 2019). Search strategy: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar were searched for articles related to COVID-19 and published between December 2019 and October 2026. Search terms were "COVID-19, SARS-CoV-2, long COVID, and post-COVID-19 condition". A list of articles was searched in detail. Documents and reports from WHO, the United States Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC), and the Infectious Diseases Society of America (IDSA) were also included. Study selection: Peer-reviewed articles published in English, together with official guidelines and reports, were considered eligible. Priority was directed to systematic reviews and meta-analyses, large RCTs, large cohort studies, and

current guidelines. Data synthesis: The evidence was constructed under the headings in this review. For each study, the study design, size, and consistency of supporting studies were considered. Disagreements between studies are reported as controversies (Guyatt et al. 2008).

Results

Virology

SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus of about 30 kilobases. It belongs to the genus Betacoronavirus, subgenus Sarbecovirus. It is the seventh coronavirus that is known to infect humans; the other six are four endemic common-cold coronaviruses (229E, NL63, OC43, HKU1) and two earlier epidemic viruses, SARS-CoV (2002) and MERS-CoV (2012) (Zhu et al. 2020).

The virion has four structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). The spike glycoprotein mediates virus entry. The S1 subunit contains the receptor-binding domain, which binds angiotensin-converting enzyme 2 (ACE2) on the host cell, and the S2 subunit mediates membrane fusion. Spike activation requires cleavage by host proteases, mainly TMPRSS2 at the cell surface and cathepsin L in endosomes (Hoffmann et al. 2020).

SARS-CoV-2 has a polybasic furin cleavage site at the S1/S2 junction, which enhances cell-surface entry and transmission (Coutard et al. 2020). The viral genome also encodes 16 non-structural proteins, including the RNA-dependent RNA polymerase (nsp12), the main protease (nsp5/3CLpro), and a proofreading exonuclease (nsp14). This proofreading activity gives coronaviruses a lower mutation rate than influenza viruses; however, extensive variation has occurred through frequent recombination (Markov et al. 2023).

Origins

In June 2025, the WHO suggested that COVID-19 has a zoonotic origin, either directly from bats or through an intermediate host (WHO 2025).

The closest known relatives of SARS-CoV-2 are bat sarbecoviruses, including RaTG13 with about 96.2% genomic identity, sampled in China in 2013, and BANAL-52 with about 96.8%, sampled in Laos in 2020 (Zhou et al. 2020, Temmam et al. 2022). But they are not close enough to be progenitors. The earliest known cases were identified at the Huanan Seafood Wholesale Market, China (Worobey et al. 2022, Crits-Christoph et al. 2024). Firstly, it was suggested that there were two early lineages, A and B (Pekar et al. 2022).

Epidemiology and the Course of the Pandemic

By mid-2026, WHO had reported more than 779 million confirmed cases and about 7.1 million deaths (WHO 2026). The exact number of deaths is expected to

be higher, especially in countries with incomplete death registration and limited testing (Msemburi et al. 2023).

Transmission occurs through respiratory aerosols and droplets, particularly in crowded and poorly ventilated indoor spaces. Also, Transmission may happen through contaminated surfaces and objects (Wang et al. 2021). More than half of transmission originated from people without symptoms, either pre-symptomatic or asymptomatic (Johansson et al. 2021). Before airborne transmission was acknowledged, preventive measures focused mainly on hand hygiene and surface disinfection (Wang et al. 2021).

The risk of severe disease increases sharply with age and is also increased by obesity, diabetes, cardiovascular and chronic lung disease, chronic kidney disease, immunosuppression, pregnancy, and male sex. Additionally, socioeconomic deprivation and occupational exposure increase this risk, and mortality was higher among ethnic minority groups and in low-income communities (Williamson et al. 2020).

Waves and Variants

The pandemic had series of waves, with the emergence of new lineages (Tegally et al. 2021, Viana et al. 2022) (Table 1).

Table 1. *Major SARS-CoV-2 Variants and their Characteristics*

Variant	Time	Special features	Effect
Ancestral (Wuhan-Hu-1)	Dec 2019	Reference genome	First global wave, spring 2020
D614G	Mid-2020	Spike stability	Replaced ancestral worldwide
Alpha (B.1.1.7)	Dec 2020	About 50% more transmissible	Winter 2020-21 waves in Europe, North America
Beta (B.1.351)	Dec 2020	E484K immune escape	Southern Africa; limited global spread
Gamma (P.1)	Jan 2021	Immune escape	Severe Manaus, Brazil wave
Delta (B.1.617.2)	May 2021	High viral loads, more severe	Deadliest global year, 2021
Omicron (B.1.1.529)	Nov 2021	30+ spike mutations, upper-airway tropism	Largest infection wave, lower severity
Omicron descendants (BA.2, BA.5, XBB, JN.1)	2022-24	Progressive immune escape	Recurrent, milder waves
XFG, NB.1.8.1, PQ.16.1.1, BA.3.2	2025-26	JN.1-lineage descendants, including the recombinant XFG; BA.3.2 is a highly divergent BA.3 descendant	Current circulation; variants under monitoring, with no evidence of added severity

Since March 2023, no new variant has been classified as a variant of concern (WHO 2026).

Post-Omicron evolution: Since late 2021, SARS-CoV-2 has followed two main patterns. The first one is antigenic drift in the dominant lineage, with the occurrence of mutations in the receptor-binding domain that confer immune escape. In some

cases, these mutations included ACE2 affinity, as in BA.2, BA.5, XBB, and JN.1. The second is saltation, in which abrupt emergence of highly divergent lineages occurs. This describes what happened with Omicron, with BA.2.86 and BA. 3.2. Prolonged infection in immunocompromised patients is thought to be the leading cause of these mutations; however, this explanation is not well proven. Moreover, recombination between the circulating lineages, such as XBB and XFG, provides a possible third source of diversity (Markov et al. 2023, Carabelli et al. 2023).

In 2026, WHO classified JN.1 as a variant of interest and XFG, NB.1.8.1, PQ.16.1.1 and BA.3.2 as variants under monitoring. For most of the year, XFG became the most prevalent lineage worldwide (WHO 2026). BA.3.2 was first reported in South Africa in late 2024. It has many spike mutations and is considered antigenically distant from other Omicron lineages. Preliminary data indicated vaccines induce cross-reactive antibodies against it (European Centre for Disease Prevention and Control 2026).

Clinical Presentation

Severe COVID-19 is an immune and vascular systemic disease. Infection starts in the nasopharyngeal epithelium, where ciliated and goblet cells expressing ACE2 enhance viral replication. In most cases, infection remains confined to the upper respiratory tract. In a minority of cases, the virus reaches the alveolar type II pneumocytes, triggering severe inflammation with recruitment of monocytes and neutrophils, which leads to cell death, loss of surfactant, and diffuse alveolar damage (Hou et al. 2020).

The clinical course has three overlapping phases. The first week is dominated by viral replication. In the second week, the host immune response becomes predominant. In patients whose clinical status deteriorates, the hyperinflammatory phase can lead to acute respiratory distress syndrome and multi-organ failure, accompanied by elevated interleukin-6, ferritin, and C-reactive protein levels (Siddiqi and Mehra 2020). That's why it is important to use antivirals early and immunomodulators later. Host factors also play a role in determining severity. Neutralizing autoantibodies against type I interferons were detected in about 10% of patients with fatal COVID-19 pneumonia (Bastard et al. 2020).

Endothelial injury and thrombosis are features of COVID-19. Severe cases are characterized by high D-dimer levels, microvascular and macrovascular thrombosis, and pulmonary intravascular coagulopathy, which increase the risk of myocardial infarction, stroke, and venous thromboembolism (Ackermann et al. 2020).

Clinical Spectrum

The median incubation period was about five days in the case of ancestral strain. It was shortened to about three days with Omicron (Wu et al. 2022). The clinical presentation ranges from asymptomatic cases to critical disease.

- Common symptoms: fever, fatigue, myalgia, headache, dry cough, sore throat, and nasal congestion.
- Early features: sudden anosmia and ageusia, more frequent with pre-Omicron variants.
- Gastrointestinal: diarrhea, nausea, and anorexia.
- Serious signs: severe dyspnea and low oxygen saturation on days 7 to 10. Some patients have marked hypoxemia with little respiratory distress, termed "silent hypoxemia".

Before vaccination, about 80% of symptomatic patients had mild disease, 15% had severe disease and needed oxygen, and 5% were critically ill (Guan et al. 2020, Wu & McGoogan 2020). These percentages have decreased markedly because of vaccination, immunity from prior infection, and the shift to less virulent Omicron lineages (Carabelli et al. 2023).

Extrapulmonary manifestations include myocarditis and arrhythmia, delirium, stroke, Guillain-Barré syndrome, acute kidney injury, and hepatic injury. Most children with COVID-19 have mild illness. However, a small number developed multisystem inflammatory syndrome in children (MIS-C) two to six weeks after infection, with fever, shock, cardiac dysfunction, and elevated inflammatory markers. Its incidence decreased after the administration of vaccination and the emergence of Omicron (Feldstein et al. 2020).

Diagnosis

Nucleic acid amplification testing, mainly RT-PCR on a nasopharyngeal or combined throat-nasal swab, remains the standard diagnostic test. Although its sensitivity and specificity are high, False-negative results are common in the early incubation period and late in illness. The accuracy of the result also depends on sampling technique and specimen type. A systematic review reported that false-negative rates of the initial RT-PCR ranged from 2% to 58% across studies (Arevalo-Rodriguez et al. 2020, Kucirka et al. 2020). False-positive results could be related to laboratory contamination, cross-reaction, and data-handling errors, and their relative impact increases when prevalence is low (Surkova et al. 2020). RT-PCR can detect viral RNA for weeks after the end of the infection. Therefore, a positive result late in the illness course does not reflect transmissibility (Cevik et al. 2021).

Since 2021, rapid antigen tests have been used for speed and accessibility. In a meta-analysis, sensitivity was about 73% in symptomatic and 55% in asymptomatic individuals. Its specificity was about 99.6%. For accuracy, it should be performed in the first days of symptoms, when viral load is highest. Serial rapid testing partly compensates for lower sensitivity (Dinnes et al. 2022).

Detection of anti-nucleocapsid antibodies indicates infection, while anti-spike antibodies indicate either infection or vaccination. Antibody titres do not reliably reflect protection; therefore, they are not recommended for assessing individual immunity outside research (Lumley et al. 2021).

Imaging studies are mainly used to assess disease severity. Chest CT typically reveals bilateral, peripheral, lower-zone ground-glass opacities, sometimes with

crazy-paving or fibrotic changes. Lung ultrasound shows B-lines and pleural irregularity. It is useful as a bedside test. Laboratory findings involve lymphopenia, elevated D-dimer, ferritin, C-reactive protein, lactate dehydrogenase, and troponin (Shi et al. 2020).

Treatment

Treatment is tailored based on the two main phases of the disease. Antiviral therapies should be used early to reduce viral replication. Immunomodulators are recommended later to suppress the dysregulated immune host response (Siddiqi and Mehra 2020, Hammond et al. 2022, Beigel et al. 2020).

Management guidelines have changed after the rise in immunity and decline of the baseline risk. Now, the WHO recommendations stratify patients with non-severe disease by their risk of hospitalization. Nirmatrelvir-ritonavir is recommended for patients with high or moderate risk. And molnupiravir or remdesivir are suggested for high-risk patients only when nirmatrelvir-ritonavir is unavailable. These alternatives are not advised for patients at moderate or low risk, because the benefit is too small and does not outweigh potential harms (Lamontagne et al. 2020). For severe and critical disease, WHO and IDSA still recommend systemic corticosteroids, in addition to interleukin-6 receptor inhibitors or baricitinib in patients with severely progressive disease (Lamontagne et al. 2020, Bhimaraj et al. 2020) (Table 2).

Antivirals for Early Disease in High-Risk Patients

Table 2. *Antivirals for High-Risk COVID-19 Patients*

Agent	Mechanism	Regimen	Features
Nirmatrelvir-ritonavir	3CL protease inhibitor	Oral, within 5 days of symptoms	Extensive drug interactions via ritonavir; requires renal dose adjustment; benefit shown in unvaccinated high-risk adults (EPIC-HR); no significant benefit in vaccinated or standard-risk adults (EPIC-SR) (Hammond et al. 2022, Hammond et al. 2024)
Remdesivir	RNA polymerase inhibitor	IV, hospitalised or 3-day outpatient course	Modest benefit; small mortality reduction in hospitalised patients receiving oxygen, but no mortality benefit in ventilated patients (WHO Solidarity Trial Consortium 2022); 87% reduction in hospitalization in unvaccinated outpatients (PINETREE) (Gottlieb et al. 2022)
Molnupiravir	Mutagenic nucleoside	Oral alternative	Lower efficacy; no reduction in hospitalization or death in vaccinated adults (PANORAMIC) (Butler et al. 2023); should be avoided in pregnancy

Monoclonal antibodies against spike became ineffective due to Omicron-lineage immunity escape. A few newer agents, such as pemivibart, are still effective against some current lineages and are used mainly for pre-exposure prophylaxis in severely immunocompromised patients (Cao et al. 2022).

Immunomodulators

In June 2020, the RECOVERY platform trial reported that Dexamethasone reduced mortality, particularly in patients who needed oxygen and mechanical ventilation. It did not show benefit for patients who did not require oxygen (RECOVERY Collaborative Group 2021a). Higher doses of corticosteroids resulted in higher mortality in patients who needed simple oxygen; thus, the recommended dose was 6 mg daily (RECOVERY Collaborative Group 2023). Interleukin-6 receptor blockers (tocilizumab, sarilumab) and the JAK inhibitor baricitinib reduced mortality in severe COVID-19 patients with progressive hypoxemia and elevated inflammatory markers (RECOVERY Collaborative Group 2021b, RECOVERY Collaborative Group 2022).

Supportive Care

Oxygen is the cornerstone of supportive care. Utilization of high-flow nasal oxygen and awake prone positioning reduces the need for intubation. When mechanical ventilation is required, low-tidal-volume techniques and prone positioning are applied. Extracorporeal membrane oxygenation is reserved for refractory severe cases. Prophylactic anticoagulants are standard in hospitalized patients, and therapeutic-dose heparin is beneficial in moderately, non-critical patients but not in critical illness (ATTACC, ACTIV-4a, and REMAP-CAP Investigators 2021).

Other Drugs

Hydroxychloroquine, lopinavir-ritonavir, ivermectin, colchicine and azithromycin were ineffective in improving clinical outcomes in large clinical trials. The large platform trials, including RECOVERY, SOLIDARITY and REMAP-CAP, addressed the role of these drugs and provided strong evidence (WHO Solidarity Trial Consortium 2021).

The evidence on the role of Convalescent plasma is uncertain. Large clinical trials, including RECOVERY, showed no mortality benefit for hospitalized patients (RECOVERY Collaborative Group 2021c), and a systematic review reported that convalescent plasma has no beneficial effect on mortality in patients with moderate-to-severe disease (Iannizzi et al. 2023). On the other hand, two RCTs found that early administration of high-titre plasma reduced progression of out-patients' condition to severe disease or hospitalization (Libster et al. 2021, Sullivan et al. 2022). WHO recommends against its use for non-severe disease and outside clinical trials in severe or critical disease (Lamontagne et al. 2020). Therefore, its role is confined to selected immunocompromised patients and remains uncertain.

Vaccines

In December 2020, the first mRNA vaccine was authorized. This occurred about 11 months after the viral genome was published, compared with the previous record of about four years (Ball 2021, Polack et al. 2020). It was estimated that the

vaccination could prevent approximately 19.8 million deaths, although such an estimate relies on assumptions based on counterfactual transmission and mortality rates (Watson et al. 2022). More than 13 billion doses have been administered worldwide (WHO 2026) (Table 3).

Table 3. *COVID-19 Vaccines*

Platform	Examples	Notes
mRNA	BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna)	Highest initial efficacy (~95% against symptomatic disease caused by the ancestral strain in RCTs); rapidly reformulated for new variants
Viral vector	ChAdOx1 (Oxford-AstraZeneca), Ad26.COV2.S (Janssen), Sputnik V	Cheaper, easier cold chain; rare thrombosis with thrombocytopenia syndrome
Inactivated	CoronaVac, BBIBP-CorV, Covaxin	Lower efficacy against infection; widely used in Asia and Latin America
Protein subunit	NVX-CoV2373 (Novavax)	Good tolerability; later to market

Protection against severe disease and death persisted longer across different variants; however, protection against infection declined within months because of immune escape (Feikin et al. 2022). The effectiveness of two-dose vaccine against Omicron infection decreased to low levels within a few months, and booster doses could restore it transiently (Andrews et al. 2022). This explains why vaccinated people got infected in 2021. In the endemic phase, most studies investigating vaccine effectiveness were observational studies, which are more vulnerable to bias from differential testing behavior and unregistered prior infection. The benefit of repeated booster doses of vaccine in healthy younger adults is small and uncertain.

Safety has been monitored continuously. One of the rare side effects of mRNA vaccines is myocarditis, especially in young male individuals after the second dose. This event occurred at a rate of a few cases per 100,000 and is usually mild. In most cases, vaccine-induced myocarditis is less frequent than myocarditis caused by COVID-19 infection itself (Witberg et al. 2021, Patone et al. 2022). However, it has been found that the administration of a second dose of mRNA-1273 in young men was associated with a higher risk of myocarditis than the infection (Patone et al. 2022). Vaccine-induced thrombocytopenia and thrombosis associated with adenoviral-vector vaccines are considered rare but more serious. This resulted in restriction of these vaccines in several countries (Greinacher et al. 2021). Additionally, anaphylactic reactions occur at a rate of 5 per million doses.

Strain genomes are now updated continuously. Recent vaccine formulations protect against JN.1, LP.8.1 and their descendants. Most vaccination programs restricted the routine boosters to older adults, immunocompromised population, pregnant women, and health workers. This is a shift away from the universal administration of booster doses (WHO 2024-2026). In 2025, the Food and Drug Administration (FDA) narrowed the updated vaccines to adults aged 65 years or older and younger people with high-risk conditions (Prasad et al. 2025).

Long COVID

Long COVID, or post-COVID-19 syndrome, is one of the long-term complications of the pandemic. WHO defines it as symptoms beginning within three months of infection, lasting at least two months and not explained by another diagnosis (Soriano et al. 2022). In 2024, a broader definition was proposed by the US National Academies of Sciences, Engineering, and Medicine: it is an infection-associated chronic condition present for at least three months that does not require laboratory confirmation of infection (National Academies of Sciences, Engineering, and Medicine 2024). The existence of different definitions of long COVID-19 makes the comparison between studies difficult. At least 65 million people worldwide have been affected (Davis et al. 2023). According to the variation in definitions, prevalence estimates range from 3% to over 20% of infections. Many studies did not include control groups, depended on self-reported symptoms, and were affected by selection bias, which may have inflated the estimates.

The syndrome includes some symptom clusters (Davis et al. 2023):

- Fatigue and post-exertional malaise, resembling myalgic encephalomyelitis/ chronic fatigue syndrome
- Cognitive impairment, brain fog, with deficits in attention, processing speed and memory
- Dysautonomia, especially postural orthostatic tachycardia syndrome
- Persistent breathlessness and decreased exercise capacity, sometimes without abnormal lung imaging
- Smell and taste disturbance, including parosmia
- Cardiovascular and thrombotic events

The underlying mechanisms are not fully understood yet and include viral persistence in tissues, autoimmunity and autoantibody formation, reactivation of latent herpesviruses such as Epstein-Barr virus, persistent microthrombosis and endothelial dysfunction, microbiome disruption, and residual organ damage from the acute illness (Davis et al. 2023, Al-Aly et al. 2024).

Risk is higher after severe acute illness, in patients with pre-existing conditions, in women, and with infection by pre-Omicron variants. On the other hand, the risk reduces with vaccination before infection by about a quarter to a half in most studies, although these data come from heterogeneous observational studies (Byambasuren et al. 2023, Xie et al. 2024). But the large number of infections makes the absolute burden high, and reinfections increase cumulative risk (Al-Aly et al. 2022, Bowe et al. 2022).

No effective treatment is available in randomized clinical trials. Management focuses on rehabilitation and symptomatic treatment. This includes pacing for post-exertional malaise, autonomic measures for postural orthostatic tachycardia syndrome, olfactory training for smell loss, and multidisciplinary approaches for other symptoms (Greenhalgh et al. 2024). Trials of antivirals, immunomodulators, and anticoagulants in long COVID have so far been small or negative; for example, a 15-day course of nirmatrelvir-ritonavir did not improve symptoms in the STOP-

PASC trial (Geng et al. 2024). Prevention may play a role in reducing the occurrence of long COVID. The COVID-OUT trial reported that metformin could reduce the incidence of long COVID by about 40% if given during acute infection (Bramante et al. 2023).

Public Health Response

The global response relied on suppression strategies, which included measures to reduce viral transmission towards zero through testing, tracing, border control and lockdowns, and mitigation strategies, which focused on flattening peaks within health systems (Flaxman et al. 2020). Countries in East Asia and Oceania implemented strict test-and-trace systems, which helped delay large waves until vaccines were available. Comparisons between countries are biased by variations in demography, geography, and reporting systems. However, the same strategies waned against Omicron's transmissibility. In December 2022, after China relaxed the restricted policy, case counts rose sharply, producing a large wave within weeks (Leung et al. 2023).

School closures, which affected more than 1.5 billion children, resulted in learning loss that was notable years later. Mental health indicators, especially anxiety and depression in adolescents and young women, deteriorated significantly. Other health programs on routine immunization, tuberculosis, HIV, and cancer screening and treatment were affected for some years. This may explain the disruption to childhood vaccination, which caused measles resurgences across several countries (Betthauser et al. 2023).

Global GDP shrank by about 3% in 2020, the deepest recession since the 1930s. This economic crisis markedly affected the low-income countries (IMF 2021).

The distribution of vaccines showed a high degree of inequity, with marked impact on low-income countries. Global efforts to waive intellectual property protections and to transfer the technology were exerted. However, these efforts were too late to affect the pandemic (Usher 2021).

Current Status

As of late 2026, SARS-CoV-2 is considered a respiratory virus with regional waves rather than global surges. Reported deaths are small, about 719 worldwide in the 28-day period till 18 October 2026, in comparison with thousands weekly in early 2021. The XFG variant is the most prevalent virus lineage for most of 2026, and no variant currently meets the criteria for a variant of concern (WHO 2026).

Consensus and Controversies

Some findings are now well established, and others are considered uncertain or contested (Table 4). Inpatient therapeutic regimens are supported by large randomized clinical trials. On the other hand, the evidence on vaccine effectiveness in the endemic phase, non-pharmaceutical measures, and long COVID depends mainly on observational studies. Conclusions, particularly on antivirals and booster doses of vaccines, were confined to non-immune populations in 2020 and 2021 and required a revision as immunity became almost universal. The concerns that remain inconclusive require long-term investigations, e.g., long COVID research. This becomes difficult as the funding and political attention are markedly declining.

Table 4. *Established Findings and Controversies*

	Established	**Uncertain**
Transmission	Mainly airborne; with substantial pre-symptomatic and asymptomatic transmission.	Effectiveness of community masking and closure of schools and businesses (Jefferson et al. 2011).
Diagnosis	RT-PCR is the standard diagnostic method; antigen tests when performed early in symptomatic disease.	Interpretation of persistent RT-PCR positivity and of cycle threshold values.
Treatment	Corticosteroids, IL-6 receptor blockers and baricitinib reduce mortality in hypoxemic patients; several other repurposed drugs are ineffective.	Effectiveness of antivirals in vaccinated or previously infected patients; role of convalescent plasma in immunocompromised patients.
Vaccines	Large reductions in severe disease and death; rare serious adverse events well characterized.	Role of repeated boosters in low-risk groups; optimal timing and antigen composition.
Variants	Continued Omicron-derived evolution with periodic saltation.	Mechanisms of saltation, whether intrinsic severity could increase.
Long COVID	Real, heterogeneous and multisystem; lower risk in case of vaccination.	Prevalence, standard definition and underlying mechanisms.

Conclusion

Now, SARS-CoV-2 is considered an endemic airborne virus that causes a spectrum of illness, and the severe disease represents a dysregulated immune and vascular reaction. At the time of the pandemic, large clinical trials could reach effective treatments with benefit on mortality for hospitalized patients and rapidly identify the ineffectiveness of repurposed drugs. Within a year, vaccines were manufactured and markedly reduced severe disease and mortality. However, this protection waned after a few months. The increased immunity drove the transition to endemicity. The pandemic showed what the scientific community can achieve in a limited critical time, including genomic sequencing, treatment protocols, and vaccines. On the other hand, delays in identifying the airborne transmission, inadequate transfer of information to the public,

and inequitable vaccine distribution can be considered failures of institutions, politics, and communication (Sachs et al. 2022).

There are still areas of uncertainty, including the role of early antivirals and repeated boosters of vaccines in vaccinated individuals, previously infected patients, and low-risk populations. This needs further randomized clinical trials conducted during the endemic phase. In addition, the value of convalescent plasma is limited and unclear. Long COVID lacks a standard definition, definitive biomarkers, clear underlying mechanisms, and an effective treatment. It is still undetermined whether a pan-sarbecovirus or mucosal vaccine can prevent the viral transmission rather than only severe disease. Intranasal forms of vaccines are still under trial, but no durable sterilizing immunity has yet been shown. Continued saltation may cause an antigenically divergent or more virulent variant. Because of decreased surveillance and genomic studies, the detection of such mutations becomes difficult.

For clinicians and health care workers, management should follow current WHO guidelines, and clinical decisions should be guided by individual risk stratification rather than applied uniformly. For public health, the priorities should be genomic investigation, continuous surveillance, providing vaccination to high-risk populations, and maintaining clinical trials to find scientific evidence for uncertain points. For future pandemics, efforts should be focused more on sustaining surveillance between emergencies, providing equitable distribution of measures, and maintaining public trust (Sachs et al. 2022).

Limitations

This study is a narrative review, not following a systematic search protocol. Therefore, this paper did not include a formal risk-of-bias assessment or meta-analysis, so selection bias cannot be fully excluded. The COVID-19 literature is huge and under continuous revision and change. Thus, some recent data, especially on circulating viral variants and guidelines, may be updated soon. Surveillance reports of the endemic phase may be biased by decreased testing and reporting and should be interpreted cautiously.

References

Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. (2020) Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19. *The New England Journal of Medicine* 383(2): 120–128.

Al-Aly Z, Bowe B, Xie Y (2022) Long COVID after breakthrough SARS-CoV-2 infection. *Nature Medicine* 28(May): 1461–1467.

Al-Aly Z, Davis H, McCorkell L, Soares L, Wulf-Hanson S, Iwasaki A, et al. (2024) Long COVID science, research and policy. *Nature Medicine* 30(Aug): 2148–2164.

Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, et al. (2022) COVID-19 vaccine effectiveness against the Omicron (B.1.1.529) variant. *The New England Journal of Medicine* 386(16): 1532–1546.

Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, Zambrano-Achig P, Del Campo R, Ciapponi A, et al. (2020) False-negative results of initial RT-PCR assays for COVID-19: a systematic review. *PLoS One* 15(12): e0242958.

ATTACC, ACTIV-4a, and REMAP-CAP Investigators (2021) Therapeutic anticoagulation with heparin in noncritically ill patients with COVID-19. *The New England Journal of Medicine* 385(9): 790–802.

Baethge C, Goldbeck-Wood S, Mertens S (2019) SANRA—a scale for the quality assessment of narrative review articles. *Research Integrity and Peer Review* 4(Mar): 5.

Ball P (2021) The lightning-fast quest for COVID vaccines and what it means for other diseases. *Nature* 589(Dec): 16–18.

Bastard P, Rosen LB, Zhang Q, Michailidis E, Hoffmann H-H, Zhang Y, et al. (2020) Autoantibodies against type I IFNs in patients with life-threatening COVID-19. *Science* 370(6515): eabd4585.

Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. (2020) Remdesivir for the treatment of COVID-19: final report. *The New England Journal of Medicine* 383(19): 1813–1826.

Betthauser BA, Bach-Mortensen AM, Engzell P (2023) A systematic review and meta-analysis of the evidence on learning during the COVID-19 pandemic. *Nature Human Behaviour* 7(Jan): 375–385.

Bhimraj A, Morgan RL, Shumaker AH, Baden L, Cheng V C-C, Edwards KM, et al. (2020) Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. *Clinical Infectious Diseases*.

Bowe B, Xie Y, Al-Aly Z (2022) Acute and postacute sequelae associated with SARS-CoV-2 reinfection. *Nature Medicine* 28: 2398–2405.

Bramante CT, Buse JB, Liebovitz DM, Nicklas JM, Puskarich MA, Cohen K, et al. (2023) Outpatient treatment of COVID-19 and incidence of post-COVID-19 condition over 10 months (COVID-OUT): a multicentre, randomised, quadruple-blind, parallel-group, phase 3 trial. *The Lancet - Infectious Diseases* 23(10): 1119–1129.

Butler CC, Hobbs FDR, Gbinigie OA, Rahman NM, Hayward G, Richards DB, et al. (2023) Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomised controlled trial. *The Lancet* 401(10373): 281–293.

Byambasuren O, Stehlik P, Clark J, Alcorn K, Glasziou P (2023) Effect of COVID-19 vaccination on long covid: systematic review. *BMJ Medicine* 2(1): e000385.

Cao Y, Wang J, Jian F, Xiao T, Song W, Yisimayi A, et al. (2022) Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. *Nature* 602(Dec): 657–663.

Carabelli AM, Peacock TP, Thorne LG, Harvey WT, Hughes J (2023) SARS-CoV-2 variant biology: immune escape, transmission and fitness. *Nature Reviews – Microbiology* 21(3): 162–177.

Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A (2021) SARS-CoV-2, SARS-CoV and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness: a systematic review and meta-analysis. *The Lancet - Microbe* 2(1): e13–e22.

Coutard B, Valle C, de Lamballerie X, Canard B, Seidah NG, Decroly E (2020) The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. *Antiviral Research* 176(Apr): 104742.

Crits-Christoph A, Levy JI, Pekar JE, Goldstein SA, Singh R, Hensel Z, et al. (2024) Genetic tracing of market wildlife and viruses at the epicenter of the COVID-19 pandemic. *Cell* 187(19): 5468–5482.

Davis HE, McCorkell L, Vogel JM, Topol EJ (2023) Long COVID: major findings, mechanisms and recommendations. *Nature Reviews Microbiology* 21(Jan): 133–146.

Dinnes J, Sharma P, Berhane S, van Wyk SS, Nyaaba N, Domen J, et al. (2022) Rapid, point-of-care antigen tests for diagnosis of SARS-CoV-2 infection. *The Cochrane Database of Systematic Reviews* 7(7): CD013705.

European Centre for Disease Prevention and Control – ECDC (2026) *SARS-CoV-2 variant update: BA.3.2 added to variants under monitoring*. Stockholm: ECDC.

Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, et al. (2022) Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *The Lancet* 399(10328): 924–944.

Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. (2020) Multisystem inflammatory syndrome in U.S. children and adolescents. *The New England Journal of Medicine* 383(4): 334–346.

Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. (2020) Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature* 584(Jun): 257–261.

Geng LN, Bonilla H, Hedlin H, Jacobson KB, Tian L, Jagannathan P, et al. (2024) Nirmatrelvir-ritonavir and symptoms in adults with postacute sequelae of SARS-CoV-2 infection: the STOP-PASC randomized clinical trial. *JAMA Internal Medicine* 184(9): 1024–1034.

Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, et al. (2022) Early remdesivir to prevent progression to severe COVID-19 in outpatients. *The New England Journal of Medicine* 386(4): 305–315.

Greenhalgh T, Sivan M, Perlowski A, Nikolich JZ (2024) Long COVID: a clinical update. *The Lancet* 404(10453): 707–724.

Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S (2021) Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *The New England Journal of Medicine* 384(22): 2092–2101.

Guan WJ, Ni ZY, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. (2020) Clinical characteristics of coronavirus disease 2019 in China. *The New England Journal of Medicine* 382(18): 1708–1720.

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336(Apr): 924–926.

Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. (2022) Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. *The New England Journal of Medicine* 386(15): 1397–1408.

Hammond J, Fountaine RJ, Yunis C, Fleishaker D, Almas M, Bao W, et al. (2024) Nirmatrelvir for vaccinated or unvaccinated adult outpatients with COVID-19. *The New England Journal of Medicine* 390(13): 1186–1195.

Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. (2020) SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 181(2): 271–280.

Hou YJ, Okuda K, Edwards CE, Martinez DR, Asakura T, Dinnon KH 3rd, et al. (2020) SARS-CoV-2 reverse genetics reveals a variable infection gradient in the respiratory tract. *Cell* 182(2): 429–446.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 395(10223): 497–506.

Iannizzi C, Chai KL, Piechotta V, Valk SJ, Kimber C, Monsef I, et al. (2023) Convalescent plasma for people with COVID-19: a living systematic review. *The Cochrane Database of Systematic Reviews* 2(2): CD013600.

International Monetary Fund – IMF (2021) *World Economic Outlook, April 2021: managing divergent recoveries*. Washington DC: IMF.

Jefferson T, Mar CBD, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. (2011) Physical interventions to interrupt or reduce the spread of respiratory viruses. *The Cochrane Database of Systematic Reviews* 7(Jul): CD006207.

Johansson MA, Quandelacy TM, Kada S, Prasad PV, Steele M, Brooks JT, et al. (2021) SARS-CoV-2 transmission from people without COVID-19 symptoms. *JAMA Network Open* 4(1): e2035057.

Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J (2020) Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Annals of Internal Medicine* 173(4): 262–267.

Lamontagne F, Agarwal A, Rochwerg B, Rochwerg B, Lamontagne F, Siemieniuk RA, et al. (2020) A living WHO guideline on drugs for COVID-19. *BMJ* 370: m3379.

Leung K, Lau EHY, Wong CKH, Leung GM, Wu JT (2023) Estimating the transmission dynamics of SARS-CoV-2 Omicron BF.7 in Beijing after adjustment of the zero-COVID policy in November–December 2022. *Nature Medicine* 29(Jan): 579–582.

Libster R, Pérez Marc G, Wappner D, Coviello S, Bianchi A, Braem V, et al. (2021) Early high-titer plasma therapy to prevent severe COVID-19 in older adults. *The New England Journal of Medicine* 384(7): 610–618.

Lumley SF, O'Donnell D, Stoesser NE, Matthews PC, Howarth A, Hatch SB, et al. (2021) Antibody status and incidence of SARS-CoV-2 infection in health care workers. *The New England Journal of Medicine* 384(6): 533–540.

Markov PV, Ghafari M, Beer M, Lythgoe K, Simmonds P, Stilianakis NI, et al. (2023) The evolution of SARS-CoV-2. *Nature Reviews Microbiology* 21(Apr): 361–379.

Msemburi W, Karlinsky A, Knutson V, Aleshin-Guendel S, Chatterji S, Wakefield J, et al. (2023) The WHO estimates of excess mortality associated with the COVID-19 pandemic. *Nature* 613(7942): 130–137.

National Academies of Sciences, Engineering, and Medicine (2024) *A long COVID definition: a chronic, systemic disease state with profound consequences*. Washington, DC: The National Academies Press.

Patone M, Mei XW, Handunnetthi L, Dixon S, Zaccardi F, Shankar-Hari M, et al. (2022) Risk of myocarditis after sequential doses of COVID-19 vaccine and SARS-CoV-2 infection by age and sex. *Circulation* 146(10): 743–754.

Pekar JE, Magee A, Parker E, Moshiri N, Izhikevich K, Havens JL, et al. (2022) The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2. *Science* 377(6609): 960–966.

Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. (2020) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *The New England Journal of Medicine* 383(27): 2603–2615.

Prasad V, Makary MA (2025) An evidence-based approach to COVID-19 vaccination. *The New England Journal of Medicine* 392(24): 2484–2486.

RECOVERY Collaborative Group (2021a) Dexamethasone in hospitalized patients with COVID-19. *The New England Journal of Medicine* 384(8): 693–704.

RECOVERY Collaborative Group (2021b) Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *The Lancet* 397(10285): 1637–1645.

RECOVERY Collaborative Group (2021c) Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial. *The Lancet* 397(10289): 2049–2059.

RECOVERY Collaborative Group (2022) Baricitinib in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial and updated meta-analysis. *The Lancet* 400(10349): 359–368.

RECOVERY Collaborative Group (2023) Higher dose corticosteroids in patients admitted to hospital with COVID-19 who are hypoxaemic but not requiring ventilatory support (RECOVERY): a randomised, controlled, open-label, platform trial. *The Lancet* 401(10387): 1499–1507.

Sachs JD, Karim SSA, Aknin L, Allen J, Brosbøl K, Colombo F (2022) The Lancet Commission on lessons for the future from the COVID-19 pandemic. *The Lancet* 400(10359): 1224–1280.

Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. (2020) Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *The Lancet – Infectious Diseases* 20(4): 425–434.

Siddiqi HK, Mehra MR (2020) COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. *The Journal of Heart and Lung Transplantation* 39(5): 405–407.

Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV, WHO Clinical Case Definition Working Group on Post-COVID-19 Condition (2022) A clinical case definition of post-COVID-19 condition by a Delphi consensus. *The Lancet – Infectious Diseases* 22(4): e102–e107.

Sullivan DJ, Gebo KA, Shoham S, Bloch EM, Lau B, Shenoy AG, et al. (2022) Early outpatient treatment for COVID-19 with convalescent plasma. *The New England Journal of Medicine* 386(18): 1700–1711.

Surkova E, Nikolayevskyy V, Drobniewski F (2020) False-positive COVID-19 results: hidden problems and costs. *The Lancet – Respiratory Medicine* 8(12): 1167–1168.

Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. (2021) Detection of a SARS-CoV-2 variant of concern in South Africa. *Nature* 592(Mar): 438–443.

Temmam S, Vongphayloth K, Baquero E, Munier S, Bonomi M, Regnault B, et al. (2022) Bat coronaviruses related to SARS-CoV-2 and infectious for human cells. *Nature* 604(Feb): 330–336.

Usher AD (2021) A beautiful idea: how COVAX has fallen short. *The Lancet* 397(10292): 2322–2325.

Viana R, Moyo S, Amoako DG, Tegally H, Scheepers C, Althaus CL, et al. (2022) Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. *Nature* 603(Jan): 679–686.

Wang CC, Prather KA, Sznitman J, Jimenez JL, Lakdawala SS, Tufekci Z, et al. (2021) Airborne transmission of respiratory viruses. *Science* 373(6558): eabd9149.

Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC (2022) Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *The Lancet – Infectious Diseases* 22(9): 1293–1302.

Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. (2020) Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 584(7821): 430–436.

Witberg G, Barda N, Hoss S, Richter I, Wiessman M, Aviv Y, et al. (2021) Myocarditis after COVID-19 vaccination in a large health care organization. *The New England Journal of Medicine* 385(23): 2132–2139.

World Health Organization – WHO (2020) *WHO Director-General's opening remarks at the media briefing on COVID-19, 11 March 2020*. Geneva: WHO.

World Health Organization – WHO (2023) *Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic*. Geneva: WHO.

World Health Organization – WHO (2025) *Scientific Advisory Group for the Origins of Novel Pathogens (SAGO): independent assessment of the origins of SARS-CoV-2*. Geneva: WHO.

World Health Organization – WHO (2026) *COVID-19 epidemiological dashboard: global circulation and variants*. WHO.

WHO Solidarity Trial Consortium (2021) Repurposed antiviral drugs for COVID-19: interim WHO Solidarity trial results. *The New England Journal of Medicine* 384: 497–511.

WHO Solidarity Trial Consortium (2022) Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. *The Lancet* 399: 1941–1953.

World Health Organization Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) (2024–2026) *Statements on the antigen composition of COVID-19 vaccines*. Geneva: WHO.

Worobey M, Levy JI, Malpica Serrano L, Crits-Christoph A, Pekar JE, Goldstein SA, et al. (2022) The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic. *Science* 377(6609): 951–959.

Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. *JAMA* 323: 1239–1242.

Wu Y, Kang L, Guo Z, Liu J, Liu M, Liang W (2022) Incubation period of COVID-19 caused by unique SARS-CoV-2 strains: a systematic review and meta-analysis. *JAMA Network Open* 5(8): e2228008.

Xie Y, Choi T, Al-Aly Z. (2024) Postacute sequelae of SARS-CoV-2 infection in the pre-Delta, Delta, and Omicron eras. *The New England Journal of Medicine* 391(6): 515–525.

Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 579(7798): 270–273.

Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. *The New England Journal of Medicine* 382(8): 727–733.