# 1 Global Challenges After a Global Challenge: Lessons Learned from the COVID-19 Pandemic

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**Abstract**

Coronavirus disease 2019 (COVID-19) has affected not only individual lives but also the world and global systems, both natural and human-made. Besides millions of deaths and environmental challenges, the rapid spread of the infection and its very high socioeconomic impact have affected healthcare, economic status and wealth, and mental health across the globe. To better appreciate the pandemic's influence, multidisciplinary and interdisciplinary approaches are needed. In this chapter, world-leading scientists from different backgrounds share collectively their views about the pandemic's footprint and discuss challenges that face the international community.

**Keywords**

COVID-19 · Post-pandemic · Physiological · Mental health · Environment · Economics · Scientific · Infodemic · Long COVID-19 · Complications

**Abbreviations**

| | |
|---|---|
| AI | Artificial intelligence |
| COVID-19 | Coronavirus disease 2019 |
| HIV | Human immunodeficiency virus |
| RdRP | RNA-dependent RNA polymerase |
| SARS-CoV-2 | Severe acute respiratory syndrome coronavirus 2 |
| SDGs | Sustainable development goals |
| WHO | World Health Organization |
| PHEIC | Public Health Emergency of International Concern |

## 1.1 Introduction

Coronavirus disease 2019 (COVID-19) has affected not only individual lives but also the world and global systems, both natural and human-made. The latter includes adverse consequences to the environment, global trade, and supply chains, as well as politics. It has been more than three years since the World Health Organization (WHO) declared the newly emerged epidemic viral infection as a Public Health Emergency of International Concern (PHEIC); since then, the world has been facing, and will be facing, many pandemic-related challenges.

Although the COVID-19 pandemic put a remarkable and perhaps unprecedented strain on healthcare infrastructure and care delivery, its impact was also felt on education systems, physiological and psychological health, economics, and the environment. Some of the pandemic's effects may only become fully apparent over time. To better appreciate the pandemic's influence, multidisciplinary and interdisciplinary approaches are needed. In this chapter, world-leading scientists from different backgrounds share collectively their views about the pandemic's footprint and discuss challenges that face the international community.

## 1.2 Interdisciplinary Approach to Combat the Virus

### 1.2.1 Modeling of COVID-19

The prediction of COVID-19's evolution was crucial. Mathematical models, computational simulations, and epidemiological simulations play a pivotal role in anticipating and controlling the pandemic and potential future epidemics (Moradian et al. 2020).

To model effectively the dynamics of a specific infection, researchers need to consider the influence of different sub-population compartments. Many variables ranging from micro-host–pathogen interactions to host-to-host encounters as well as the prevailing cultural, social, economic, and local customs worldwide need to be taken into account. Mathematical modeling may help to minimize the effects of the epidemic by understanding the virus transmission mechanisms, thus providing the opportunity to predict the spread of the virus and controlling the pandemic. As an example, the relevant compartments of the asymptomatic persons and, most important, the super-spreaders have been used to model the COVID-19 transmission dynamics (Ndaïrou et al. 2020).

Most of the mathematical models contain ordinary or partial differential equations. These mathematical tools, when combined with large quantities of data along with machine learning and artificial intelligence, can create new technologies to facilitate prevention and combat viral epidemics (Palaniappan et al. 2022), highlighting the potential of interdisciplinary studies to address complex problems.

### 1.2.2 Virus Detection

Early detection of COVID-19 is crucial for health policy. As such, sensitive, robust, and reliable sensors are needed. Researchers have been proposing and testing new techniques and kits necessary for virus detection but not adequate sensitivity, selectivity, and scalability have been achieved so far. Lately, technologies involving nanomaterial-based sensors have been developed, characterized by the potential for a rapid coronavirus detection (Naikoo et al. 2022). These technologies are not invasive and may afford real-time results at low fabrication costs. We highlight surface plasmon resonance and localized surface plasmon resonance sensors (Lee et al. 2018) that detect the viral nucleic-acid particles and nucleocapsid antibodies against coronavirus in undiluted human serum, exhaled breath sensors based on inorganic or organic nanomaterials that rely on a change in the electrical resistance caused by the interaction with the analyte (Shan et al. 2020; Naikoo et al. 2021), graphene-based field-effect transistor (FET)-based biosensors (Seo et al. 2020), electrochemical sensors (Mujawar et al. 2020; Maduraiveeran et al. 2018), and colorimetric sensors that are based on gold nanoparticles (AuNPs) linked to thiol modified antisense oligonucleotides (Moitra et al. 2020). Yet, nanomaterial-based sensors for COVID-19 detection did not fully achieve the requirements for commercialization. Accuracy needs to improve together with reduction of false positives. On better news, artificial intelligence (AI) hold promises for addressing these challenges (Jain et al. 2021). The achievement of reliable and wide-spreadable sensors may allow mass COVID-19 detection along with its large area monitoring that in turn will provide a clear view on the rapid progression of viral infections.

Finally, sensors may be important for reducing the risks of infections in a different way. Given that the virus is present in aerosols in the exhaled breath of infected persons, and the inhalation of high doses of these aerosols may infect healthy persons, it is pivotal to monitor the presence of exhaled breath in closed environments in order to alert or tart a ventilation process. Forcing ventilation can decrease the presence of aerosols indoors and decrease the risk of spreading infection. This can be achieved via air quality sensors (Bosch Sensortec 2019).

### 1.2.3 Development of New Vaccines

The pandemic has pushed scientists to rapidly develop, validate, and clinically translate next-generation vaccines. The successful approval of vaccines against COVID-19 has led to the administration of billions of doses worldwide, protected people from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and saved many lives (Zheng et al. 2022). The existing types of COVID-19 vaccines include at least one of the following four approaches: (i) nucleic-acid vaccines (mainly mRNA encapsulated in lipid nanoparticles) able to instruct cells to produce the SARS-CoV-2 spike protein; (ii) inactivated vaccines derived from the coronavirus itself; (iii) protein vaccines based on the spike protein or its receptor-binding domain; and (iv) viral-vector vaccines, which adopt modified viruses to shuttle genetic instructions for synthesizing the spike protein into cells (Chavda et al. 2021; Ndwandwe and Wiysonge 2021; Deng et al. 2022).

However, challenges still exist for the COVID-19 vaccines. As the viral variants can evade the immunity provided by the original vaccination, the upgrade and improvement of COVID-19 vaccines are ongoing (Callaway 2023). Consequently, vaccines are currently developed as an upgrade of previous versions, such as the bivalent vaccines that comprise portions of the original virus and a variant (e.g., Omicron). In addition, new vaccines are currently developed relying on new technologies and nanosized platforms. These include mosaic vaccines based on nanoparticles supporting coronavirus proteins, and their RBDs derived from multiple coronavirus variants. The common objective of these new vaccines is to provide a long-lasting protection to the patient and overcome viral (present and future) variants. Furthermore, these new vaccines will become cheaper and even more potent, while minimizing side effects (Yamamoto 2022).

### 1.2.4 Looking for Treatments

The pandemic propelled drug development and repurposing of existing anticancer and anti-inflammatory drugs. Given that the SARS-CoV-2 virus infection led to COVID-19, a serious inflammatory condition, many existing drugs were used to relieve symptoms, such as corticosteroids (e.g., dexamethasone). These drugs relieved symptoms but did not control or reduce the viral infection. Several drugs, which were registered for other viral infections (e.g., human immunodeficiency virus [HIV]) or were in development by various pharmaceutical companies and research institutes, were immediately investigated for their antiviral SARS-CoV-2 activity. Antiviral drugs are targeted against either host factors or viral factors. The best known host factor is angiotensin-converting enzyme 2 (ACE2), a receptor responsible for the uptake of the virus. The major disadvantage of ACE2 targeting is its normal cellular function (Jackson et al. 2022). Targeting the viral life cycle (i.e., replication) is more likely to be specific, as it addresses a viral-encoded component of the reproduction machinery in the cell. This is the backbone of the successful treatment of HIV infections. Such practice led to rapid development and registration of the nucleoside analogs remdesivir and molnupiriavir, drugs inhibiting RNA-dependent RNA polymerase (RdRP) (Lee et al. 2022a; Beigel et al. 2020; von Delft et al. 2023). Viral proteases are essential in the viral life cycle, and nirmatrelvir is an example of a drug inhibiting SARS-CoV-2 proteases (Hammond et al. 2022). This drug inhibits Mpro (3CL protease) and is combined with ritonavir, which inhibits CYP3A4/CYP450 to increase its half-life. However, there is a problem with these drugs. As has been observed with HIV infection, the virus mutates rapidly, leading to drug resistance. This can be solved effectively by developing combinations of drugs directed to different viral targets, such as RdRP and Mpro. It can also be solved by repurposing already registered anticancer drugs, which are likely or proven to be effective; examples are antimetabolites such as 6-mercaptopurine or antifolates such as methotrexate (Stegmann et al. 2021; Bayoumy et al. 2020; Mohamed et al. 2021a). For instance, methotrexate enhances the efficacy of remdesivir, whereas inhibition of dihydroorotate dehydrogenase potentiates the effect of molnupiravir (Stegmann et al. 2022).

The development of these combinations is rapidly proceeding. With experience in designing combinations for HIV treatment and cancer, more effective combination treatments will likely be available both for SARS-CoV-2 and other viral infections.

## 1.3 Medical and Health Challenges

### 1.3.1 Long COVID-19

Many patients experience difficult, even life-threatening conditions, days and weeks following infection with SARS-CoV-2, and for high-risk patients immediate mortality remains a danger (Rezaei et al. 2021). Nevertheless, most infected people will survive the acute episode, although the health challenges may not end quickly. A good number of patients face a range of ongoing complications after COVID-19 recovery, a condition named long COVID-19. It is estimated that more than 10% of patients develop long COVID-19, and more than 65 million individuals worldwide suffer from it. Multiple organs and systems are affected by long COVID-19 with diverse clinical manifestations, including those that resemble chronic fatigue syndrome/myalgic encephalomyelitis and postural orthostatic tachycardia syndrome (Davis et al. 2021; Ceban et al. 2022; Larsen et al. 2022). Incidences of long COVID-19 are most frequent in hospitalized patients, followed by non-hospitalized and vaccinated individuals (Davis et al. 2023). Patients present with clinical manifestations of the organ system and tissues involved, including neurological and cognitive system (memory loss, cognitive impairment, paresthesia, dizziness, and balance issues, sensitivity to light and noise, loss of smell or taste, autonomic dysfunction, tinnitus, hearing loss, vertigo), reproductive system (menstrual irregularities), respiratory system (shortness of breath, cough), gastrointestinal system (nausea, abdominal pain, loss of appetite, heartburn, constipation), dysautonomia, chronic fatigue syndrome/myalgic encephalomyelitis (postexertional malaise, unrefreshing sleep, cognitive impairment, and/or orthostatic intolerance), vascular tissue and organ damage (increased risk of deep vein thrombosis, pulmonary embolism, bleeding), and endocrine disorders (low cortisol) (Nalbandian et al. 2021; Han et al. 2022).

Various mechanisms have been proposed to explain long COVID-19 symptoms. ACE2, which is well recognized as the COVID-19 entry portal into cells, is also expressed in different non-respiratory tissues. Therefore, viral replication in ACE2-expressing cells in different tissues may induce a local inflammatory response, which has been suggested to contribute to prolonged COVID-19 pathophysiology (Khazaal et al. 2022). In addition, the host immune system may be a culprit. Activation of the innate immune system can contribute to disease pathology (Lucas et al. 2020). For instance, SARS-CoV-2 nucleocapsid (N)-protein and spike proteins can trigger complement activation in different ways, which might induce tissue damage and thrombosis (Flude et al. 2021; Yu et al. 2020). These findings have prompted clinical studies on the use of complement inhibitors, such as AMY-101, with successful therapeutic outcomes in COVID-19 patients (Soung et al. 2022; Mastaglio et al. 2020).

However, the misdirected immune response is not limited to innate immunity, in view of the frequently present autoantibodies that target immunomodulatory proteins (such as anti-type I interferon neutralizing antibodies) and the considerable increase in autoantibody reactivities frequently detected in COVID-19 patients (Wang et al. 2021a). As an example, a type of autoantibody targeting the orexin/hypocretin receptor HCRTR2 impedes orexin signaling, which plays a crucial role in wakefulness and appetite regulation (Nixon et al. 2015). Many cytokines and chemokines are elevated, and several autoantibodies have been observed in affected individuals, including autoantibodies against ACE2, ADRB2/β2-adrenoceptor, CHRM2/muscarinic M2 receptor, AGTR1/angiotensin II AT1 receptor, and the angiotensin 1–7-MAS1 receptor (Davis et al. 2023).

In addition, prolonged inflammatory state due to the persistence of the virus in some body tissues (Li et al. 2020a; Wu et al. 2020; Yong 2021) can lead to endovascular and tissue fibrosis. These may be responsible for some lung injuries and cardiac problems post-COVID-19, which, in turn, may trigger more complications in other organs (Hama Amin et al. 2022; Liu et al. 2020). Autoimmunity is also a contributing mechanism to long COVID-19 (Rojas et al. 2022; Chang et al. 2023). The evidence for long COVID is supported by the long-term complications that occur following earlier outbreaks of SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) (Ahmed et al. 2020; Hui et al. 2005; Lee et al. 2019). Although some post-COVID-19 health complications are recognized, others may reveal over time. Regular follow-up of patients who suffer from post-COVID-19 complications is helpful in identifying long-term complications.

### 1.3.2 Chronic Diseases

Disrupted follow-up of patients with chronic diseases has attracted the medical community's attention during the pandemic. Autoimmune diseases (e.g., inflammatory bowel disease, multiple sclerosis), rheumatological diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus), congenital disorders, primary immunodeficiency diseases, neurological diseases (e.g., Alzheimer's disease, dementia), cardiometabolic diseases (e.g., heart failure, obesity, diabetes mellitus), cancers, and chronic diseases (e.g., kidney disease, asthma) place a heavy burden on patients' families and the healthcare system. However, the pandemic, mandatory lockdown and home confinement, as well as fear of infection, caused a remarkable disruption in medical follow-up of chronic diseases (Barach et al. 2020). In addition, patients with chronic diseases may be more susceptible to COVID-19, and patients infected with COVID-19 may be at risk of developing chronic conditions (Davis et al. 2021; Han et al. 2022; Papadopoulou et al. 2021; Yazdanpanah and Rezaei 2022; Kunutsor and Laukkanen 2020). Next, we consider relevant examples.

#### 1.3.2.1 Alzheimer's Disease

Reports of the impact of COVID-19 on nursing home residents early in the pandemic raised the alarm for Alzheimer's disease (AD) (Perry 2020). With nearly two-thirds of nursing home residents suffering from dementia, mostly from AD, and estimates of over 60% of COVID-19 deaths in nursing homes (Gaugler et al. 2014; Neumann 2020), the alarm was justified. Epidemiological studies demonstrated that AD patients are more susceptible to COVID-19 (Reyes-Bueno et al. 2020; Wang et al. 2021b), and, conversely, those recovered from COVID-19 are more susceptible to AD onset (Wang et al. 2022a). As long COVID evolves, it is critical to evaluate the coincidence of AD for understanding and reducing the underlying risk factors.

#### 1.3.2.2 Cancer

Delays in screening and early symptom assessment brought on by COVID-19 impacted the capacity of the health system and will likely lead to a surge in cancer cases in the near future, although the short-term effect is a decline in reported cancer cases due to disrupted diagnosis and screening programs. However, the expected increase in cancer cases and cancer-related mortality could be explained by the disrupted follow-up and missed or delayed regular screening programs due to changes in healthcare system priorities during the pandemic, lockdown, and fear of visiting health-related facilities (Oakes et al. 2023; Siegel et al. 2022, 2023). The role of COVID-19 itself in triggering cancer formation is still under debate. Multiple mechanisms are being considered to explain a potential effect of COVID-19 on carcinogenesis and cancer progression. In particular, increased production and prolonged presence of pro-inflammatory cytokines, T-cell depletion leading to host immune dysfunction, sustained activation of oncogenic signaling pathways such as JAK-STAT, MAPK, and NFKB/NF-κB, hypoxia-induced oxidative stress, and a prolonged inflammatory environment have been proposed as explanations of the link between COVID-19 and tumor formation and progression (Del Valle et al. 2020; André et al. 2022; Li et al. 2020b; Satarker et al. 2021; Goel et al. 2021; Abassi et al. 2020; Muz et al. 2015; Greten and Grivennikov 2019).

During SARS-CoV infection, non-structural protein 3 (Nsp3) and endoribonuclease Nsp15 provoke degradation of tumor suppressor protein TP53 and RB transcriptional corepressor 1 (RB1), in preclinical models, respectively (Ma-Lauer et al. 2016; Bhardwaj et al. 2012; Fujiyoshi et al. 2021). Moreover, in silico studies on SARS-CoV-2 proteins revealed that the S2 subunit interacts with TP53 as well as BRCA1 and BRCA2 proteins (Gorodetska et al. 2019; Mantovani et al. 2019; Singh and Bharara 2020). Taken together, the SARS-CoV viral family has the potential functional capacity to induce genomic instability by impairing the function of tumor suppressor proteins.

One of the most important mechanisms associated with cancer is macroautophagy (hereafter autophagy) (Gaebler et al. 2021). Autophagy is responsible for removing damaged organelles and misfolded proteins, and defects in autophagy are associated with several pathological conditions including cancer (Levine and Kroemer 2019; Alizadeh et al. 2023). As a homeostatic mechanism, autophagy crosstalks with other such pathways including the unfolded protein response, the induction of which also could be an initiator for cancer (Dastghaib et al. 2020; Høyer-Hansen and Jäättelä 2007). In general, autophagy is considered a double-edged sword: It could be a mechanism against cancer or a mechanism to promote cancer progression (White 2015). Both SARS-CoV-2 receptors, angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) are highly expressed in the human gastrointestinal tract; thus, SARS-CoV-2 is able to infect and replicate in human enterocytes (Zang et al. 2020). In a recent investigation on the gastrointestinal biopsies of 14 patients, researchers located virus nucleic acid and antigens in 50% of the cases (Gaebler et al. 2021). These results were repeated in the nasopharyngeal specimens obtained from individuals with previous SARS-CoV-2 infection (Habibzadeh et al. 2020, 2021). Therefore, continuous expression of viral nucleic acids could have significant long-term effects in COVID-19 survivors. Importantly, SARS-COV-2 proteins could interact with the autophagy machinery and induce changes in autophagy flux in mammalian cells. As an example, ORF3a protein interacts with VPS39 and induces autophagy flux inhibition via targeting autophagosome and lysosome interactions (Zhang et al. 2021). Nsp15 blocks the initial stage of autophagy (induction), whereas ORF7a protein decreases lysosomal acidification and slows down the autophagy flux (Hayn et al. 2021). Therefore, SARS-COV-2 infection could reduce autophagy flux via targeting both the initiation and degradation steps of autophagy.

The effects of COVID-19 on cancer formation and progression are not simply attributable to a single direct mechanism but are likely a cumulative consequence of multiple mechanisms. Of note, the currently available statistics may reflect only the tip of the iceberg, as the effect of COVID-19 on cancer trends will take years to ascertain.

Furthermore, the effect of the COVID-19 pandemic is not limited to cancer pathophysiology; indeed, treatment of cancers has been severely affected during the pandemic. The development of cancer therapy has suffered greatly, especially in blood cancers. Many of the available most effective therapeutics are B-cell-depleting agents, leading to a great susceptibility to COVID-19. Recently, highly effective drugs have failed to receive regulatory approval, because of the incidence of COVID-19 in clinical trials. Physicians need to balance treatment efficacy with COVID-19 risk (Cheson 2022).

#### 1.3.2.3 Obesity

According to a recent report by the WHO, more than one billion individuals are affected by obesity and the number is growing (World Health Organization 2022). The pandemic worsened this trend. Lockdown or mandatory home confinement has increased the risk of obesity through multiple mechanisms (Ghanemi et al. 2020; Tan et al. 2020). Fear of getting infected with COVID-19 by visiting outdoor public places, such as food markets, caused many individuals to choose highly processed food products containing large amounts of calories (especially in the form of saturated fats) and extra salt, with long shelf lives but low nutritional value, rather than fresh products. Moreover, the pandemic had a negative impact on mental health (Hettich et al. 2022). Mental health problems are mutually associated with disruption of normal sleep cycles and sleep deprivation (Zhao et al. 2022). The combination of sleep disturbance and psychological problems such as stress, anxiety, and depression, may result in increased food consumption, which, when associated with a lack of physical activity (due to home confinement), considerably increases the risk of obesity. Mental health problems are also associated with increased alcohol intake (Grossman et al. 2020), which is another source of nutritionally empty calories. From a socioeconomic point of view, as numerous businesses were closed during the pandemic, many employees faced unemployment and financial difficulties. As a result, some families could not afford fresh healthy food, and instead used more junk foods or preserved foods, which cost less. In addition, both fear of visiting public places and financial problems led to a noteworthy decline in the use of public gyms and healthcare facilities for weight control, which further intensified the obesity trend (Ghanemi et al. 2020; Tan et al. 2020). Obesity is strongly linked to cardiovascular diseases, diabetes mellitus, and metabolic complications, as well as musculoskeletal disorders such as osteoarthritis; moreover, it is a risk factor for some types of cancer. As such, when the obesity trend is accelerated due to the pandemic, more complications and a heavier burden are to be expected in the near future. This merits a multidisciplinary call for global action.

#### 1.3.2.4 Cardiovascular Diseases

Various cardiovascular complications are associated with long COVID. These include fatigue, chest pain, and shortness of breath, as well as autonomic manifestations such as postural orthostatic tachycardia (i.e., a low volume of blood returning to the heart upon standing). All these symptoms can lead to greater anxiety and disability. Key cardiovascular issues that have been reported beyond the acute phase of COVID-19 include myocardial inflammation, myocardial infarction, right ventricular dysfunction, and arrhythmias (Al-Aly et al. 2021; Raman et al. 2022; Lorente-Ros et al. 2023; Dale et al. 2023). There is also some evidence of myocardial edema, active inflammation, as well as both left and right ventricular dysfunction. Overall, there is an increased risk of cardiovascular outcomes, as evidenced by large-scale observational studies, such as coronary artery disease, cardiomyopathy, and arrhythmias, compared to the general population (Abbasi 2022). Mechanisms of how various cardiovascular outcomes are linked to COVID-19 are not adequately understood, but COVID-19 likely modulates the long-term risk of these, and other cardiovascular complications often prevalent among individuals suffering greatly from COVID-19. Although the acute cardiovascular consequences of COVID-19 were more prominent in the hospitalized patients compared to those enduring a milder illness, the heightened risk of long-term cardiovascular events was observed even in patients who endured mild forms of the illness and were not hospitalized (Al-Aly et al. 2021).

During the pandemic, cardiovascular surgery was all but halted except for emergency operations such as for aortic dissection. A recent study examined (Ad et al. 2021) the effects of the COVID-19 pandemic in 67 adult cardiac surgery institutions in Canada and the USA. Non-urgent surgery markedly dwindled during the month of March 2020 in nearly all institutions, resulting in a decline to 45% of baseline. Hospitals with a high burden of patients hospitalized with COVID-19 showed decline trends in total volume similar to institutions in areas with fewer cases of COVID-19. As a proportion of total surgical volume, there was a relative increase in coronary artery bypass grafting surgery, heart transplantation, and the use of extracorporeal membrane oxygenation but a decrease in valvular operations. With the end of the pandemic, cardiac surgical volumes normalized, but the hospital staffing including nurses and respiratory therapies showed high turnover, markedly affecting patient care. Staff shortages continue to be a problem to the present day and probably to the future.

### 1.3.3 Outbreaks of Vaccine-Preventable Diseases

A large proportion of healthcare resources and facilities were devoted to the pandemic. Even where resources were available, fear of visiting healthcare centers resulted in considerable disruption of routine childhood vaccination programs in parts of the world. In addition, some authorities dictated vaccination against COVID-19, likely prompting opposition and increased fear for other vaccinations. Failure to receive life-saving childhood vaccines increases the risk of future large outbreaks of infectious diseases. Indeed, during the first two months of 2022, globally reported measles cases showed a 79% increase compared to the same period in 2021, which raises concerns of possible outbreaks of vaccine-preventable diseases with potential fatal outcomes (World Health Organization JNR 2022). Due to the highly contagious nature of measles, as social distancing and strict health-related protocols weaken and vaccination rates decline, the disease could spread quickly. The same is true for other vaccine-preventable infectious diseases, perhaps at a more gradual pace. Besides its acute impact on general health, measles temporarily impairs the immune system and predisposes the patient to a variety of secondary bacterial and viral infections, which could be devastating for children. The outbreak of vaccine-preventable diseases is a worldwide serious threat requiring global action.

More generally, a post-COVID rebound has been acknowledged also in non-preventable infectious diseases such as hand-foot-and-mouth disease (HFMD) and some infectious respiratory diseases as a result of the loss of immunity following COVID-19 social distancing measures (Farahat et al. 2022; Lee et al. 2022b). Although the situation may normalize in the years to come, it is unclear how long this "immunity debt" will last and what its consequences will be.

### 1.3.4 Repercussion for Young Children

Many people suffered increases in anxiety, depression, and stress during COVID-19 (Muñoz-Vela et al. 2023). Domestic violence also increased (Huldani et al. 2022). If a pregnant woman is exposed to such increased stress, her child is at greater risk of a range of neurodevelopmental problems, including attention deficit hyperactivity disorder (ADHD), conduct disorder, anxiety, and depression, as well as autism spectrum disorders (Glover et al. 2018). Prenatal infection independently predicts child social and communication problems (O'Connor et al. 2022) and the children are also at increased risk of some physical problems, such as asthma. All these conditions will likely be more frequent among the children of women who were pregnant during the COVID-19 pandemic. There should be extra screening programs for these children and early intervention to help.

## 1.4 Psychological and Mental Health Challenges

### 1.4.1 Stress, Grief, and Mental Disorders

The pandemic disrupted life and brought many coping challenges to individuals and families. Lockdowns, distancing, and strict health protocols affected mental health (Xiong et al. 2020). In particular, isolation, home confinement, deprivation from social interactions, persistent fear of being infected, loss of friends and family members, and long-term hospitalization worsened mental health (Gruber et al. 2021). Isolation had particularly adverse consequences when family members or friends were not allowed to visit dying family members in hospitals or residential care homes for the elderly; these consequences included guilt for being unable to express an appropriate "goodbye" to loved ones (Szuhany et al. 2021).

In addition, many businesses were closed, and the workers faced unemployment and financial difficulties. Relatedly, mental health deteriorated due to the unavailability of mental healthcare services, especially during the first weeks of the pandemic when online services were just about to be established (Li et al. 2020c). The psychological repercussions of the pandemic were most prevalent in vulnerable populations, such as children and older adults. Moreover, healthcare personnel experienced long periods of isolation from family besides long hours of working in hospitals and healthcare centers, which put considerable psychological strain on them. Anxiety, depression, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), and sleep disturbances were commonly reported during the pandemic (Zeng et al. 2023; Peng et al. 2023; Ghahramani et al. 2022; Theberath et al. 2022).

Maladaptive behaviors such as self-harm ideation, unprotected sex, aggressive behavior, hoarding, binge eating episodes, drug abuse, and alcohol consumption were also increasingly observed (Pedrini et al. 2022; Nowak et al. 2020). A multidisciplinary, long-term action is needed to prevent serious physical and psychosocial complications (Holmes et al. 2020).

### 1.4.2 Information Overload and Misinformation

Infodemic, defined as the combination of excessively mostly correct and relevant information with incorrect or unreliable information that is typically widespread, has become a challenge since the early days of the pandemic (Naeem and Bhatti 2020). Infodemic leads to the accumulation of false or distorted news, causes uncertainty, provokes emotional distress, and negatively affects mental health. When prolonged, infodemic may foster alternative coping strategies, such as neglecting pandemic-related information, which may deprive people of receiving effective health-related information to combat the pandemic (Soroya et al. 2021; Zarocostas 2020). Infodemic, information overload, and misinformation also challenged the acceptance of the COVID-19 vaccination program in many susceptible communities, with harmful consequences (Singh et al. 2022; Chen et al. 2022). Infodemic and misinformation resulted in a significant social pathology during the peak of the infection and beyond, as they created a divide between abiding and non-complying citizens, and generated friction in otherwise socially cohesive groups (Mohamed et al. 2021b).

### 1.4.3 COVID-19 Vaccine Hesitancy

Under the COVID-19 campaign worldwide, many people manifested vaccine refusal or hesitancy. A study analyzing COVID-19 vaccine hesitancy in 23 countries showed that this is the result of misperceptions about the safety, efficacy, and risks posed by the vaccine, as well as mistrust in the science and clinical validation of vaccine development or in the institutions responsible for vaccination campaigns (Lazarus et al. 2022). Other factors associated with vaccine hesitancy varied by country and included personal experience with COVID-19 (e.g., loss of a family member, sickness) and demographic characteristics (e.g., gender, education, income). For example, one study (Lazarus et al. 2022) showed that low education levels and low household income are correlated with high levels of hesitancy in 19 and 11 countries, respectively, among the 23 included. In contrast, a loss of income due to the pandemic and loss of a family member were factors associated with vaccine acceptance in some countries. Likely, people who lost their jobs, lost their socioeconomic status, or were sick desired to quickly return to normality and were more prone to accept the COVID-19 vaccination. In the same study, although these cases of vaccine hesitancy accounted for 24.8% in June 2021, the reported vaccine acceptance was as high as 75.2% among the 23 countries (Lazarus et al. 2022). However, this percentage of acceptance is lower than the estimation needed to control the pandemic's progress. The misperception of vaccine safety and efficacy has been also associated with wrong or inaccurate communication and dissemination, often politicized (Aliasin et al. 2022; Larson et al. 2022). Finally, negative vaccine respondents may be more willing to accept a vaccine if recommended by their trusted doctor.

The challenges for the ongoing vaccination campaigns are thus to succeed in overcoming such misperception and resistance and expanding vaccine access in low- and middle-income countries. Such campaigns would need to include the importance of the correct information and communication by trusted sources throughout the entire population, which could improve perceptions of vaccine safety and efficacy and increase vaccine acceptance (Shakeel et al. 2022).

## 1.5 Digital Transformation Challenges

### 1.5.1 Education

Due to closure of schools, universities, and other educational centers, educational authorities started considering alternative routes for mandated education programs. Digitalization in education and e-learning had been expected to become part of routine educational programs, particularly as a supplemental tool, but the pandemic pushed the plans rapidly in practice and quickly added virtual learning methods to established curriculums during the middle of a semester. Although neither the education system nor the students were ready for the unprecedented shift, they had to adapt quickly. Post-pandemic educational models have become topics of scholarly interest (Peimani and Kamalipour 2021; O'Dea and Stern 2022). Despite some concern that digital technologies could change the conventional role played by universities and educational institutions in modifying social life, digitalization of university education is inevitable and the process is well underway (Peimani and Kamalipour 2021). It has been generally accepted that online education cannot replace face-to-face education and in-person classes; yet, digitalization and remote learning methods are helpful in redesigning and developing novel learning and teaching programs. Indeed, the pandemic-induced virtual learning methods could be considered a model for evaluating institutional, local, national, and global efforts to introduce digitalization into education, and for providing an opportunity to assess innovative pedagogical approaches, students' perception and expectations, and the psychological effects of online learning and teaching (O'Dea and Stern 2022; Zhao and Watterston 2021). The role of online education in primary school requires special mention. Engaging children to behind-the-computer learning is challenging, given that interindividual learning capabilities are different and remote education does not support the social growth of children to the same extend as in-person education (Alsubaie 2022). It is important to address how the shift in the education model during the pandemic has affected the overall student's ability to participate in life-long learning and to develop a sense of professionalism.

Closure of schools and universities had a different impact in developing versus developed countries, due to the great gap in access to the internet (and, sometimes, also to electricity) and in information and communications technology infrastructures. Indeed, there is a massive regional variation in internet penetration globally. In the poorest (vs. wealthiest) countries, the percentage of people with internet connectivity is still very low. Improving the situation would require a considerable investment, which is unlikely to occur. As such, it is worth considering low-cost solutions that could bridge the digital divide such as the community communication center (C3) model, massive open online courses (MOOCs), use of social media as a learning platform, and use of digital platforms (Osman 2022).

To be more concrete with regard to higher education, financial strain, and research disruption are key challenges. Many universities faced financial difficulties as a result of the pandemic, due to a decline in enrollment and government funding, which reduced their revenue. These financial difficulties will likely continue to impact on higher education institutions for years to come (Dubey and Pandey 2020). The pandemic has disrupted research in many fields, with laboratories and research facilities having to close temporarily. These disruptions are likely to have a lasting influence and may change the way research is conducted in the future. In fact, pandemic-related effects on the supply chain for many reagents, consumable products, and equipment items are still being experienced by researchers globally.

The technology for virtualizing training, meetings between research teams, and international collaborations and supervision has undergone an extraordinary but uneven evolution in a very short time, depending on a university's technical capacities. Developments included the installation of digitized techniques both in the training process and the defense phase of doctoral theses, leading to a better economic return. The possibility of holding a greater number of virtual meetings of higher quality makes the training process more flexible and increases the capacity for internationalization. Regarding the defense of doctoral theses, digital technology has worked well, making examination committees more international and effective. The protocol and solemnity of the process may have been affected, but the economic cost has been lowered (Mullen 2021; Raju 2021).

### 1.5.2 Careers

A change in careers occurred, starting at the early days of the pandemic and lockdown. Many non-essential employees switched to working remotely from home, and many companies deployed automatic systems and used robots to continue work with the lowest risk of spreading the infection. Permanent career changes are likely in the post-pandemic era.

Some companies have considered flexible workplace arrangements (in-person and remote), as they realized that remote working during the pandemic could be more efficient and often save physical space, financially benefiting the company. In addition, employees' transportation and meal expenses may decrease. The possibility of working remotely and the widespread application of virtual meetings limits business travel, which reduces companies' expenses and saves time (Hanaei et al. 2021, 2022). However, online conferences and online meetings may provide reduced opportunities for informal social interactions, which could otherwise culminate in stimulating ideas. Before the pandemic, informal contacts at conferences were considered by many as the most important features or opportunities.

Conversely, whereas business travels may be reduced, tourism and leisure-related businesses are expected to experience a surge in demand post-pandemic (Lund et al. 2021). Furthermore, both businesses and consumers have found e-commerce more convenient and likely will continue to extend it post-pandemic. Many companies have started to use automation and artificial intelligence (AI), initiating a quick adoption of these technologies in work categories with a high level of physical interaction (direct human-to-human contact) such as in warehouses, call centers, and grocery stores. Application of automation and AI is predicted to continue and even expand to other work categories in the post-pandemic era. The demand for healthcare-related workers may increase, as the pandemic has alerted attention to health. Overall, low-wage occupations as well as those of part-time and minority workers are predicted to be vulnerable jobs facing cuts post-pandemic (McKinsey Global Institute 2021; Battisti et al. 2022).

### 1.5.3 Tele-Healthcare

Tele-healthcare is the application of distant communication and information technologies to deliver healthcare as well as promote and monitor patient's self-management via constant monitoring and personalized feedback. During the pandemic, a considerable burden was imposed on healthcare staff, which triggered accelerated in-practice utilization of robotic and AI technologies in healthcare settings. For instance, disinfection of the hospitals' environment, patients' risk assessment, and delivery and supply chain activities were conducted using robotic and AI technologies (Sarker et al. 2021). However, due to the high expenses for developing robotic and AI-aiding technologies and lack of proper infrastructure, healthcare settings in some regions of the world did not benefit from these technologies. The COVID-19 pandemic sped up the tele-healthcare revolution. Although many patients and physicians prefer in-person clinical visit and care, tele-healthcare and "home visits" are predicted to become popular and perhaps the norm. A strong surveillance system and proper infrastructure are essential for continuous and extensive use of tele-healthcare; otherwise, serious health issues may occur, particularly in regions with underdeveloped infrastructure (Sarker et al. 2021; Hollander and Carr 2020). Different challenges are associated with widespread application of tele-health. For example, lack of face-to-face physical contact may negatively affect the quality of visits as emotional information is more likely to be missed. Another challenge will be the overuse of available services when they are unnecessary, which may result in mismanagement of the patient's chief health complaint. Similar to digitalization in other fields, such as education, poor internet access in some regions is a big challenge for tele-healthcare (Anaya et al. 2022; Omboni et al.

2022). Although tele-healthcare has been a great resource during the pandemic crisis, it is arguable to what extent the widespread application of robotics, AI, and advanced technologies in a vital situation, such as human health, would be safe and useful in the post-pandemic era.

## 1.6 Scientific Challenges

### 1.6.1 Data Disclosure Process

The health toll caused by the COVID-19 crisis called for the collection of a large volume of data and a speed-up in the flow of information at an unprecedented scale and magnitude. The scientific community adapted rather promptly by facilitating the exchange of information between research groups, creating rules governing publishing in such cases, and ultimately through a sharp rise in the use of preprint archives. The perceived value of preprint manuscripts increased considerably, as they became a source of information for the media (Watson 2022). This trend has drawbacks: the pertinent manuscript has not undergone peer review and hence may entail mistakes.

Similarly, public repositories of raw data, especially of genetic sequences, boomed to facilitate storage and shared analysis. Although this was largely a salutary measure, particular cases invited caution by the scientific community, as some repositories (the Global Initiative on Sharing All Influenza Data [GISAID], in particular) have operated based on terms and policies contrary to the best interest and ethical needs (Enserink 2023).

## 1.7 Economic Challenges

The pandemic had an enormous on global economy. However, the pandemic's consequences were most severe among emerging economies, exacerbating their fragility. With the lockdown and closure of many businesses, over 50% of households (not only in emerging but also in advanced economies) were unable to keep up basic consumption for more than 90 days in the face of income loss. In addition, an average business was unable to cover expenses for more than 55 days with cash reserves. Overall, the pandemic had a huge influence on global poverty, which increased at a rate unobserved in a generation. Disproportionate unemployment and income loss resulted in a remarkable rise in fiscal inequality nationally and globally (World Bank 2022a).

The World Bank estimated that recovery from the pandemic-induced crisis would be similarly unequal to its initial economic effects. In the post-pandemic era, high-income countries are expected to recover at a faster pace than low-income countries. As the interest rates rise worldwide, the low-income countries' currencies will depreciate, making it difficult to pay back their debts (which they incurred by borrowing in foreign currency during the pandemic) and hindering their economic recovery (World Bank 2022b). Inequality in economic development has been a global challenge but was exacerbated by the pandemic. The swift trend of digitalization contributed to an increase in the use of robots and automated systems for work that was previously carried out by low/middle-skilled workers, thus raising unemployment and inequality (World Bank 2022a; Park et al. 2022).

Interestingly, the economic crisis caused by the pandemic has provided an opportunity to facilitate transformation to a more efficient and sustainable global economy. Climate change has always been a global challenge, and different measures, including economic practices, have been suggested to tackle global warming. Revising the cost of carbon emissions and supporting green economy approaches and the application of sustainable technologies are important practices to slow down climate change (Drews et al. 2022; Savin et al. 2022). The pandemic led to an inevitable economic slowdown, which varied between countries, offering governments the opportunity to adopt green economic approaches (World Bank 2022b; Sandbrook et al. 2022).

Furthermore, the increased healthcare expenses caused by the pandemic resulted in reallocation of funds. Also, large amounts of money were spent on vaccine development programs. Consequently, the allocation of large sums of money to health-related sectors has inevitably reduced the budget for other sectors.

On a related topic, additional funding needs to be committed to worldwide health monitoring programs. For example, the USA ended funding for the Predict program that was run by the US Agency for International Development (USAID) and was acting as an early warning system for pandemics, just months before the outbreak of the current pandemic. Similarly, the Centers for Disease Control and Prevention (CDC), the leading public health agency in the USA, is chronically underfunded, and there has been a consistent decline in independent funding for the WHO. Overall, public health is receiving less funding than that devoted to individualized medicine, undermining preparedness for coping with new pandemics.

## 1.8 Environmental Challenges

### 1.8.1 Climate Change, Recycling, and Air Pollution

Deforestation to build farms or pastures results in migration of wild species to new habitats, which leads to contact among different species (wild-wild, wild-domestic, and wild-human contacts) that would not have previously interacted when living in separate habitats. Furthermore, as shown in the case of bats, which face multiple and synergistic threats (Kingston et al. 2021), environmental stress is responsible for increased viral shedding (Eby et al. 2023). These processes facilitate the spread of emerging infectious diseases (Wolfe et al. 2007; Rohr et al. 2020).

Biodiversity affects human health; it is reported that about 75% of anti-infection medications are derived from natural products (Romanelli et al. 2015). Moreover, the checks and balances of natural systems help to prevent contagious pathogens from worldwide spread and becoming a pandemic (Everard et al. 2020).

Climate change is considered the biggest global environmental threat, which compounds the toll on mental health brought on by the pandemic (Kornei 2023). It is estimated that a further 1.5 °C increase in global temperature can happen by 2040 (McNeely 2021). The global temperature rise causes a sea level rise, and extreme climatic events such as droughts, floods, heat waves, extensive forest fires, and more dust emissions. Hence, population movement and changes in animals' habitat raises the possibility of spreading new infections. Also, prolonged wildfire seasons induced by climate change produce a huge amount of carbon dioxide ($CO_2$) that, in addition to regular anthropogenic inputs, exacerbates global warming and climate change (Landrum and Holland 2020; Hugelius et al. 2020) resulting in a negative downward cycle. Emissions of particulate matter from such fires have a deleterious impact on society (e.g., destroyed communities) and public health.

During the pandemic, environmental changes were accelerated. As the pandemic inflicted serious economic problems and priorities changed in budget allocation, environmental protection agencies weakened, allowing easier exploitation of natural resources. Moreover, in some regions, particularly tropical areas, people started to attack wildlife and protected species and to cut trees due to unemployment and loss of income (McNeely 2021; Badola 2020). Bats and to a lesser extent pangolins have been stigmatized and increasingly persecuted (Gupta et al. 2022; Lu et al. 2021).

Increased plastic wastes also pose an environmental challenge, as the use of personal protection equipment, plastic-packaged food, and disposable utensils increased considerably during the pandemic. A safe process to eliminate plastic waste is necessary on both national and global scales to preserve the environment from greater damage (Vanapalli et al. 2021).

The pandemic has also raised concerns about global recycling efforts to mitigate environmental challenges, and in particular materials that have been exposed to the virus. New guidelines and regulations have been formulated regarding waste management (Das et al. 2021). These include specific requirements for the handling of potentially contaminated materials such as medical masks, gloves, and suits. Overall, the pandemic has presented a new set of challenges for waste recycling, and adherence to new guidelines can minimize the spread of the virus while sustaining the continued global recycling efforts (Das et al. 2021; Sarkodie and Owusu 2021).

Air pollution decreased in some cities following lockdowns and home confinement regulations. Reduced rates of transportation and limited activity of large industries resulted in lower global consumption of fossil fuels, which, in turn, slightly lessened the emission of greenhouse gas (Forster et al. 2020; International Energy Agency 2020). This experience has encouraged some governments to speed up the development of renewable infrastructure, such as wind and solar power generation.

During lockdowns, the world learned to still be connected without much physical presence or international travel. Although the latter has rebounded substantially (Lund et al. 2021), a certain level of reduced travel to and from offices has been achieved, as flexible workplace arrangement is maintained. This may contribute to a reduction in emissions of greenhouse gases in the long run.

### 1.8.2 Food Systems

The pandemic increased global food insecurity in almost every country by slashing incomes and disrupting food supply chains. The conditions during the pandemic were worsened by Russia's invasion of Ukraine. According to the World Food Program (WFP), due to the compounding effects of social, political, and economic crises, the total number of food insecure people rose from 276 to 323 million (World Food Programme 2023). The pandemic continues to wreak havoc on global hunger and poverty—especially on the poorest and most vulnerable populations. In particular, the pandemic had an impact upon the agri-food systems and their economy, stressing critical factors like food production, demand, price hikes, security, and supply chain resilience (Sridhar et al. 2023). Also, the pandemic posed huge barriers in providing affordable and nutritious food to poor people in developing countries. A lesson learned is the need to build a resilient food system. This can be achieved by adopting sustainable agricultural practices with a prime focus on techniques like urban agriculture, crop rotation, hydroponics, and family farming. Scientific advances in using modern digital tools such as artificial intelligence, machine learning, deep learning, and blockchain technology can contribute toward developing sustainable agri-food systems for a self-reliant society (Sridhar et al. 2023).

### 1.8.3 Energy

The spread of SARS-CoV-2 had a negative impact upon the economic growth of many countries. For example, according to the International Energy Agency (IEA) report published in 2020, the US gross domestic product (GDP) decreased by 7.4% in 2020. As a result of the economic slowdown, energy consumption saw a worldwide reduction. Of note, the pattern of energy consumption differed across countries. Travel restrictions and lockdowns had a considerable influence on energy demand and consequently on the need for oil and other forms of energy. By mid-April 2020, weekly energy demand had fallen by 25% for countries in complete lockdown and 18% for those in partial lockdown. The fall in demand led to a sharp fall in the price of natural gas and oil, reaching a decade low in April 2021 as the virus spread around the world. Renewable energy proved to be more resilient than other forms of energy. Electricity systems increased the shares of renewables in their operation, as they operated effectively, albeit under reduced load conditions (International Energy Agency 2022; Guida et al. 2020).

Besides its drastic effects on demand and energy prices, the pandemic has revealed the crucial role of energy in current society. Without energy, vital functions of the health system and the critical telecommunication system would collapse. It is suggested that given the surplus of energy supplies, the importance of efficient, resilient energy networks for the transmission and distribution of electrical energy in such extreme conditions cannot be overstated. During the pandemic, network operators have taken successful mitigation measures to ensure continuity and maximization of operations both for field and office activities. In some cases, grid maintenance works have been postponed or canceled, due to travel restrictions without risking system operation in short or medium terms. Moreover, hygiene and sanitary measures, especially for operational staff and travel restriction or cancelation of arrangements to prevent virus contamination, have been imposed. The transmission and distribution supply industry has been able to continue its essential operations to provide network operators with the necessary equipment and services, although its activity has been affected by reduced market demand and supply chain disruptions (International Renewable Energy Agency 2020).

The global economy recovered at record speed in 2021. As energy intensity improvements were postponed, global energy demand increased by 5.4%, and the demand for all fossil fuels grew by at least 5% in 2021. The historic plunge in global energy consumption in the early months of 2020 that drove the price of many fossil fuels to their lowest level in decades has rebounded fast since mid-2021. Oil prices have returned to around or above USD 100/barrel, and coal and natural gas prices have reached record levels (International Energy Agency 2022).

Surging energy demand was in part met by increased use of coal, resulting in a jump in emissions in 2021, the largest annual increase in global $CO_2$ emissions from the energy sector ever recorded. This contrasted with a fall of about 8% in $CO_2$ emissions growth in 2020 compared to 2019, the largest annual drop since the Second World War. The rebound of global economy among other factors, like the impact of weather-related events on demand and electricity generation, has led to a global energy crisis with energy prices touching record levels in many markets. The global energy crisis has hurt households, industries, and entire economies around the world, with the poorest and most vulnerable suffering particular hardship. One of the striking results of the combination of the COVID-19 pandemic and the energy crisis is a reversal of global progress on electricity access for the first time in more than a decade (International Energy Agency 2022).

The increasing trend of energy prices was exacerbated in early 2022 by the Ukraine conflict, pointing to the need for increased energy security by reducing dependence on imported fuels (International Energy Agency 2022). Moreover, concerns about climate change have led several countries to accelerate their plans to reach net zero emissions through faster deployment of renewable energy sources, both in the power sector and beyond (Guida et al. 2020).

During the pandemic, forced stays at home increased, and therefore, the management of energy consumption became crucial (Karami et al. 2014). As a solution for solving this challenge, Smart Homes provide a solution in the framework of Smart Grid and Smart Cities (El-Dessouki and Saeed 2021). Microgrids, as novel network structures, provide the most effective way to control local energy resources and supply critical loads increasing the system resilience in case of rare events, like the pandemic and natural disasters (Schwaegerl and Tao 2013). In a Smart Grid framework, it is possible to realize the e-health infrastructure, distance working, and e-learning, while also tracing the ill people in the city (a very important consideration during the outbreak of infectious diseases). Investment in infrastructures for the development of Smart Grids and Smart Cities will play a key role in future outbreaks of infectious diseases.

In some parts of the world, political institutions have invested a large portion of public savings to carry out an energy and ecological transition. For example, Next-Generation EU (NGEU) is the European Union economic recovery package to support the EU member states in recovering from the COVID-19 pandemic, especially those that have been particularly hard hit. The instrument is worth €750 billion and, among various initiatives, the complete substitution of combustion vehicles with electric ones has been decided and will be fully adopted starting in 2035. This mandate has pushed researchers to find new rechargeable battery solutions, in terms of safety, recycling, raw materials, and engineering (Fagiolari et al. 2022; Siccardi et al. 2022; Gandolfo et al. 2022).

### 1.8.4 Ocean and Marine Studies

Humans have become increasingly reliant on the ocean, which cover 70% of the planet. Thus, it is not surprising to find ocean interactions with SARS-CoV-2 in multiple ways—both positive and negative. Marine scientists have made numerous contributions regarding COVID-19 transmission, detection, and the search for drug treatment. Early work by scientists at the University of California San Diego identified the airborne transmission of COVID-19 that confirms the effectiveness of masking (Prather et al. 2020) and pioneered the surveillance and early detection of COVID-19 using campus wastewater (Karthikeyan et al. 2021). Active compounds derived from marine organisms, including flavonoids, tannins, alkaloids, terpenoids, peptides, lectins, polysaccharides, and lipids, have been found to influence COVID-19 entry into cells, replication, and release from cells. Marine sponges and algae in particular produce RdRp inhibitors or exhibit general antiviral properties (Geahchan et al. 2021; Rahman et al. 2022).

Ocean-based livelihoods were affected by the pandemic with reductions in fishing, recreation, and tourism. This hit particularly hard for tropical island countries reliant on tourism as a primary source of income, and recovery is just now happening. Marine science observation contributes to the knowledge of weather, climate, and ocean hazards as well as basic science. For open ocean scientific observing, a COVID-19 impacts survey in April 2020 revealed that the cancelation of ship activity meant that existing moored equipment could not be serviced, limited operations of autonomous underwater vehicles (AUVs) and gliders, and no reseeding of fundamental drifter arrays like ARGO (Heslop et al. 2020).

A direct negative effect of the pandemic on the ocean was the generation of medical waste including 129 billion masks and 65 billion gloves every month (Prata et al. 2020), leading to significant plastic excess in the ocean (Wang et al. 2022b). It is estimated that 25,000 tons of single-use plastic entered the global ocean, creating danger to marine ecosystems (Peng et al. 2021). In contrast, the limited activities of humans during 2020 and parts of 2021 reduced other human impacts on the ocean from tropical waters to Antarctica. There was a 70.2% decrease in marine traffic within Exclusive Economic Zones associated with restrictions on human mobility and in consumer supply and demand (March et al. 2021). Reduced noise, ship strikes of mammals, less commercial and recreational fish catching, and less direct human contact all offer some respite to marine ecosystems.

For marine science projects engaging stakeholders, engagement was more difficult, and the move to an internet-based, digital mode of operation created distinct disadvantages for specific regions and groups (e.g., artisanal fishers, aquaculture farmers) (Köpsel et al. 2021). Marine science is still catching up but with some changed practices. Funding agencies work harder to support early career scientists in transition between jobs, conferences are now routinely hybrid, and ships are back in action but with the COVID-19 precautions in place.

### 1.8.5 Geographical Studies

Time and space are researched by geographers, who traced the spread of the pandemic via maps and graphs and by studying travel behavior (Rose-Redwood et al. 2020; Bissell 2021; Franch-Pardo et al. 2020; Xi et al. 2023). Several research teams contributed to the accumulated knowledge, spanning countries such as Spain (Maza and Hierro 2022), Sweden (Florida and Mellander 2022), Denmark (Holmager et al. 2021), and Italy (Ascani et al. 2021). This knowledge helped to prevent the pandemic's impact on human health (Brinkman and Mangum 2022; Gaskin et al. 2021). Also, geographers analyzed the role of climate and weather on the spread of the coronavirus, which is highly affected by atmospheric conditions (Yang et al. 2021). Geographical studies were useful for developing the understanding and knowledge of the pandemic (Franch-Pardo et al. 2021; Maiti et al. 2021). As discussed in previous sections, the pandemic opened a new challenge for the environment (e.g., increased plastic waste), biodiversity (e.g., execution of some species and wildlife overuse due to economic problems in some areas), and soil security (e.g., soil security being affected as it is closely linked to water, food, energy; environment security being affected) (Geraghty and Kerski 2020; El-Ramady et al. 2021). Hence, geographical studies can help to tackle environmental and perhaps long-lasting, challenges.

## 1.9 Sustainable Development Goals

Sustainable development goals (SDGs) were adopted by the UN General Assembly on September 25, 2015, and agreed upon by 193 countries under the 2030 Agenda for Sustainable Development. The SDGs were formulated to align the world to act toward achieving a better quality of life and sustainable growth, as well as to mitigate the effect of climate change. There are 17 SDGs classifiable into five groups:

- *People*: no poverty, zero hunger, good health and well-being, quality education, and gender equality
- *Planet*: drinking water and sanitation, climate action, responsible consumption and production, life below water, and life on land
- *Prosperity*: affordable and clean energy for all, reduced inequality, sustainable cities and communities, decent work and economic growth, and industry, innovation and infrastructure
- *Peace*: peace, justice and strong institutions
- *Partnership*: partnerships for achieving the targets of goals.

With the emergence of the COVID-19 pandemic, progress toward achieving SDGs is likely to be hindered. Hence, the pandemic may be a distraction from achieving SDGs. Yet, the pandemic could be viewed as an opportunity to identify pitfalls in the route toward achieving the SDGs.

## 1.10 Future Perspectives and Conclusions

The spreading of COVID-19 represented an unprecedented challenge for humanity. This is not only because of the complexity of protecting public health and the need to quickly develop and administer effective vaccines but also because of immediate repercussions to the global economy. Besides millions of deaths, the rapid diffusion of the infection and its very high socioeconomic impact have affected healthcare, economic status and wealth, and mental health across the globe. Yet, COVID-19 also constituted an opportunity, as it tested individuals' and societies' capability to react to an existential threat. The lessons learned may pay off in preparing for another virus outbreak. Science can play a critical role in shaping the future agenda and political decisions.

In most healthy people, the SARS-CoV-2 infection is asymptomatic and mild, although it can occasionally result in severe or life-threatening illness, or permanent disabling symptoms. The pandemic proved that several characteristics mainly affecting the immune response of humans have a significant impact on the consequence of infection-host interaction. Therefore cases with higher susceptibility should be identified and protected or vaccinated compared to other immunocompetent cases to avoid the same adverse consequences observed during the early phase of the pandemic. The human immune function, the key factor in determining the severity of COVID-19 illness, is substantially diminished by age, with the over 65-year-olds having the highest likelihood of needing intensive care. Comorbidities such as obesity, metabolic syndrome, and chronic liver and kidney diseases associated with immune dysregulation are associated with severe COVID-19 illness. Also, men are more vulnerable than women due to the impact of X-chromosome-located immune genes on the final response against the virus, as many genetic defects have been identified in X-linked patterns (e.g., TLR7 deficiency). The presence of neutralizing autoantibodies against immune components (e.g., type I interferons) was strongly over-represented among individuals who developed life-threatening COVID-19. Young children appear to be less severely affected compared to people with other respiratory viral infections, but those with inborn errors of immunity could present severe COVID-19 mainly with defects in interferon pathways. Therefore, active identification of cases with immune susceptibility to other viral infections, mainly zoonotic respiratory pathogens, should be conducted at high speed and in advance to prevent the impact of the next potential pandemic on this vulnerable group of patients and manage better the prioritization of treatment and vaccination. However, given the relatively small group of patients with such defects, it is necessary to consider the available resources and think of the best strategy to protect both vulnerable populations and the meet the healthcare-related needs of the overall population.

Long COVID-19 is associated with more than 200 symptoms that affect multiple organ systems. Consequently, there will be a great number of new conditions requiring novel treatment strategies. Therefore, from the medical point of view, new recommendations and guidelines are essential for each medical discipline. Moreover, it will be a great challenge to define standards for diagnostics. The question will arise "What is long COVID?." There will be a risk that doctors classify patients with a rare, unknown, or even unrecognized disease as a patient with COVID-19 complications.

The pandemic has opened up new research priorities. For example, in medical sciences, it will be necessary to identify the pathobiochemical mechanisms by which the SARS-CoV-2 mediates its pleiotropic effect on different organs. Receptor and downstream signaling must be investigated. It would be ideal to pinpoint biomarkers with high sensitivity and specificity to identify patients suffering from long COVID-19. In addition, there are many patients that are assumed to have developed diseases after vaccination. Therefore, there is a need to establish strategies to define what lesions were induced by the vaccination. In addition, there is an urgent need for strategies to cure or improve post-vaccination sequelae. Finally, mental health issues (psychological distress, depression, anxiety, stress symptoms, suicidal thoughts) associated with COVID-19 are more prominent in women than men. The reasons need to be understood.

Some recommended treatments for COVID-19 are challenging. IgG antibodies formed specifically against enveloped viruses can undergo a unique form of glycosylation (afucosylation); although these antibodies can be effective in eliminating cancer cells, they can also amplify cytokine storms and immune-mediated pathologies, which could contribute to the severity of COVID-19 (Larsen et al. 2021). Further research is essential to design proper medications for COVID-19. In biological, chemical, and physical sciences, the importance of interdisciplinary work to develop preventive vaccines, diagnostic tools, and therapeutic agents has been thoroughly highlighted by the pandemic. Collaborative studies between scientists from different disciplines such as environmental, biological, and chemical sciences are crucial in studying the origin of SARS-CoV-2 and how to prevent future viral spreads. Scientists from environmental sciences, economics, and politics need to work together to develop protocols about how to protect nature, biodiversity, and the ecosystem. Taken together, as scientific inquiry becomes increasingly interdisciplinary, research that integrates insights from multiple fields will only become more important in the years ahead.

During the pandemic, social media have been used as a platform for spreading various conspiracy theories about the source and consequences of COVID-19. Better ways to communicate health information and prevent the spread of misinformation are needed.

Inflation and the disruption of supply chains lead to families making difficult financial decisions regarding basic needs. Consumer prices rose 7.1% from November 2021 to November 2022, with food costs up 10.6%, prompting the 2023 World Economic Forum to name the cost-of-living crisis as the most significant short-term global risk. Strategies for alleviating poverty through the widespread promotion of medium-term practices of food storage on a yearly or bi-yearly basis should also be encouraged to avoid the 55–90 days individual support limit observed during COVID-19. Such practices have the potential to alleviate inequality and promote economic recovery in future pandemics.

The pandemic has had a notable political impact, with many governments around the world facing criticism for their handling of the crisis. It has also led to increased nationalism and racism in some countries. In addition, it has highlighted existing health disparities and inequities, particularly in vulnerable populations.

Anthropogenic ecological disequilibria could and did generate a global health crisis. Yet, it is still something that people and particularly, to a lesser extent, the scientific community, have not yet fully come to terms with. Yet, the COVID-19 crisis apparently started due to habitat clearance putting pressure on wildlife, and wildlife trade markets, which act as potential spillover sites. We have now entered the paradigms of "One Earth" and "One Health." The creation of international networks to prevent outbreaks and pandemics is another task that was started but remains to be finalized. In particular, it is important to remember that the COVID pandemic is of zoonotic nature. Hence, given the environmental factors that will make spillovers more frequent in the future, the fostering of networks, such as Preventing Zoonotic Disease Emergence/PREZODE, focused on the prevention of such events is crucial.

There are also positive lessons learned. The pandemic has increased awareness of public health and resulted in increased investment and focus on healthcare and research. The development and use of mRNA vaccines have opened the door to create vaccines for numerous other viruses that were previously not amenable to preventative measures. The development of mRNA-loaded nanoparticle-based vaccines, like the ones introduced by Pfizer-BioNTech and Moderna, has showcased the unprecedented potential of mRNA technology and has opened the field for the development of next-generation lipid-based nanoparticle vaccines for other viral and bacterial infections to improve preparation for future threats, and for other types of disease, such as solid tumors. Indeed, encouraging results from early clinical trials with mRNA-loaded nanoparticle-based vaccines as a monotherapy or in combination with immunotherapy have been obtained in patients with resected solid tumors and gastrointestinal cancer (Lorentzen et al. 2022). The ongoing studies on next-generation mRNA cancer vaccines are more likely to succeed in combination with immunotherapeutic treatments such as adoptive cell therapy and immune checkpoint inhibitors. Nevertheless, several challenges remain and include identification of individual cancer neoantigens, validation of the most feasible vaccine administration methods, and regulatory hurdles.

The pandemic period has accelerated the introduction of digital tools and new teaching methods. These will also be important in the future, in the case of teacher unavailability, public transport strikes, student indisposition, or development of online courses. In engineering sciences, many countries have moved to spend a share of public money to accelerate environmental and energy policies, paving the way to a more sustainable world. In this context, Smart Grid technologies have proved to increase the system resilience by supplying critical loads in case of rare events, like pandemics and natural disasters.

The role of science and academia during global crises has also come to the fore. First, the safeguarding of freedom of expression, academic freedom, debate, and protection of international whistleblowers are crucial for science to operate properly. The COVID crisis has demonstrated shortcomings in these aspects. Second, science needs to have voices. Structures (e.g., venues, communication media, and official speakers) are necessary to ensure that vocal minorities do not take over the public dialog and that scientists can express the majority of the community's opinion and thereby are in a position to counter any potential political agendas that are contrary to the public interest.

Pandemics have threatened the health and well-being of societies, and the global order, in the past. The crucial roles of science and public health, vaccination programs, the WHO, and all other mutually beneficial international collaborations must continue to play a central role in informing healthcare policy and delivery. Now that we are at what is considered the end of the pandemic, we should look back, and by assessing the toll we as humans paid in each of these areas, we can learn how to be better prepared for the next pandemic. It will help if scientists understand issues outside their immediate areas of expertise/interest and see how the different challenges are interrelated. In addition to tackling the many challenges in this article, we need to consider what will happen in the next pandemic. What have we done to try to prevent or at least mitigate the impact of that next threat to global health?

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## References

Abbasi J (2022) The COVID heart—one year after SARS-CoV-2 infection, patients have an array of increased cardiovascular risks. JAMA 327(12):1113–1114

Abassi Z, Higazi AAR, Kinaneh S, Armaly Z, Skorecki K, Heyman SN (2020) ACE2, COVID-19 infection, inflammation, and coagulopathy: missing pieces in the puzzle. Front Physiol 11:574753

Ad N, Luc JG, Nguyen TC, Arora RC, Balkhy HH, Bender EM et al (2021) Cardiac surgery in North America and coronavirus disease 2019 (COVID-19): regional variability in burden and impact. J Thorac Cardiovasc Surg 162(3):893–903.e4

Ahmed H, Patel K, Greenwood DC, Halpin S, Lewthwaite P, Salawu A et al (2020) Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: a systematic review and meta-analysis. J Rehabil Med 52(5):jrm00063

Al-Aly Z, Xie Y, Bowe B (2021) High-dimensional characterization of post-acute sequelae of COVID-19. Nature 594(7862):259–264

Aliasin MM, Yazdanpanah N, Rezaei N (2022) Neurological and neuropsychological adverse effects of SARS-CoV-2 vaccines—where do we stand? Rev Neurosci 33(7):721–743

Alizadeh J, Kavoosi M, Singh N, Lorzadeh S, Ravandi A, Kidane B et al (2023) Regulation of autophagy via carbohydrate and lipid metabolism in cancer. Cancers 15(8)

Alsubaie MA (2022) Distance education and the social literacy of elementary school students during the COVID-19 pandemic. Heliyon 8(7):e09811

Anaya YB-M, Bañuelos Mota A, Hernandez GD, Osorio A, Hayes-Bautista DE (2022) Post-pandemic telehealth policy for primary care: an equity perspective. J Am Board Fam Med 35(3):588

André S, Picard M, Cezar R, Roux-Dalvai F, Alleaume-Butaux A, Soundaramourty C et al (2022) T cell apoptosis characterizes severe COVID-19 disease. Cell Death Differ 29(8):1486–1499

Ascani A, Faggian A, Montresor S (2021) The geography of COVID-19 and the structure of local economies: the case of Italy. J Reg Sci 61(2):407–441

Badola S (2020) Indian wildlife amidst the COVID-19 crisis: an analysis of status of poaching and illegal wildlife trade. TRAFFIC India office

Barach P, Fisher SD, Adams MJ, Burstein GR, Brophy PD, Kuo DZ et al (2020) Disruption of healthcare: will the COVID pandemic worsen non-COVID outcomes and disease outbreaks? Prog Pediatr Cardiol 59:101254

Battisti E, Alfiero S, Leonidou E (2022) Remote working and digital transformation during the COVID-19 pandemic: economic–financial impacts and psychological drivers for employees. J Bus Res 150:38–50

Bayoumy AB, Ansari AR, De Abreu RA, Peters GJ, Mulder CJ (2020) Multi-drug therapy schedules for SARS-COV-2: smart repurposing of old drugs. J Explor Res Pharmacol 5:29–30

Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC et al (2020) Remdesivir for the treatment of COVID-19—final report. N Engl J Med 383(19):1813–1826

Bhardwaj K, Liu P, Leibowitz JL, Kao CC (2012) The coronavirus endoribonuclease Nsp15 interacts with retinoblastoma tumor suppressor protein. J Virol 86(8):4294–4304

Bissell D (2021) A changing sense of place: geography and COVID-19. Geogr Res 59(2):150–159

Bosch Sensortec. How sensing solutions help to fight against the spread of COVID-19. Available from: https://www.bosch-sensortec.com/news-and-stories/stories/how-sensing-solutions-help-to-fight-against-the-spread-of-covid-19.html

Brinkman J, Mangum K (2022) JUE insight: the geography of travel behavior in the early phase of the COVID-19 pandemic. J Urban Econ 127:103384

Callaway E (2023) The next generation of coronavirus vaccines. Nature 614:22–25

Ceban F, Ling S, Lui LM, Lee Y, Gill H, Teopiz KM et al (2022) Fatigue and cognitive impairment in post-COVID-19 syndrome: a systematic review and meta-analysis. Brain Behav Immunity 101:93–135

Chang R, Chen TY-T, Wang SI, Hung YM, Chen HY, Wei CJ (2023) Risk of autoimmune diseases in patients with COVID-19: a retrospective cohort study. eClinicalMedicine 56:101783

Chavda VP, Hossain MK, Beladiya J, Apostolopoulos V (2021) Nucleic acid vaccines for COVID-19: a paradigm shift in the vaccine development arena. Biologics 1(3):337–356

Chen X, Lee W, Lin F (2022) Infodemic, institutional trust, and COVID-19 vaccine hesitancy: a cross-national survey. Int J Environ Res Public Health 19(13)

Cheson BD (2022) Death and clinical trials in the plague years. The ASCO Post. Available from: https://ascopost.com/issues/july-10-2022/death-and-clinical-trials-in-the-plague-years/

Dale CE, Takhar R, Carragher R, Katsoulis M, Torabi F, Duffield S et al (2023) The impact of the COVID-19 pandemic on cardiovascular disease prevention and management. Nat Med 29(1):219–225

Das AK, Islam MN, Billah MM, Sarker A (2021) COVID-19 pandemic and healthcare solid waste management strategy—a mini-review. Sci Total Environ 778:146220

Dastghaib S, Shojaei S, Mostafavi-Pour Z, Sharma P, Patterson JB, Samali A et al (2020) Simvastatin induces unfolded protein response and enhances temozolomide-induced cell death in glioblastoma cells. Cells 9(11)

Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y et al (2021) Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. eClinicalMedicine 38:101019

Davis HE, McCorkell L, Vogel JM, Topol EJ (2023) Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol 1–14

Del Valle DM, Kim-Schulze S, Huang H-H, Beckmann ND, Nirenberg S, Wang B et al (2020) An inflammatory cytokine signature predicts COVID-19 severity and survival. Nat Med 26(10):1636–1643

Deng S, Liang H, Chen P, Li Y, Li Z, Fan S et al (2022) Viral vector vaccine development and application during the COVID-19 pandemic. Microorganisms 10(7):1450

Drews S, Savin I, Van Den Bergh JC, Villamayor-Tomás S (2022) Climate concern and policy acceptance before and after COVID-19. Ecol Econ 199:107507

Dubey P, Pandey D (2020) Distance learning in higher education during pandemic: challenges and opportunities. Int J Indian Psychol 8(2):43–46

Eby P, Peel AJ, Hoegh A, Madden W, Giles JR, Hudson PJ et al (2023) Pathogen spillover driven by rapid changes in bat ecology. Nature 613(7943):340–344

El-Dessouki I, Saeed N (eds) (2021) Smart grid integration into smart cities. In: 2021 IEEE international smart cities conference (ISC2), 7–10 Sept 2021

El-Ramady HR, Singh A, Rajput VD, Amer MM, Omara AE-D, Elsakhawy T et al (2021) Environment, biodiversity and soil security: a new dimension in the era of COVID-19. Environ Biodivers Soil Secur 5(2021):1–14

Enserink M (2023) Dispute simmers over who first shared SARS-CoV-2's genome. Science. Available from: https://www.science.org/content/article/dispute-simmers-over-who-first-shared-sars-cov-2-s-genome

Everard M, Johnston P, Santillo D, Staddon C (2020) The role of ecosystems in mitigation and management of COVID-19 and other zoonoses. Environ Sci Policy 111:7–17

Fagiolari L, Versaci D, Di Berardino F, Amici J, Francia C, Bodoardo S et al (2022) An exploratory study of $MoS_2$ as anode material for potassium batteries. Batteries 8(11)

Farahat RA, Shaheen N, Kundu M, Shaheen A, Abdelaal A (2022) The resurfacing of hand, foot, and mouth disease: are we on the verge of another epidemic? Ann Med Surg 81:104419

Florida R, Mellander C (2022) The geography of COVID-19 in Sweden. Ann Reg Sci 68(1):125–150
Flude BM, Nannetti G, Mitchell P, Compton N, Richards C, Heurich M et al (2021) Targeting the complement serine protease MASP-2 as a therapeutic strategy for coronavirus infections. Viruses 13(2):312
Forster PM, Forster HI, Evans MJ, Gidden MJ, Jones CD, Keller CA et al (2020) Current and future global climate impacts resulting from COVID-19. Nat Clim Change 10(10):913–919
Franch-Pardo I, Napoletano BM, Rosete-Verges F, Billa L (2020) Spatial analysis and GIS in the study of COVID-19. A review. Sci Total Environ 739:140033
Franch-Pardo I, Desjardins MR, Barea-Navarro I, Cerdà A (2021) A review of GIS methodologies to analyze the dynamics of COVID-19 in the second half of 2020. Trans GIS 25(5):2191–2239
Fujiyoshi K, Bruford EA, Mroz P, Sims CL, O'Leary TJ, Lo AWI et al (2021) Opinion: standardizing gene product nomenclature—a call to action. Proc Natl Acad Sci USA 118(3)
Gaebler C, Wang Z, Lorenzi JCC, Muecksch F, Finkin S, Tokuyama M et al (2021) Evolution of antibody immunity to SARS-CoV-2. Nature 591(7851):639–644
Gandolfo M, Amici J, Fagiolari L, Francia C, Bodoardo S, Bella F (2022) Designing photocured macromolecular matrices for stable potassium batteries. Sustain Mater Technol 34:e00504
Gaskin DJ, Zare H, Delarmente BA (2021) Geographic disparities in COVID-19 infections and deaths: the role of transportation. Transp Policy 102:35–46
Gaugler JE, Yu F, Davila HW, Shippee T (2014) Alzheimer's disease and nursing homes. Health Aff (Proj Hope) 33(4):650–657
Geahchan S, Ehrlich H, Rahman MA (2021) The antiviral applications of marine resources for COVID-19 treatment: an overview. Mar Drugs 19(8)
Geraghty E, Kerski J (2020) The impact of COVID-19 on geography, GIS, and education. J Read J Res Didact Geogr 2
Ghahramani S, Kasraei H, Hayati R, Tabrizi R, Marzaleh MA (2022) Health care workers' mental health in the face of COVID-19: a systematic review and meta-analysis. Int J Psychiatry Clin Pract 1–10
Ghanemi A, Yoshioka M, St-Amand J (2020) Will an obesity pandemic replace the coronavirus disease-2019 (COVID-19) pandemic? Med Hypotheses 144:110042
Glover V, O'Donnell KJ, O'Connor TG, Fisher J (2018) Prenatal maternal stress, fetal programming, and mechanisms underlying later psychopathology—a global perspective. Dev Psychopathol 30(3):843–854
Goel S, Saheb Sharif-Askari F, Saheb Sharif Askari N, Madkhana B, Alwaa AM, Mahboub B et al (2021) SARS-CoV-2 switches 'on' MAPK and NFκB signaling via the reduction of nuclear DUSP1 and DUSP5 expression. Front Pharmacol 12:631879
Gorodetska I, Kozeretska I, Dubrovska A (2019) BRCA genes: the role in genome stability, cancer stemness and therapy resistance. J Cancer 10(9):2109–2127
Greten FR, Grivennikov SI (2019) Inflammation and cancer: triggers, mechanisms, and consequences. Immunity 51(1):27–41
Grossman ER, Benjamin-Neelon SE, Sonnenschein S (2020) Alcohol consumption during the COVID-19 pandemic: a cross-sectional survey of US adults. Int J Environ Res Public Health 17(24)
Gruber J, Prinstein MJ, Clark LA, Rottenberg J, Abramowitz JS, Albano AM et al (2021) Mental health and clinical psychological science in the time of COVID-19: challenges, opportunities, and a call to action. Am Psychol 76:409–426
Guida G, Hatziargyriou N, Russo E (2020) ETIP SNET views on post COVID 19 recovery. Available from: https://smart-networks-energy-transition.ec.europa.eu/news/etip-snet-views-post-covid-19-recovery
Gupta SK, Minocha R, Thapa PJ, Srivastava M, Dandekar T (2022) Role of the pangolin in origin of SARS-CoV-2: an evolutionary perspective. Int J Mol Sci 23(16)
Habibzadeh P, Sajadi MM, Emami A, Karimi MH, Yadollahie M, Kucheki M et al (2020) Rate of re-positive RT-PCR test among patients recovered from COVID-19. Biochem Med 30(3):030401
Habibzadeh P, Mofatteh M, Silawi M, Ghavami S, Faghihi MA (2021) Molecular diagnostic assays for COVID-19: an overview. Crit Rev Clin Lab Sci 58(6):385–398
Hama Amin BJ, Kakamad FH, Ahmed GS, Ahmed SF, Abdulla BA, Mohammed SH et al (2022) Post COVID-19 pulmonary fibrosis; a meta-analysis study. Ann Med Surg 77:103590
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. N Engl J Med 386(15):1397–1408
Han Q, Zheng B, Daines L, Sheikh A (2022) Long-term sequelae of COVID-19: a systematic review and meta-analysis of one-year follow-up studies on post-COVID symptoms. Pathogens (Basel, Switzerland) 11(2)
Hanaei S, Sarzaeim M, Yazdanpanah N, Pirkoohi ZR, Ziaei H, Mohamed K et al (2021) The hybrid USERN 2020 congress: new standards for events in practice. Acta Med Iran
Hanaei S, Takian A, Majdzadeh R, Maboloc CR, Grossmann I, Gomes O et al (2022) Emerging standards and the hybrid model for organizing scientific events during and after the COVID-19 pandemic. Disaster Med Public Health Prep 16(3):1172–1177
Hayn M, Hirschenberger M, Koepke L, Nchioua R, Straub JH, Klute S et al (2021) Systematic functional analysis of SARS-CoV-2 proteins uncovers viral innate immune antagonists and remaining vulnerabilities. Cell Rep 35(7):109126
Heslop A, Fischer A, Tanhua T, Legler D, Belbeoch M, Kramp M et al (2020) COVID-19's impact on the ocean observing system and our ability to forecast weather and predict climate change. Glob Ocean Observ Syst

Hettich N, Entringer TM, Kroeger H, Schmidt P, Tibubos AN, Braehler E et al (2022) Impact of the COVID-19 pandemic on depression, anxiety, loneliness, and satisfaction in the German general population: a longitudinal analysis. Soc Psychiatry Psychiatr Epidemiol 57(12):2481–2490
Hollander JE, Carr BG (2020) Virtually perfect? Telemedicine for COVID-19. N Engl J Med 382(18):1679–1681
Holmager TL, Lynge E, Kann CE, St-Martin G (2021) Geography of COVID-19 in Denmark. Scand J Public Health 49(1):88–95
Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L et al (2020) Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. Lancet Psychiatry 7(6):547–560
Høyer-Hansen M, Jäättelä M (2007) Connecting endoplasmic reticulum stress to autophagy by unfolded protein response and calcium. Cell Death Differ 14(9):1576–1582
Hugelius G, Loisel J, Chadburn S, Jackson RB, Jones M, MacDonald G et al (2020) Large stocks of peatland carbon and nitrogen are vulnerable to permafrost thaw. Proc Natl Acad Sci 117(34):20438–20446
Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G et al (2005) Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. Thorax 60(5):401–409
Huldani H, Kamal Abdelbasset W, Abdalkareem Jasim S, Suksatan W, Turki Jalil A, Thangavelu L et al (2022) Intimate partner violence against pregnant women during the COVID-19 pandemic: a systematic review and meta-analysis. Women Health 62(6):556–564
International Energy Agency (2020) Global energy review. Available from: https://www.iea.org/reports/global-energy-review-2020
International Energy Agency (2022) World energy outlook. Available from: https://www.iea.org/reports/world-energy-outlook-2022
International Renewable Energy Agency (2020) Post-COVID recovery: an agenda for resilience, development and equality. Available from: https://www.irena.org/publications/2020/Jun/Post-COVID-Recovery
Jackson CB, Farzan M, Chen B, Choe H (2022) Mechanisms of SARS-CoV-2 entry into cells. Nat Rev Mol Cell Biol 23(1):3–20
Jain S, Nehra M, Kumar R, Dilbaghi N, Hu T, Kumar S et al (2021) Internet of medical things (IoMT)-integrated biosensors for point-of-care testing of infectious diseases. Biosens Bioelectron 179:113074
Karami H, Sanjari MJ, Hosseinian SH, Gharehpetian GB (2014) An optimal dispatch algorithm for managing residential distributed energy resources. IEEE Trans Smart Grid 5(5):2360–2367
Karthikeyan S, Nguyen A, McDonald D, Zong Y, Ronquillo N, Ren J et al (2021) Rapid, large-scale wastewater surveillance and automated reporting system enable early detection of nearly 85% of COVID-19 cases on a university campus. mSystems 6(4):e0079321
Khazaal S, Harb J, Rima M, Annweiler C, Wu Y, Cao Z et al (2022) The pathophysiology of long COVID throughout the renin-angiotensin system. Molecules (Basel, Switzerland) 27(9)
Kingston T, Florens FV, Vincenot CE (2021) Crumbling island keystones: threat diversity and intensification on islands push large island fruit bats to the brink. EcoEvoRxiv. Preprint publication
Köpsel V, de Moura Kiipper G, Peck MA (2021) Stakeholder engagement vs. social distancing—how does the COVID-19 pandemic affect participatory research in EU marine science projects? Marit Stud 20(2):189–205
Kornei K (2023) The mental toll of climate change. Eos. Available from: https://eos.org/features/the-mental-toll-of-climate-change
Kunutsor SK, Laukkanen JA (2020) Renal complications in COVID-19: a systematic review and meta-analysis. Ann Med 52(7):345–353
Landrum L, Holland MM (2020) Extremes become routine in an emerging new Arctic. Nat Clim Change 10(12):1108–1115
Larsen MD, de Graaf EL, Sonneveld ME, Plomp HR, Nouta J, Hoepel W et al (2021) Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity. Science (New York, NY) 371(6532):eabc8378
Larsen NW, Stiles LE, Shaik R, Schneider L, Muppidi S, Tsui CT et al (2022) Characterization of autonomic symptom burden in long COVID: a global survey of 2,314 adults. Medrxiv
Larson HJ, Gakidou E, Murray CJ (2022) The vaccine-hesitant moment. N Engl J Med 387(1):58–65
Lazarus JV, Wyka K, White TM, Picchio CA, Rabin K, Ratzan SC et al (2022) Revisiting COVID-19 vaccine hesitancy around the world using data from 23 countries in 2021. Nat Commun 13(1):3801
Lee T, Ahn J-H, Park SY, Kim G-H, Kim J, Kim T-H et al (2018) Recent advances in AIV biosensors composed of nanobio hybrid material. Micromachines 9(12)
Lee SH, Shin HS, Park HY, Kim JL, Lee JJ, Lee H et al (2019) Depression as a mediator of chronic fatigue and post-traumatic stress symptoms in Middle East respiratory syndrome survivors. Psychiatry Investig 16(1):59–64
Lee TC, Murthy S, Del Corpo O, Senécal J, Butler-Laporte G, Sohani ZN et al (2022a) Remdesivir for the treatment of COVID-19: a systematic review and meta-analysis. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis 28(9):1203–1210
Lee SS, Viboud C, Petersen E (2022b) Understanding the rebound of influenza in the post COVID-19 pandemic period holds important clues for epidemiology and control. Int J Infect Dis IJID Off Publ Int Soc Infect Dis 122:1002–1004

Levine B, Kroemer G (2019) Biological functions of autophagy genes: a disease perspective. Cell 176(1–2):11–42

Li Q, Zheng XS, Shen XR, Si HR, Wang X, Wang Q et al (2020a) Prolonged shedding of severe acute respiratory syndrome coronavirus 2 in patients with COVID-19. Emerg Microbes Infect 9(1):2571–2577

Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P et al (2020b) Coronavirus infections and immune responses. J Med Virol 92(4):424–432

Li W, Yang Y, Liu ZH, Zhao YJ, Zhang Q, Zhang L et al (2020c) Progression of mental health services during the COVID-19 outbreak in China. Int J Biol Sci 16(10):1732–1738

Liu PP, Blet A, Smyth D, Li H (2020) The science underlying COVID-19: implications for the cardiovascular system. Circulation 142(1):68–78

Lorente-Ros M, Das S, Elias J, Frishman WH, Aronow WS (2023) Cardiovascular manifestations of the long COVID syndrome. Cardiol Rev

Lorentzen CL, Haanen JB, Met Ö, Svane IM (2022) Clinical advances and ongoing trials on mRNA vaccines for cancer treatment. Lancet Oncol 23(10):e450–e458

Lu M, Wang X, Ye H, Wang H, Qiu S, Zhang H et al (2021) Does public fear that bats spread COVID-19 jeopardize bat conservation? Biol Conserv 254:108952

Lucas C, Wong P, Klein J, Castro TBR, Silva J, Sundaram M et al (2020) Longitudinal analyses reveal immunological misfiring in severe COVID-19. Nature 584(7821):463–469

Lund SAM, Manyika J, Smit S, Ellingrud K, Robinson O (2021) The future of work after COVID-19. McKinsey Global Institute. Available from: https://www.mckinsey.com/featured-insights/future-of-work/the-future-of-work-after-covid-19

Maduraiveeran G, Sasidharan M, Ganesan V (2018) Electrochemical sensor and biosensor platforms based on advanced nanomaterials for biological and biomedical applications. Biosens Bioelectron 103:113–129

Maiti A, Zhang Q, Sannigrahi S, Pramanik S, Chakraborti S, Cerda A et al (2021) Exploring spatiotemporal effects of the driving factors on COVID-19 incidences in the contiguous United States. Sustain Cities Soc 68:102784

Ma-Lauer Y, Carbajo-Lozoya J, Hein MY, Müller MA, Deng W, Lei J et al (2016) p53 down-regulates SARS coronavirus replication and is targeted by the SARS-unique domain and PLpro via E3 ubiquitin ligase RCHY1. Proc Natl Acad Sci USA 113(35):E5192–E5201

Mantovani F, Collavin L, Del Sal G (2019) Mutant p53 as a guardian of the cancer cell. Cell Death Differ 26(2):199–212

March D, Metcalfe K, Tintoré J, Godley BJ (2021) Tracking the global reduction of marine traffic during the COVID-19 pandemic. Nat Commun 12(1):2415

Mastaglio S, Ruggeri A, Risitano AM, Angelillo P, Yancopoulou D, Mastellos DC et al (2020) The first case of COVID-19 treated with the complement C3 inhibitor AMY-101. Clin Immunol 215:108450

Maza A, Hierro M (2022) Modelling changing patterns in the COVID-19 geographical distribution: Madrid's case. Geogr Res 60(2):218–231

McKinsey Global Institute (2021) The future of work after COVID-19. Available from: https://www.mckinsey.com/featured-insights/future-of-work/the-future-of-work-after-covid-19

McNeely JA (2021) Nature and COVID-19: the pandemic, the environment, and the way ahead. Ambio 50(4):767–781

Mohamed K, Yazdanpanah N, Saghazadeh A, Rezaei N (2021a) Computational drug discovery and repurposing for the treatment of COVID-19: a systematic review. Bioorg Chem 106:104490

Mohamed K, Yazdanpanah N, Saghazadeh A, Rezaei N (2021b) Cognitive biases affecting the maintenance of COVID-19 pandemic. Acta Bio-Med Atenei Parmensis 92(2):e2021102

Moitra P, Alafeef M, Dighe K, Frieman MB, Pan D (2020) Selective naked-eye detection of SARS-CoV-2 mediated by N gene targeted antisense oligonucleotide capped plasmonic nanoparticles. ACS Nano 14(6):7617–7627

Moradian N, Ochs HD, Sedikies C, Hamblin MR, Camargo CA Jr, Martinez JA et al (2020) The urgent need for integrated science to fight COVID-19 pandemic and beyond. J Transl Med 18(1):205

Mujawar MA, Gohel H, Bhardwaj SK, Srinivasan S, Hickman N, Kaushik A (2020) Nano-enabled biosensing systems for intelligent healthcare: towards COVID-19 management. Mater Today Chem 17:100306

Mullen CA (2021) Online doctoral mentoring in a pandemic: help or hindrance to academic progress on dissertations? Int J Mentor Coach Educ 10(2):139–157

Muñoz-Vela FJ, Rodríguez-Díaz L, Gómez-Salgado J, Fernández-Carrasco FJ, Allande-Cussó R, Vázquez-Lara JM et al (2023) Fear and anxiety in pregnant women during the COVID-19 pandemic: a systematic review. Int J Public Health 41

Muz B, de la Puente P, Azab F, Azab AK (2015) The role of hypoxia in cancer progression, angiogenesis, metastasis, and resistance to therapy. Hypoxia (Auckland, NZ) 3:83–92

Naeem SB, Bhatti R (2020) The COVID-19 'infodemic': a new front for information professionals. Health Info Libr J 37(3):233–239

Naikoo GA, Awan T, Hassan IU, Salim H, Arshad F, Ahmed W et al (2021) Nanomaterials-based sensors for respiratory viral detection: a review. IEEE Sens J 21(16):17643–17656

Naikoo GA, Arshad F, Hassan IU, Awan T, Salim H, Pedram MZ et al (2022) Nanomaterials-based sensors for the detection of COVID-19: a review. Bioeng Transl Med 7(3):e10305

Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS et al (2021) Post-acute COVID-19 syndrome. Nat Med 27(4):601–615

Ndaïrou F, Area I, Nieto JJ, Torres DFM (2020) Mathematical modeling of COVID-19 transmission dynamics with a case study of Wuhan. Chaos Solitons Fractals 135:109846

Ndwandwe D, Wiysonge CS (2021) COVID-19 vaccines. Curr Opin Immunol 71:111–116

Neumann A (2020) It has the highest death rate of any nursing home in the US. The Guardian. Available from: https://www.theguardian.com/us-news/2020/oct/28/nursing-homes-america-new-jersey-coronavirus

Nixon JP, Mavanji V, Butterick TA, Billington CJ, Kotz CM, Teske JA (2015) Sleep disorders, obesity, and aging: the role of orexin. Ageing Res Rev 20:63–73

Nowak B, Brzóska P, Piotrowski J, Sedikides C, Żemojtel-Piotrowska M, Jonason PK (2020) Adaptive and maladaptive behavior during the COVID-19 pandemic: the roles of dark triad traits, collective narcissism, and health beliefs. Personality Individ Differ 167:110232

O'Connor TG, Ciesla AA, Sefair AV, Thornburg LL, Brown AS, Glover V et al (2022) Maternal prenatal infection and anxiety predict neurodevelopmental outcomes in middle childhood. J Psychopathol Clin Sci 131(4):422

O'Dea XC, Stern J (2022) Virtually the same?: Online higher education in the post COVID-19 era. Br J Educ Technol J Counc Educ Technol 53(3):437–442

Oakes AH, Boyce K, Patton C, Jain S (2023) Rates of routine cancer screening and diagnosis before vs after the COVID-19 pandemic. JAMA Oncol 9(1):145–146

Omboni S, Padwal RS, Alessa T, Benczúr B, Green BB, Hubbard I et al (2022) The worldwide impact of telemedicine during COVID-19: current evidence and recommendations for the future. Connect Health 1:7–35

Osman AJK (2022) The impact of COVID-19 on education systems in the commonwealth. The Commonwealth iLibrary. Available from: https://www.thecommonwealth-ilibrary.org/index.php/comsec/catalog/book/950

Palaniappan S, Ragavi V, David B, Pathur Nisha S (2022) Prediction of epidemic disease dynamics on the infection risk using machine learning algorithms. SN Comput Sci 3(1):47

Papadopoulou A, Musa H, Sivaganesan M, McCoy D, Deloukas P, Marouli E (2021) COVID-19 susceptibility variants associate with blood clots, thrombophlebitis and circulatory diseases. PLoS ONE 16(9):e0256988

Park YC, Beck T, Obstfeld M, Acemoğlu D (2022) Prospects of the global economy after COVID-19. CEPR Press. Available from: https://cepr.org/voxeu/columns/prospects-global-economy-after-covid-19

Pedrini L, Meloni S, Lanfredi M, Ferrari C, Geviti A, Cattaneo A et al (2022) Adolescents' mental health and maladaptive behaviors before the COVID-19 pandemic and 1-year after: analysis of trajectories over time and associated factors. Child Adolesc Psychiatry Ment Health 16(1):42

Peimani N, Kamalipour H (2021) Online education in the post COVID-19 era: students' perception and learning experience. Educ Sci [Internet] 11(10)

Peng Y, Wu P, Schartup AT, Zhang Y (2021) Plastic waste release caused by COVID-19 and its fate in the global ocean. Proc Natl Acad Sci 118(47):e2111530118

Peng P, Hao Y, Liu Y, Chen S, Wang Y, Yang Q et al (2023) The prevalence and risk factors of mental problems in medical students during COVID-19 pandemic: a systematic review and meta-analysis. J Affect Disord 321:167–181

Perry G (2020) Alzheimer's disease patients in the crosshairs of COVID-19. J Alzheimer's Dis JAD 76(1):1

Prata JC, Silva ALP, Walker TR, Duarte AC, Rocha-Santos T (2020) COVID-19 pandemic repercussions on the use and management of plastics. Environ Sci Technol 54(13):7760–7765

Prather KA, Marr LC, Schooley RT, McDiarmid MA, Wilson ME, Milton DK (2020) Airborne transmission of SARS-CoV-2. Science (New York, NY) 370(6514):303–304

Rahman MM, Islam MR, Shohag S, Hossain ME, Shah M, Shuvo S et al (2022) Multifaceted role of natural sources for COVID-19 pandemic as marine drugs. Environ Sci Pollut Res 29(31):46527–46550

Raju V (2021) Implementing flexible systems in doctoral viva defense through virtual mechanism. Glob J Flex Syst Manag 22(2):127–139

Raman B, Bluemke DA, Lüscher TF, Neubauer S (2022) Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. Eur Heart J 43(11):1157–1172

Reyes-Bueno JA, Mena-Vázquez N, Ojea-Ortega T, Gonzalez-Sotomayor MM, Cabezudo-Garcia P, Ciano-Petersen NL et al (2020) Case fatality of COVID-19 in patients with neurodegenerative dementia. Neurología (Engl Ed) 35(9):639–645

Rezaei N, Ashkevarian S, Fathi MK, Hanaei S, Kolahchi Z, Ladi Seyedian S-S et al (2021) Introduction on coronavirus disease (COVID-19) pandemic: the global challenge. In: Rezaei N (ed) Coronavirus disease—COVID-19. Springer International Publishing, Cham, pp 1–22

Rohr JR, Civitello DJ, Halliday FW, Hudson PJ, Lafferty KD, Wood CL et al (2020) Towards common ground in the biodiversity–disease debate. Nat Ecol Evol 4(1):24–33

Rojas M, Rodríguez Y, Acosta-Ampudia Y, Monsalve DM, Zhu C, Li Q-Z et al (2022) Autoimmunity is a hallmark of post-COVID syndrome. J Transl Med 20(1):129

Romanelli C, Cooper D, Campbell-Lendrum D, Maiero M, Karesh WB, Hunter D et al (eds) (2015) Connecting global priorities: biodiversity and human health: a state of knowledge review. World Health Organisation/Secretariat of the UN Convention on Biological Diversity

Rose-Redwood R, Kitchin R, Apostolopoulou E, Rickards L, Blackman T, Crampton J et al (2020) Geographies of the COVID-19 pandemic. Dialog Hum Geogr 10(2):97–106

Sandbrook C, Gómez-Baggethun E, Adams WM (2022) Biodiversity conservation in a post-COVID-19 economy. Oryx 56(2):277–283

Sarker S, Jamal L, Ahmed SF, Irtisam N (2021) Robotics and artificial intelligence in healthcare during COVID-19 pandemic: a systematic review. Robot Auton Syst 146:103902

Sarkodie SA, Owusu PA (2021) Impact of COVID-19 pandemic on waste management. Environ Dev Sustain 23(5):7951–7960

Satarker S, Tom AA, Shaji RA, Alosious A, Luvis M, Nampoothiri M (2021) JAK-STAT pathway inhibition and their implications in COVID-19 therapy. Postgrad Med 133(5):489–507

Savin I, Drews S, Van Den Bergh J, Villamayor-Tomas S (2022) Public expectations about the impact of COVID-19 on climate action by citizens and government. PLoS ONE 17(6):e0266979

Schwaegerl C, Tao L (2013) The microgrids concept. In: Hatziargyriou N (ed) Microgrids: architectures and control. Wiley-IEEE Press, pp 1–24

Seo G, Lee G, Kim MJ, Baek S-H, Choi M, Ku KB et al (2020) Rapid detection of COVID-19 causative virus (SARS-CoV-2) in human nasopharyngeal swab specimens using field-effect transistor-based biosensor. ACS Nano 14(4):5135–5142

Shakeel CS, Mujeeb AA, Mirza MS, Chaudhry B, Khan SJ (2022) Global COVID-19 vaccine acceptance: a systematic review of associated social and behavioral factors. Vaccines 10(1)

Shan B, Broza YY, Li W, Wang Y, Wu S, Liu Z et al (2020) Multiplexed nanomaterial-based sensor array for detection of COVID-19 in exhaled breath. ACS Nano 14(9):12125–12132

Siccardi S, Amici J, Colombi S, Carvalho JT, Versaci D, Quartarone E et al (2022) UV-cured self-healing gel polymer electrolyte toward safer room temperature lithium metal batteries. Electrochim Acta 433:141265

Siegel RL, Miller KD, Fuchs HE, Jemal A (2022) Cancer statistics, 2022. CA Cancer J Clin 72(1):7–33

Siegel RL, Miller KD, Wagle NS, Jemal A (2023) Cancer statistics, 2023. CA Cancer J Clin 73(1):17–48

Singh N, Bharara SA (2020) S2 subunit of SARS-nCoV-2 interacts with tumor suppressor protein p53 and BRCA: an in silico study. Transl Oncol 13(10):100814

Singh K, Lima G, Cha M, Cha C, Kulshrestha J, Ahn YY et al (2022) Misinformation, believability, and vaccine acceptance over 40 countries: takeaways from the initial phase of the COVID-19 infodemic. PLoS ONE 17(2):e0263381

Soroya SH, Farooq A, Mahmood K, Isoaho J, Zara S-e (2021) From information seeking to information avoidance: understanding the health information behavior during a global health crisis. Inf Process Manag 58(2):102440

Soung AL, Vanderheiden A, Nordvig AS, Sissoko CA, Canoll P, Mariani MB et al (2022) COVID-19 induces CNS cytokine expression and loss of hippocampal neurogenesis. Brain 145(12):4193–4201

Sridhar A, Balakrishnan A, Jacob MM, Sillanpää M, Dayanandan N (2023) Global impact of COVID-19 on agriculture: role of sustainable agriculture and digital farming. Environ Sci Pollut Res 30(15):42509–42525

Stegmann KM, Dickmanns A, Gerber S, Nikolova V, Klemke L, Manzini V et al (2021) The folate antagonist methotrexate diminishes replication of the coronavirus SARS-CoV-2 and enhances the antiviral efficacy of remdesivir in cell culture models. Virus Res 302:198469

Stegmann KM, Dickmanns A, Heinen N, Blaurock C, Karrasch T, Breithaupt A et al (2022) Inhibitors of dihydroorotate dehydrogenase cooperate with molnupiravir and N4-hydroxycytidine to suppress SARS-CoV-2 replication. Iscience 25(5):104293

Szuhany KL, Malgaroli M, Miron CD, Simon NM (2021) Prolonged grief disorder: course, diagnosis, assessment, and treatment. Focus (Am Psychiatr Publ) 19(2):161–172

Tan M, He FJ, MacGregor GA (2020) Obesity and COVID-19: the role of the food industry. BMJ 369:m2237

Theberath M, Bauer D, Chen W, Salinas M, Mohabbat AB, Yang J et al (2022) Effects of COVID-19 pandemic on mental health of children and adolescents: a systematic review of survey studies. SAGE Open Med 10:20503121221086710

Vanapalli KR, Sharma HB, Ranjan VP, Samal B, Bhattacharya J, Dubey BK et al (2021) Challenges and strategies for effective plastic waste management during and post COVID-19 pandemic. Sci Total Environ 750:141514

von Delft A, Hall MD, Kwong AD, Purcell LA, Saikatendu KS, Schmitz U et al (2023) Accelerating antiviral drug discovery: lessons from COVID-19. Nat Rev Drug Discov 1–19

Wang EY, Mao T, Klein J, Dai Y, Huck JD, Jaycox JR et al (2021a) Diverse functional autoantibodies in patients with COVID-19. Nature 595(7866):283–288

Wang Q, Xu R, Volkow ND (2021b) Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. World Psychiatry Off J World Psychiatr Assoc (WPA) 20(1):124–130

Wang L, Davis PB, Volkow ND, Berger NA, Kaelber DC, Xu R (2022a) Association of COVID-19 with new-onset Alzheimer's disease. J Alzheimer's Dis JAD 89(2):411–414

Wang Q, Huang R, Li R (2022b) Impact of the COVID-19 pandemic on research on marine plastic pollution—a bibliometric-based assessment. Mar Policy 146:105285

Watson C (2022) Rise of the preprint: how rapid data sharing during COVID-19 has changed science forever. Nat Med 28(1):2–5

White E (2015) The role for autophagy in cancer. J Clin Investig 125(1):42–46

Wolfe ND, Dunavan CP, Diamond J (2007) Origins of major human infectious diseases. Nature 447(7142):279–283

World Bank (2022a) World development report 2022. Chapter 1. The economic impacts of the COVID-19 crisis 2022. Available from: https://www.worldbank.org/en/publication/wdr2022/brief/chapter-1-introduction-the-economic-impacts-of-the-covid-19-crisis

World Bank (2022b) World development report 2022. Chapter 6. Policy priorities for the recovery. Available from: https://www.worldbank.org/en/publication/wdr2022/brief/chapter-6-policy-priorities-for-the-recovery

World Food Programme (2023) Food insecurity. Available from: https://www.wfp.org/

World Health Organization (2022) World obesity day 2022—accelerating action to stop obesity 2022. Available from: https://www.who.int/news/item/04-03-2022-world-obesity-day-2022-accelerating-action-to-stop-obesity#:~:text=More%20than%201%20billion%20people,they%20are%20overweight%20or%20obese

World Health Organization JNR (2022) UNICEF and WHO warn of perfect storm of conditions for measles outbreaks, affecting children. Available from: https://www.who.int/news/item/27-04-2022-unicef-and-who-warn-of--perfect-storm--of-conditions-for-measles-outbreaks--affecting-children

Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X et al (2020) Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. Lancet Gastroenterol Hepatol 5(5):434–435

Xi J, Liu X, Wang J, Yao L, Zhou C (2023) A systematic review of COVID-19 geographical research: machine learning and bibliometric approach. Ann Am Assoc Geogr 113(3):581–598

Xiong J, Lipsitz O, Nasri F, Lui LMW, Gill H, Phan L et al (2020) Impact of COVID-19 pandemic on mental health in the general population: a systematic review. J Affect Disord 277:55–64

Yamamoto K (2022) Adverse effects of COVID-19 vaccines and measures to prevent them. Virol J 19(1):1–3

Yang X-D, Li H-L, Cao Y-E (2021) Influence of meteorological factors on the COVID-19 transmission with season and geographic location. Int J Environ Res Public Health 18(2):484

Yazdanpanah N, Rezaei N (2022) Autoimmune complications of COVID-19. J Med Virol 94(1):54–62

Yong SJ (2021) Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infect Dis (Lond Engl) 53(10):737–754

Yu J, Yuan X, Chen H, Chaturvedi S, Braunstein EM, Brodsky RA (2020) Direct activation of the alternative complement pathway by SARS-CoV-2 spike proteins is blocked by factor D inhibition. Blood 136(18):2080–2089

Zang R, Gomez Castro MF, McCune BT, Zeng Q, Rothlauf PW, Sonnek NM et al (2020) TMPRSS2 and TMPRSS4 promote SARS-CoV-2 infection of human small intestinal enterocytes. Sci Immunol 5(47)

Zarocostas J (2020) How to fight an infodemic. The Lancet 395(10225):676

Zeng N, Zhao Y-M, Yan W, Li C, Lu Q-D, Liu L et al (2023) A systematic review and meta-analysis of long term physical and mental sequelae of COVID-19 pandemic: call for research priority and action. Mol Psychiatry 28(1):423–433

Zhang Y, Sun H, Pei R, Mao B, Zhao Z, Li H et al (2021) The SARS-CoV-2 protein ORF3a inhibits fusion of autophagosomes with lysosomes. Cell Discov 7(1):31

Zhao Y, Watterston J (2021) The changes we need: education post COVID-19. J Educ Change 22(1):3–12

Zhao J, Xu J, He Y, Xiang M (2022) Children and adolescents' sleep patterns and their associations with mental health during the COVID-19 pandemic in Shanghai, China. J Affect Disord 301:337–344

Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W (2022) Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. Int J Infect Dis 114:252–260