



## Review article

# Microbial ecology and evolution is key to pandemics: using the coronavirus model to mitigate future public health challenges



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## ABSTRACT

Pandemics are global challenges that lead to total disruption of human activities. From the inception of human existence, all pandemics have resulted in loss of human lives. The coronavirus disease caused by SAR-CoV-2 began in China and is now at the global scale with an increase in mortality and morbidity. Numerous anthropogenic activities have been implicated in the emergence and severity of pandemics, including COVID-19. These activities cause changes in microbial ecology, leading to evolution due to mutation and recombination. This review hypothesized that an understanding of these anthropogenic activities would explain the dynamics of pandemics. The recent coronavirus model was used to study issues leading to microbial evolution, towards preventing future pandemics. Our review highlighted anthropogenic activities, including deforestation, mining activities, waste treatment, burning of fossil fuel, as well as international travels as drivers of microbial evolution leading to pandemics. Furthermore, human-animal interaction has also been implicated in pandemic incidents. Our study recommends substantial control of such anthropogenic activities as having been highlighted as ways to reduce the frequency of mutation, reduce pathogenic reservoirs, and the emergence of infectious diseases.

## 1. Introduction

Pandemics are global epidemics that result in numerous sicknesses and deaths, causing massive disruption in the socio-economic conditions of the world. The history of humanity has witnessed numerous pandemics, including smallpox, plague, cholera, and flu.

Although pandemics are reportedly spread via communication and trade lines, the 1918 Spanish flu caused by the Influenza A virus, H1N1, which claimed about 20 million human lives worldwide, was transmitted from one region to the other through military mobilization and trench warfare. Other factors that made for ease of spread include limited access to good health care services and poor sanitation (Akin and Gözel, 2020;

Johnson and Mueller, 2002). The H2N2 influenza virus strain, first found in China, was responsible for the 1957 pandemic (Asian flu). Most deaths resulted from secondary bacterial pneumonia, and the mortality rate was 1 per 4000 infected individuals. While the Spanish flu had higher mortality in individuals aged 20–34 and pregnant women, the mortality in Asian flu was higher among children and older adults (Potter, 2001). People younger than 50 years were more susceptible to the virus, and infectivity was higher among children (Akin and Gözel, 2020) probably due to the weak immune system in children and older people. A decade after the Asian flu came the Hong Kong flu caused by the Influenza virus strain H3N2, with the highest case-fatality rate found in children and estimated mortality of 500 000 to 2 million deaths worldwide (Reperant

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et al., 2016). A new influenza virus pandemic caused by the H1N1 strain (swine flu) emanated from Mexico in April 2009 and spread across many countries within a few weeks. After influenza A virus came the coronavirus pandemics (COVID 19) of the 21st century, spreading worldwide due to international travels and lack of surveillance. Outbreaks of coronavirus infections have occurred previously; the 2003 and 2012 outbreaks of the severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS), respectively. Although they primarily occurred at the regional level, they caused severe diseases in the human population. In addition, among the common cold viruses, four coronavirus strains are etiologic agents of the common cold, although they are associated with milder symptoms (Singh and Yi, 2021).

Microbial ecology enables the study of biological invasions and a deeper understanding of the mechanisms involved in human transportation of microorganisms and the ability of these organisms to become established, readily adapt, and rapidly spread in the new environment, as can be seen in other pandemics/epidemic cases listed above, especially in the present case of SARS-CoV-2 (Frederickson and Reese, 2021; Nuñez et al., 2020). With the phylogenetic tools available in microbial evolution, a better understanding of the new viruses responsible for these pandemics is possible. For example, whether the Delta variant or even the most recent Omicron variant of the SARS-CoV-2 are spreading due to adaptation or demographic reasons is determined by evolution (Frederickson and Reese, 2021; Otto et al., 2021).

This review aims to elucidate the role of microbial evolution, ecology, and human activities on disease outbreaks, and the need to regulate certain anthropogenic activities and human-animal proximity to avert future disease outbreaks, which will serve as a tool to mitigate future public health challenges.

### 1.1. COVID 19: a case study of viral pandemics

Coronaviruses belong to the family of Coronaviridae capable of causing diseases in humans and animals. Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus are the four genera that make up this family (Hossain et al., 2021), and these genera infect different animal species. While mammals are known to primarily harbor the Alphacoronaviruses and Betacoronaviruses, the Deltacoronaviruses are primarily seen in birds. Several researchers have also reported that Gammacoronaviruses can be found in some cetaceans (King et al., 2018; Singh and Yi, 2021; Woo et al., 2014). Coronaviruses are positive-stranded RNA viruses capable of inhabiting hosts with or without any disease symptoms. Although many of the described human coronaviruses cause diseases of the upper respiratory tract in humans and are generally mild, other strains could cause fatal illnesses, implicated for diseases such as SARS, MERS, and the present COVID-19 (Abdel-Moneim, 2014; Hui et al., 2020; Zhong et al., 2003). Mammals, especially bats, have been identified as the main reservoirs of SARS, MERS, and COVID-19 coronaviruses, and they are classified as Sarbecovirus, with Betacoronavirus as their genera.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes COVID-19, which is transmitted from person-to-person mainly through respiratory droplets (Akin and Gözel, 2020). SARS-CoV-2 got its name from SARS coronavirus (SARS-CoV) as the variations in the nucleotide bases that make up their genetic material has a close relationship (Hossain et al., 2021). The interaction between the receptor-binding domain (RBD) of spike (S) protein on SARS-CoV-2 and the angiotensin-converting enzyme 2 (ACE2) cellular receptor on the host causes viral entry into the host cell. Outbreaks of SARS-CoV-2 occurred towards the end of December 2019 in Wuhan, China, and were believed to originate from bats, as shown by genome sequence with similar evolutionary characteristics (Singh and Yi, 2021). Studies have shown that SARS-CoV-2 can recognize ACE2 receptors of various animals such as monkeys, cats, pigs, orangutans with comparable efficiency as in humans (Ge et al., 2013; Ma et al., 2015). The risk of future transfer of these coronaviruses implicated in recent outbreaks between species is high because certain human activities such as hunting involves close contact

with wild mammals bearing these viruses. Most significantly, SARS-related coronaviruses frequently appear in bats (Ge et al., 2013) and are likely the proximal source of SARS-CoV-2, increasing the inevitability of future outbreaks. Animal studies have shown that cats and ferrets can be infected by SARS-CoV-2 isolated from humans (Shi et al., 2020). However, very few studies have investigated the presence of the virus in animals, particularly animal pets kept by humans. Furthermore, coronaviruses undergo frequent recombination (Masters, 2006) which can lead to an entirely new strain.

A significant challenge that impedes the fight against COVID-19 is that the many asymptomatic patients of the disease can transmit the etiologic agent at the same frequency as the symptomatic patients (Høiby, 2021). Another vital characteristic of SARS-CoV-2 is its tendency for genetic recombination across host species boundaries, as discussed above. Sadly, it seems that such recombination events already occurred in SARS-CoV-2, consequently birthing the evolution of a potent strain with the capacity to infect human cells more effectively (Singh and Yi, 2021). The S protein of SARS-CoV-2 possesses the characteristics for both purifying selection and genetic recombination, resulting in a competent S protein that infects humans and can infect many other mammals. Furthermore, the global spread of SARS-CoV-2 across human society has increased the chances of added mutations to the viral genome improving its chances for future recombination (Singh and Yi, 2021).

There is still considerable uncertainty as to the future because of COVID-19. Theoretically, however, three possible events exist; 1) Just like SARS-CoV, SARS-CoV-2 may vanish since no other important zoonotic reservoirs besides bats have been established. 2) It may become established in a zoonotic reservoir close to humans, just like MERS, which have camels as hosts. 3) It may become endemic in humans, just like the four common cold coronaviruses NL63, OC43, HKU1, and 229E, with a universal spread and no known zoonotic reservoir (Høiby, 2021; Peters et al., 2020).

### 1.2. Microbial evolution in pandemics

The term microbial evolution refers to genetic alterations in microorganisms that are retained over time (Ewald and Ewald, 2018). Factors such as the ease with which microorganisms adapt to new environments, short generation and doubling times, and high rates of mutation and genome flexibility combine to foster an increase in the evolution of microbes. These changes could result from selective pressure, such as antibiotics, which the organisms adapt to and develop resistance to overtime, or in the absence of selective pressure, such as spontaneous mutations. Besides these mutations, there is the horizontal gene transfer (HGT) which is considered one of the main ways by which microbial evolution results and involves the transfer of a gene that could either be found in the DNA of the donor bacterium or its mobile genetic element known as plasmids (Jain et al., 2002). HGT can occur between the same or different species of microorganisms, and although it can be genetically engineered, it occurs naturally in the environment, vigorously promoting microbial evolution.

One critical mechanism by which emerging infections affect humans and spread in population is via zoonotic transmission of pathogens. This cross-species transmission has accelerated over time because of increased interaction between humans and animals. These interactions occur through animal farming, trading of animal-based products, hunting, trades in exotic pets, and wet markets. Climate changes and land use have also been implicated as risk factors for transmitting pathogens in the wild to humans. Some of the pathogens that have spread to other regions because of climate change include West Nile, Dengue, Chikungunya, Zika viruses, and this is primarily due to the expansion of habitats that can harbor these zoonotic vector-borne pathogens (Caminade et al., 2019; Piret and Boivin, 2021). Acquisition of drug resistance genes by pathogens has also led to their increased geographical spread. Diseases such as cholera, malaria tuberculosis are all implicated (Morens et al., 2008; Piret and Boivin, 2021). The use of biological pathogens as weapons also helps

in the spread of pathogens. Some infectious agents such as *Yersinia pestis*, *Bacillus anthracis* are engineered to be more virulent, easily transmissible to humans, and resistant to antibiotics (Narayanan et al., 2018; Oliveira et al., 2020). The above-mentioned factors result in the introduction of harmful pathogens into the human population, mainly from endemic to non-endemic regions, ultimately resulting in disease outbreaks that may (if proactive public health measures are proactively implemented) or may not be contained.

The sarbecoviruses, which are the subgenus of the beta-coronaviruses to which SARS-CoV and SARS-CoV-2 belong, undergo frequent genetic recombination across host-species boundaries (Boni et al., 2020; Singh and Yi, 2021). Two important factors that characterize variant spread are how frequently they arise within individuals and their rate of transmissibility (Lythgoe et al., 2021). Two variants of concern, which emerged in late December 2020; the Kent variant (lineage B.1.1.7 or VOC202012/01) and the South African variant (lineage B.1.351 or 20H/501Y.V2) have spread to various countries and have been identified to result from N501Y mutations that affect the receptor-binding domain of the spike glycoprotein and are associated with increased host receptor binding ability (Pottage et al., 2021). Tasakis and colleagues, in their 2020 to early 2021 study in the United States of America, detected accumulating Single Nucleotide Variations (SNVs) encoding amino acid changes in the SARS-CoV-2 genome, with a pattern suggestive of RNA editing enzymes as major mutators of SARS-CoV-2 genomes. They also stated that increased prevalence of the B.1.1.7 variant with additional mutations in the spike proteins, which was observed in early 2021, may have arisen from the observed accumulation of new low-frequency replacement mutations in the Spike protein of SARS-CoV-2, and a hypermutable glutamine residue near the putative furin cleavage site, detected in the last quarter of 2020 (Tasakis et al., 2021). Moreso, in the analysis of 300 000 high-quality genome sequences of the variants of SARS-CoV-2, Rochman and co-workers reported that the ongoing evolution of SARS-CoV-2 is mainly characterized by purifying selection (Rochman et al., 2021). The involvement of the S protein in this purifying selection, together with the virus's propensity to undergo genetic recombination, ultimately resulted in an S protein capable of infecting both humans and other mammalian cells (Singh and Yi, 2021). In addition to the evolutions observed in the S protein, the region of the nucleocapsid protein connected with nuclear localization signals (NLS) are enriched with positively selected amino acid replacements which form a strongly connected network of apparent epistatic interactions and are signatures of primary partitions in the SARS-CoV-2 phylogeny (Rochman et al., 2021). The present evolution of the viral genome, together with the viral diversity and adaptation between and within various geographic regions, may further prolong the epidemic and may prompt the development of variant-specific vaccines to combat the COVID pandemic. There is an increased infectivity rate of these new variants, and a deeper understanding of the evolutionary trends of the SARS-CoV-2 variants' genome would aid in effectively controlling the pandemic and making better-informed decisions on vaccine development.

Emerging infectious diseases, implicated in epidemics and pandemics, result primarily from the inter-species transmission of viruses from animals to humans. This animal-human viral transmission can occur through genetic mechanisms such as recombination and mutations that give a virus new feature and enable the virus to bind and enter a new host cell with greater efficiency, avoid the immune system, and modify its virulence as in the case of the coronaviruses (CoVs). Studies have shown that bats are the primary reservoirs for several CoVs, including SARS-CoV and MERS-CoV, and that genetic recombination of viruses within a species is an essential evolutionary process that gives rise to genetic diversity and results in new viral characteristics (Longdon et al., 2014; Shahhosseini et al., 2021). Several structural and non-structural proteins are present in CoVs, with the Spike protein, S-protein being the most studied structural protein and plays a significant role in the pathogenicity of SARS-CoV.

Generally, RNA viruses to which SARS-CoV-2 belongs to are known to be more genetically diverse than DNA viruses, and this is attributed to

their error-prone polymerase/reverse transcriptase (about 10-4/site/replication cycle). RNA viruses incorporate radical mutations in their genome due to their lack of proofreading activity and readily adapt to changing environmental conditions (Elena and Sanjuán, 2005; Parvez and Parveen, 2017). On the other hand, a high mutation rate is closely linked with viral virulence and the ability of the virus to evolve (Akkiz, 2021). Secondly, mutations also arise because of recombination between two viral lineages, and finally, genomic diversity may emerge as a result of the host RNA editing system (Akkiz, 2021; van Dorp et al., 2020).

Shahhosseini and colleagues, in their study, applied computational genomics to determine the origin and pathogenicity of SARS-CoV-2. The comparison of amino acids at S-protein indicated that Pangolin-CoV had the highest similarity to SARS-CoV-2 compared to SARS-CoV. Additionally, the critical residues that bind to ACE2 are 100% identical in Pangolin-CoV and SARS-CoV, which indicates that natural selection might have occurred in Pangolin resulting in new viral trait that recognize the ACE2 receptor (Shahhosseini et al., 2021). From the phylogenetic tree, SARS-CoV-2 is shown to have the closest evolutionary relationship with Bat-SL-CoV-2. However, the receptor-binding domain (RBD) of Bat-SL-CoV-2 showed a low amino acid identity (78%) to SARS-CoV-2, unlike the RBD of Pangolin-CoV with 98% at the amino acid level (Li, 2020). This suggests that SARS-CoV-2 may not have been transmitted directly from bats to humans, but mutations in Pangolin gave the CoV features that enabled it to bind to ACE2, suggesting that Pangolin may have been an intermediate host. To further clarify the possibility that even though SARS-CoV-2 has the highest similarity to Bat-SL-CoV-2 when comparing the complete virus genome, SARS-CoV-2 may not have originated from bats, recombination events were explored. Shahhosseini and co-workers studied Bootscanning curves and compared phylogenetic tree topology of major and minor parental viruses and revealed recombination events between Bat-SL-CoV-2 and Pangolin-CoV with the position of breakpoint pairs at RBD. As a result of this recombination event, the critical residues of RBD from Pangolin-CoV integrated to Bat-SL-CoV-2, and then zoonotic transmission occurred by a recombinant virus with the capability to bind to ACE2. They further proposed that several mutations in the recombinant CoV led to the emergence of different variants of SARS-CoV-2 in the human community with new features for rapid transmission and severity (Shahhosseini et al., 2021).

The emergence of infectious diseases in new regions is mainly driven by the movement of pathogens, particularly via trade and travel. Local emergence, however, occurs because of various factors that involve both environmental and socio-economic variations. Moreover, the transmission of viruses is usually higher in more densely populated regions compared to sparse regions with migration enhancing their spread (Elena and Sanjuán, 2005; Parvez and Parveen, 2017). Most of these viral diseases can be called "crowd disease," as a relatively high-host density is needed for their persistence (Parvez and Parveen, 2017; Simmonds, 2001).

Yuan and colleagues in their study showed that the SARS-CoV-2 genome had a high genetic variation between different regions. They analyzed 11183 whole genomes of SARS-CoV-2 and showed that 60 of the 119 identified single nucleotide polymorphisms were nucleotide substitutions from C to T and represented the most abundant transition (Yuan et al., 2021). Nucleotide C to T transitions signifies less CpG abundance resulting from cytosine methylation and deamination into T (Simmonds, 2020; Yuan et al., 2021). This mutation necessitates a rapid adaptation and evolution of the virus in the host. SARS-CoV-2 has been reported to have the most extreme CpG deficiency compared to other known betacoronaviruses, and this feature contributes to evasion of host anti-viral defense mechanisms (Xia, 2020; Yuan et al., 2021).

The accumulation of mutations in the SARS-CoV-2 genome is relatively slow compared to other RNA viruses, such as the HIV/influenza virus (Akkiz, 2021; Callaway, 2020 Korber et al., 2020; Bakhshandeh et al., 2021). This could be because Coronaviruses have evolved a genetic proofreading mechanism that corrects any grave error during the replication process and SARS-CoV-2 sequence diversity is very low (Akkiz,

2021; Korber et al., 2020; Grubaugh et al., 2018). As a result, SARS-CoV-2 has been reported to incorporate only two single-nucleotide polymorphisms per month in its genome. Although the mutation rate of SARS-CoV-2 is relatively slow, about 12 000 mutations have already been identified in its genome, and researchers are tirelessly working to determine whether any evolutionary advantage is conferred by these mutations (Callaway, 2020). The fidelity of viral enzymes that replicate nucleic acids as SARS-CoV-2 RNA dependent RNA polymerase (RdRp) affect the mutagenic capability of the virus (Akkiz, 2021; Callaway, 2020), and this mutation rate plays a pivotal role in viral evolution and genome variability by conferring the ability to evade the immune response (Wang et al., 2020).

Since the mode of spread of SARS-CoV-2 is primarily via respiratory droplets from infected persons (direct) or through fomites in the immediate environment around the infected person (indirect) (World Health Organization, 2020), the virus spreads fast and efficiently within a given population compared to other viruses such as HIV and poliovirus.

Since the outbreak of COVID-19 in Wuhan, China, several variants have been isolated in different regions of the world with differences in infectivity and severity. There have been numerous reports of SARS-CoV-2 genome mutations and implications on the viral infectivity, disease severity, and potential evasion of immune response (Janik et al., 2021; Pachetti et al., 2020; Yao et al., 2020). Pachetti and co-workers reported that a point mutation at position 14408 on the SARS-CoV-2 genome (within the RdRp) is implicated in an increased mutation rate (Pachetti et al., 2020), suggesting that this mutation impacts the fidelity of the viral replication. Yao and co. showed that different mutations on the SARS-CoV-2 spike protein affect replication dynamics and infectivity (Yao et al., 2020), suggesting that some mutations can influence disease severity in patients.

The SARS-CoV-2 Interagency Group (SIG), in collaboration with the Center for Disease Control and Prevention (CDC), have developed a classification system in which variants of SARS-CoV-2 are classified into variants of interest (B.1.526, B.1.525, B.1.427/B.1.429 and P.2), concern (B.1.1.7, B.1.351 and P.1), and of high consequences. The detailed lineages of these variants have been extensively reviewed in (Janik et al., 2021). Interestingly, all reported variants share a specific mutation on the spike protein D614G. Interestingly, many researchers have found the D614G mutation to increase the viral load and higher infectivity, while others have reported no effects on viral infectivity (Volz et al., 2021; Zhang et al., 2020). Zhang and co-workers reported that D614G enhanced S protein incorporation into virions suggesting that D614G helps in virion packaging (Zhang et al., 2020). Korber and coworkers reported that D614G increases the viral load in the upper respiratory tract leading to higher infectivity (Korber et al., 2020) without a concomitant increase in. Zhang and coworkers reported that pseudoviruses carrying glycine at 614 on the spike protein infect ACE2-expressing cells more effectively than the D614 but do not alter binding or neutralization sensitivity (Zhang et al., 2020). Li et al. reported that mutations on glycosylated amino acids on the spike protein impact infectivity and sensitivity to neutralizing antibodies (Li, 2020). Li and coworkers also showed that D614G alongside A475V, L452R, V483A, and F490L mutations showed resistance to neutralizing antibodies. The authors further showed that deletions on glycosylated amino acids decreased viral infectivity. At the same time, N234Q was remarkably resistant to neutralizing antibodies, suggesting that mutation at critical amino acid positions on the spike protein not only influences virus infectivity but can help them evade treatment. It remains to be seen what other mutations would be discovered and how they could impact the currently available vaccines. In summary, the above-cited works support the claim that mutation aids virus evolution during the pandemic.

### 1.3. Methodology

This review was conducted following the methodological framework of various academic articles. The process involved a thorough review and

involved searching for the most detailed and relevant works. Our search focused on the keywords for the current review. Specifically, databases for data on ecology, evolution, pandemic, coronavirus, and anthropogenic were searched. A further search was conducted for anthropogenic activities, effects on the environment as well as contribution to pandemics. Using the available information, we synthesized the link between microbial ecology and evolution. All data used for this review were secondary data. All secondary data were collected through online search engines, particularly Google, Google Scholar, PubMed, Scopus, and Web of Science. The search was restricted to the first 100 hits and all articles were subjected to primary sorting and screening. Further screening was done to select relevant papers written in the English Language. Inclusion criteria were based on recent articles that discussed relevant keywords in the present review. A total of 150 research articles were selected initially. Further sorting reduced articles to 115 based on similarities and repetitions. The inclusion and exclusion criteria were applied to arrive at the eventual number of articles used for this review.

## 2. Exploring ecology and link to pandemic

COVID19 is an excellent example of a zoonosis that spreads from wildlife to humans. Similarly, human civilization has witnessed many diseases like this (Lloyd-Smith et al., 2009). Bubonic plague, cholera, and smallpox, for example, were introduced by Europeans to Africans to minimize human exposure to animals, law enforcement, education programs for at-risk groups to prevent virus contamination, and giving viable alternatives to bushmeat hunting, which is always linked with the poorest communities, can all help reduce the animal-human interface and Americans, and these diseases destroyed native communities. Other diseases in non-human primates include HIV/AIDS, yellow fever, Zika, and dengue fever. Similarly, measles evolved from rinderpest, a disease circulating in livestock for decades but was now exclusively found in humans. Although such emergence is no longer new, the world is more connected now than ever because of globalization. Once a spillover event has happened, connectivity increases disease spread, but the frequency and volume of those occurrences are also growing because of global environmental changes.

Understanding these underlying mechanisms of pathogen spillover and the role of biodiversity in pathogen transmission might aid in the development of proactive ecological interventions to prevent and mitigate pathogen spillover (Guégan et al., 2020; Olival et al., 2017). Indeed, ecosystem management and other efforts to preserve the diversity of species, such as rewilding, restoration, and wildlife reserves management, reduced illegal wildlife trading, habitat loss, population decrease, can be used to prevent and limit pathogen emergence and transmission. Furthermore, the demographic boom and genetic homogeneity resulting from intensive farming systems might operate as amplifiers and edge-hosts of novel diseases, resulting in rising emergence rates from domestic animals. Improving host diversity in farming techniques can help minimize domestic animals' involvement in the emergence of novel pathogens (Zhu et al., 2000).

With approximately 40% of the Earth's land surface already converted to farmland or pasture, most land-use changes in recent decades have occurred in tropical and subtropical forests, which are some of the world's most significant biodiversity hotspots (Whitmee et al., 2015). The increasing exposure of human populations to pathogens due to habitat encroachment and settlement into natural systems is another cause of emergence (Guégan et al., 2020). Human activities such as consumption of bushmeats, agricultural and recreational activities, and wildlife trading amplify increased exposure to formerly isolated wildlife. To minimize human exposure to animals, law enforcement, education programs for at-risk groups to prevent virus contamination, and providing viable alternatives to bushmeat hunting, which is always linked with the poorest communities, can help reduce the animal-human interface.

While we now have a firm grasp of pathogen spillover's evolutionary and ecological mechanisms, we still do not know which ecological actions will lower human disease loads and pandemic risk the most

effectively. There are empirical examples, such as employing landscape management to adjust bat distribution and lower the risk of bat-borne infections on shrimp farms to control the spread of schistosomiasis by reducing the snail, which serves as an intermediate host (Sokolow et al., 2019). Nonetheless, they are in short supply (Sokolow et al., 2019). In this sense, integrating data collection of pathogens and evaluation methods (e.g., quasi-experimental, observational) with the plethora of ecological management and conservation projects is one of the most promising opportunities in the ecology of diseases.

### 2.1. Public health impacts of Covid-19

COVID-19 has adversely affected global public health, and the long-term effect on mental health and lifestyle could increase the burden associated with cardiovascular diseases. The social distance measure encourages a sedentary lifestyle and abrupt lifestyle changes (Steptoe and Kivimäki, 2012). Previous studies have also shown that anxiety and stress harm glycemic control and increase blood pressure (Marcovecchio and Chiarelli, 2012; Sparrenberger et al., 2009) and medication compliance (Kretchy et al., 2014). Despite the large body of evidence from previous studies suggesting the expected health implications of an outbreak of infectious diseases (GPMB, 2019; Yamey et al., 2017), the world has not invested enough in prevention and preparedness efforts to reduce the occurrence of epidemics. Although developed countries have adequate real-time surveillance and sound health systems to manage the spread of infectious diseases, there is still a need for public health capacity in low-income and high-risk nations. Collective action is needed between governmental and other private companies in building facilities and funding research for quick response and detection of new pathogens of epidemic potential (Katz et al., 2018; Yamey et al., 2017). The Coalition for Epidemic Preparedness Innovations (CEPI), a pragmatic partnership that was launched in 2017, has been tracking efforts and activities towards COVID-19 vaccine development and is seeking strengthened international cooperation to ensure that, once vaccines are developed, the number of vaccines manufactured are sufficient and that all nations, have equitable access to vaccines (Thanh Le et al., 2020). Additionally, to effectively manage the outbreak, affected countries may

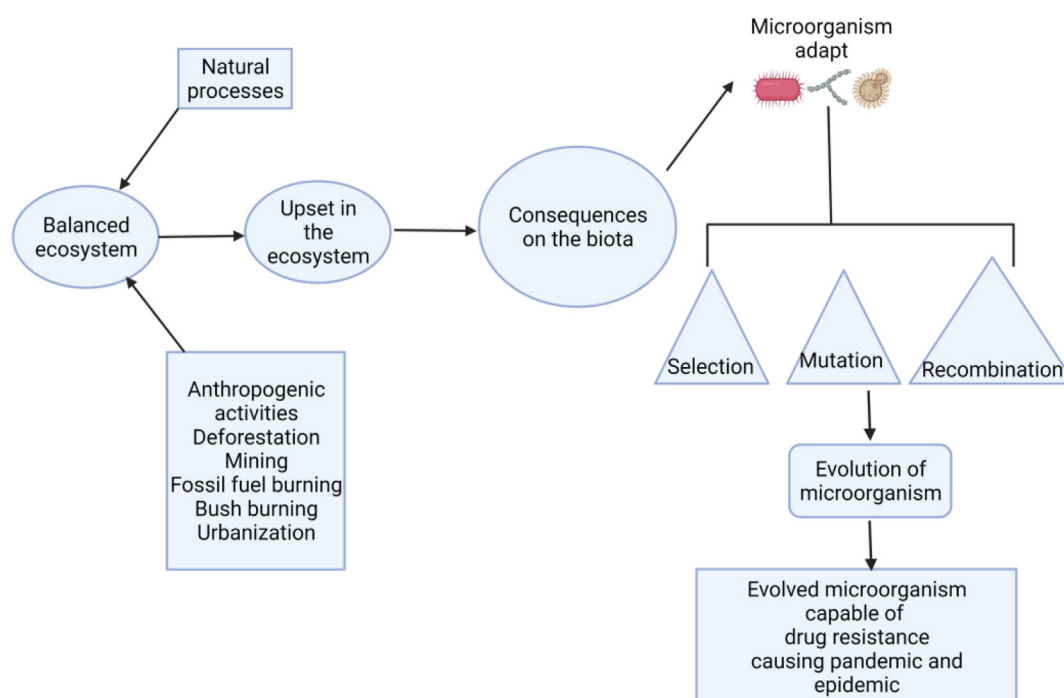
benefit from exchanging technological innovations such as health Quick Response (QR) which are useful in contact tracing.

### 3. Factors driving ecological changes and contributions to pandemic

The ecosystem, sometimes described as the life support system (LSS), is designed to sustain life (Jiang et al., 2021). An ecological balance in the ecosystem maintains proper ecological functions of the environment. Conversely, an imbalance in the ecosystem will entail changes in the ecological functions and various effects, usually resulting in irreversible changes to the system. The change in the system is what we call evolution (Figure 1). Evolution has led to consequences such as selection on the positive side (Dey and Loewenstein, 2020; Bonnet et al., 2019) as well as antibiotic resistance (Kraemer et al., 2019) and pandemics on the negative (Dey and Loewenstein, 2020; Martínez, 2018) (Figure 1). Evolution also changes in all the ecosystem components; biotic and abiotic.

Biotic and abiotic components drive ecological changes and disrupt the ecosystem. In response to ecological changes, organisms use adaptive mechanisms, including mutation (Dey and Loewenstein, 2020). For example, studies have shown that innate and environmentally induced mutation account for the ever-rising levels of antibiotic resistance (Kraemer et al., 2019). Specifically, studies by Kraemer et al. (2019) posit that antibiotic pollution resulting from indiscriminate use and unsafe disposal of antimicrobial substances has encouraged horizontal gene transfer in the LSS. Similarly, the COVID-19's Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has evolved from previous coronaviruses (Singh and Soojin, 2021; Dey and Loewenstein, 2020; Tang et al., 2020). Singh and Soojin (2021) suggest that the quick recombination and mutation, especially in the spike (S) proteins, of the SARS-CoV-2, is key to its infectivity and severity. Furthermore, organisms progress from environmental to professional pathogens through adaptation (Gagneux, 2018).

Although natural processes may explain ecological changes, anthropogenic activities are mostly blamed (Burrell et al., 2020; Rahman et al., 2020; Zhang et al., 2020). Further, anthropogenic-induced ecological changes are essential to microbial mutations and evolution (Martínez,



**Figure 1.** Summary of activities leading to an upset in the life support system. The uncontrolled imbalance in the LSS resulting from anthropogenic and natural processes could lead to evolution of the biota through various routes with possible consequences.

2018). Martínez (2018) proposed exaptation to be responsible for virulence due to changes in the habitat function. This virulence has been phenomenal, challenging to manage, and results in epidemics and pandemics. Singh and Soojin (2021) reported that SARS-CoV-2 has a zoonotic origin and resulted from previous coronaviruses. The evolution of the COVID-19 virus from earlier viruses shows evidence of specialized selection and multiple recombinations as well as geographic-induced changes (Singh and Soojin (2021); Tang et al., 2020). There is increasing evidence that pandemics, such as COVID-19, will be more recurrent, evidenced by frequent coronavirus pandemics recently and the abundance of such viruses in other mammals such as bats and rodents (Tang et al., 2020; Cui et al., 2019). The transition from the environment to pathogenic forms happens in steps, beginning with the ability to survive engulfing organisms and climaxing with host-to-host transmission (Gagneux, 2018). Stressors may have forced the microbial ancestors to transform into pathogenic strains. Evidence shows a reduction in the genetic material of pathogenic *Mycobacterium*, and these changes occur by horizontal gene transfer (Veyrier et al., 2011).

### 3.1. Anthropogenic activities

Anthropogenic activities increase the transmission of viruses into humans and progress to explosive levels (Priyadarsini et al., 2020). It is believed that anthropogenic activities that have altered the environment have placed such primary hosts of microorganisms, like SARS-CoV-2, at the receiving end leading to adaptive evolutions in both the host and the viruses. The review by Tang et al. (2020) posits that the host bats shape the evolution of these coronaviruses. These anthropogenic activities have become more rampant now and may account for the quicker repeat of these outbreaks. We considered anthropogenic activities in the environment that may account for the ecological changes leading to the evolution of mutant strains.

Further, we hypothesized that understanding the emergence of the COVID-19 pandemic would provide a good tool for predicting future occurrences. Certain anthropogenic activities leading to evolution have been considered in more detail.

#### 3.1.1. Deforestation

With the transition of life from water to land, the terrestrial environment possessed numerous favorable conditions for microbial proliferation. Deforestation recently occurs at an alarming rate and with grave consequences on biogeochemical cycles, microbial diversity, emission of greenhouse gases, and carbon sinks (Brancalion et al., 2020; Kooch et al., 2018; Kroeger et al., 2018; Tian et al., 2018). Deforestation has been an age-long anthropogenic consequence of urbanization and others, implicated for primary concerns such as food shortage (Kooch et al., 2018). More so, deforestation has been linked to changes in soil biogeochemistry, leading to severe consequences (Kooch et al., 2018; Kassa et al., 2017).

Microorganisms occupy an integral position in the maintenance of ecosystem functions and are sensitive to changes in environmental conditions (Kooch et al., 2018). Remarkable changes in the soil microbial community have been reported due to deforestation (Tian et al., 2018).

According to Vittor et al. (2020), deforestation has reduced the gap between wild animals and the human population and could explain the easy introduction of SARS-CoV-2 and other pathogens. Southeast Asia, the region of origin of the SARS-CoV-2, is known for deforestation due to population increase (Afelt et al., 2018). This anthropogenic-deforested environment has led to an increase in bat species hosting more coronaviruses (Vittor et al. (2020)), upsetting natural selection and may provide favorable conditions for viral disease transmission. Hill and Uckless suggested that the evolution of host species also results in an evolution of the colonizing viruses and could result in more virulent species (Hill and Uckless, 2020). Afelt et al. (2018) suggest that the reduced gap between animal and human dwellings could make transmission of coronaviruses easier. For instance, deforestation would bring houses closer to forests,

and these houses will be lit, attracting insects and insect-feeding bats closer to homes. This food web transition to unsafe distances to homes could increase the transmission of the viruses to humans through infection of domestic animals and deposition of Bat urine and feces, and the proximity of humans and animals is an essential factor in disease emergence (Afelt et al., 2018). With over 3,000 CoVs still in Bats (Anthony et al., 2017), more coronavirus diseases have been predicted to emerge from the globally most deforested Southeast Asia (Afelt et al., 2018). This evolution may be by horizontal gene transfer or innate mutation leading to virulent strains (Abdoulaye et al., 2021). This places the region at high risk of disease emergence and re-emergence considering the population explosion, poor sanitary conditions (Afelt et al., 2018), and probably the feeding habits in this region.

#### 3.1.2. Coal mining

Coal mining is an important activity and has recently progressed to highly efficient methods (Feng et al., 2019). These more advanced methods offer appreciable improvement in efficiency but with severe environmental consequences due to the generated waste (Feng et al., 2019; Sun et al., 2019). Pyrite is a vital waste usually stable until exposed to oxygen and water (Sun et al., 2019). This exposure leads to Acid Mine Drainage (AMD) (Sun et al., 2019). The AMD negatively affects microbial diversity, enhancing the proliferation of acidophilic microbes and leading to imbalanced microbe to microbe interactions (Sun et al., 2019). Researchers have implicated AMD for the highest microbial evolution compared with other conditions (Liu et al., 2021). This evolution could include virulent strains, noting the position of Hill and Uckless (2020).

Further, the nutrient and heavy metal content changes in coal mine environments affect the microbial population (Dang et al., 2019). These nutrients and heavy metal content changes will impact the microbial composition, causing mutation and evolution of organisms. These changes could be linked to the conversion from environmental organisms to pathogens. Coronaviruses have evolved successfully to the current pathogenic SARS-CoV-2, likely in response to environmental changes (Pujol et al., 2020).

#### 3.1.3. Refuse treatment land mines/landfills

Refuse disposal is a serious environmental challenge. Microbial waste treatment in landfills has been employed due to numerous advantages (Sekhohola-Dlamini and Tekere, 2020). Most integral is the ability of microorganisms in the dumpsites to degrade the waste towards mineralization. The presence of complex waste matter, including xenobiotics, makes this process complex, requiring corresponding microbial community functions and structures (Phale et al., 2019). The principle is the requirement for carbon by all life forms, such that microorganisms usually break down organic polymers to access carbon and other nutrients. Waste management in landfills is an anthropogenic initiated process that restricts microorganisms to sometimes undesired substrate metabolism and co-metabolism due to the complex substrate and environment (Sekhohola-Dlamini and Tekere, 2020). The process involves several syntrophic microbes leading to the transformation of the complex substrates and xenobiotics into simple polymers and subsequent mineralization. The perpetual evolution in the microbial population accounts for the ability of organisms to cope with the dynamics of the biotic and abiotic factors to continue to drive the decomposition reactions of the landfill (Hassan et al., 2018). Reactions such as hydrolysis, fermentation, methanogenesis, and acetogenesis are common in landfill waste management. These reactions are highly specialized, and only specialized, evolved organisms have been found to partake. The Landfill environment presents a harsh artificial environment, and the ubiquity of microbes ensures that they still adapt. This adaptation is made possible by evolution, mutation, and recombination. Thus, the landfill environment may lead to the evolution of organisms with undesired traits that may result in disease outbreaks. Shammi and colleagues have blamed poor waste management for the spread of Coronavirus in Asia (Shammi et al., 2021).

### 3.1.4. Fossil fuel burning

Man has continued to burn fossil fuels to meet needs but has burnt at a much higher rate in recent times. The industrial revolution has led to enormous oil, gas, and coal volumes within 50 years (Pirani, 2018). The release of greenhouse gases, including Carbon dioxide, remains a notable consequence of the combustion of fossil fuels (Franta, 2018). This increased release of greenhouse gases is the single most crucial factor expediting climate change with numerous consequences. Climate change has been blamed for weather conditions that have affected virtually all biotic and abiotic components of the LSS. Microorganisms are integral to the extent of climate change due to fossil fuel and the effect of climate change on the environment (Cavichioli et al., 2019).

The place of microorganisms in biogeochemical cycling, especially the carbon cycle (Jansson and Hofmøckel, 2020), explains their importance in the extent and effect of climate changes while placing them at the receiving end. Gagneux (2018) has implicated the controlled fires by humans for the evolution of *Mycobacterium* from environmental species to professional pathogens.

The soil environment is dynamic in terms of biotic and abiotic components is high in microbial diversity but has become more unpredictable with the effects of climate change (Jansson and Hofmøckel, 2020). It has been shown that microbes require unique traits to survive impacts of climate change such as elevated carbon and temperature have been and the acquisition of these traits distorts the dynamics of microbial diversity. For instance, increased temperature has been shown to affect the lipid component of the cell membrane that could lead to shifts in the genetic material of organisms and eventually mutation (Jansson and Hofmøckel, 2020). This mutation may affect the infectivity and severity of viruses, leading to pandemics.

Climate change could also affect the distribution of viral vectors and increase the risk of disease outbreaks (Aregbesola et al., 2019). Further, the zoonotic Bat vectors of SARS-CoVs have increased in species, expediting the evolution and transmission of CoVs over the years. Climate change has strongly influenced this evolution and transmission, leading to disease outbreaks (Beyer et al., 2021). The effects of climate change leading to selection is another suggestion for the emergence of the SARS-CoV-2 (Yan Yam, 2020).

### 3.1.5. International travel as drivers of viral pandemics

Travels have been listed among the modern drivers of pandemics (Kubota et al., 2020; Wu, 2021). The recent COVID-19 originated in Wuhan, China, in November 2019 but was quickly transmitted to all continents by February 2020 (Lalaoui et al., 2020). This transmission to other climes was due to international travels. China is known for its relevance in international trade and as an essential destination to businesses. Before the suspension on international travels, heavy traffic in and out of China could explain the transmission of the SARS-CoV-2 virus to the pandemic state.

SARS-CoV-2 spread first within the People's Republic of China (PRC) and then to other countries worldwide. This spread within PRC states was more of person-to-person infection, moving to states due to inland travels. The spread was faster initially due to the lack of information on the etiology of the disease. However, with increased awareness of the etiology, movement restrictions were suggested as a good control measure.

## 4. Strategies for the prevention of possible future pandemics

The strategies aim to prevent a future pandemic and thus reduce the hazards it poses to human health. Knowing the factors contributing to pandemics can help prevent future disease outbreaks. In the transmission of infections, pathogen-laden droplets and aerosols generated during respiratory events such as speaking, coughing, and sneezing play significant roles (Bhattacharjee and Bose, 2021; Ngonghala et al., 2020). Therefore, adopting a robust strategy in use, prioritizing, and management of ideal personal protective equipment (PPEs) to provide optimum

from the future biological, chemical, radiological, mechanical, and thermal global and domestic pandemic is necessary (Bhattacharjee and Bose, 2021; Ngonghala et al., 2020).

Previous studies reported the selection of a High-Performing, reusable and washable, well-designed multi-layered homemade cloth mask with different compositions optimally designed with cotton, polyester, nylon, chiffon, silk, or linen non-woven textile fabric blends can serve as an alternative to scarce medical masks by providing better performance in blocking airborne droplets and ensuring good breathability (Bhattacharjee and Bose, 2021; Ngonghala et al., 2020). The cloth mask must be characterized by a water-resistant outer layer of polyester/nylon with a positively charged middle layer made with blends to attract the negatively charged aerosols and particles by electrostatic force and a hydrophilic inner layer made with cotton to provide comfort by absorbing expelled droplets and humidity. Further principles regarding the design and manufacturing of these cloth masks worldwide, adoption of personal hygiene practices, and social distancing should be provided by the government to flatten the curve of a high prevalence of disease occurrences (Bhattacharjee and Bose, 2021; Ngonghala et al., 2020). The safety of workers' health from different professions, notably emergency respondents, calls for the selection of appropriate protective clothing that must have dependable barrier protection, easy to wear, comfortable and ease of washing, maintenance, and correctly designed and cover the entire skin is required even though the anxiety, higher costs, physical discomfort and strain of PPEs (Bhattacharjee et al., 2019; Bhattacharjee and Bose, 2021; Cano-Vicent et al., 2021). The virtue of Multifunctional and unique properties in Graphene modified fabrics such as antimicrobial properties, Flame resistance, Ultraviolet resistance, chemical activity, electrical and Thermal Conductivity, Mechanical Properties, toxicity toward bacteria and some aquatic organisms, and non-toxicity to humans in the medical application have proven its a high potential (Bhattacharjee et al., 2019) to overcome the limitations of conventional protective clothing with all its limitations (Bhattacharjee et al., 2019). Based on the current state of human health and the quest to prevent future pandemics and changes in disease distribution associated with combustion emissions, promotion of sustainable development and decrease in global warming, greenhouse gas emissions, and other combustion emissions to improve air quality, of paramount importance. Harmful emissions that attract and seizes atmospheric carbon to reduce the levels of carbon dioxide, conventional mitigation that reduces fossil-based CO<sub>2</sub> emissions, and radiative forcing technologies that alter the earth's radiative energy budget to reduce global temperatures or stabilize or are some of the strategies proposed and adopted for reducing global warming and carbon emission and climate change (Fawzy et al., 2020). Biochar, bioenergy carbon capture and storage, direct air carbon capture, and storage, enhanced weathering, fertilization of ocean, alkalinity enhancement of ocean, soil carbon sequestration, afforestation and reforestation, wetland construction, and restoration are the main harmful emissions techniques widely discussed in the literature include as well as alternative negative emissions utilization and adaptation (Fawzy et al., 2020; Parthasarathy and Narayanan, 2014). Some conventional mitigation involves decarbonization technologies that reduce CO<sub>2</sub> emissions, such as the use of renewable energy sources (wind and solar), fuel switching from coal to gas, efficiency gains through enhancement of fuel efficiency combustion and improving turbine generator efficiencies, nuclear power, and carbon capture storage and utilization.

The main radiative forcing geoengineering techniques discussed in the literature include marine sky brightening, cirrus cloud thinning, stratospheric aerosol injection, space-based mirrors, surface-based brightening, and various radiation management techniques (Fawzy et al., 2020; Parthasarathy and Narayanan, 2014).

Additionally, effective carbon pricing mechanisms that emphasize carbon removal need to be developed and introduced. There should be enhanced financial support, research technology funding, and accessibility. The introduction of an efficient market-based mechanism to incentivize project developers to establish carbon removal projects

should be made available by the government and financial industry for further actions. It is imperative to establish an environmental impact assessment and wildlife trade regulation in the livestock or farming process, improve biosecurity in international and domestic trading and detect the interaction between wildlife population and transportation of dangerous pathogens (Mishra et al., 2021). Pre-surveillance outbreaks should be harmonized in different health, agricultural, and forestry sectors. People with regular contact with animals related to their occupation and livelihood and patients having one symptom or another should be screened and included as cost-effective surveillance to identify novel microbe spillovers (Russell et al., 2020). Research institutes should be able to collaborate and screen animals, both domestic and wildlife; and people, to isolate and characterize the genetic sequence of organisms, high-risk human populations with cell-mediated immunity responses and antibodies to wildlife-origin as well as the risk factors in human behaviors and biotic environment (Bozzuto et al. 2020). Any imported animals must be screened for specific diseases to prevent alien diseases. Market biosecurity concerning good sanitation and hygiene practices should be improved (Daszak et al. 2020; George et al., 2019; Wang et al., 2021).

Improvements in regulation, policy, and check-ups in traditional food markets are also mechanisms for preventing future pandemic disease outbreaks (Aday and Aday, 2020). A high percentage of the human population depends on informal public food markets in spaces where small-scale retailers come together to sell fresh produce, meat from domestic animals, and in some cases, from wild animals and fish. Because zoonosis constitutes a higher percentage of pandemics, to reduce risks of future zoonotic diseases, restaurants, supermarkets, and meat storage facilities should be inspected regularly to detect and eliminate diseased animals (Espejo et al., 2020), meat that originates from a wild and domestic animal, and the different abattoirs should also be subject to similarly stringent sanitary standards. Some regulations like proper sewage treatment and disposal, testing of municipal waters for contamination, and quality control checks ensure that current good manufacturing practices in industries are maintained.

Studies have revealed that 98% of the population vulnerable to diseases would have been exposed to some degree of pollution (Coccia 2021). Mitigation activities such as sustainable environment policy to Secure Indigenous Peoples' Land Rights, reduce air, water, Promote the Benefits of Sustainable Agroforestry, Protect Coastal Wetlands, land pollution, and improvement in urban ventilation play a vital role in reducing future pandemics (Fan et al., 2016). Urban planning that supports more sustainable mobility and improves public respiratory health and as an engine of socio-economic change must be used by countries to redesign cities for people. The hazards of the association between disease outbreaks globally and environmental pollution must induce a decrease in the motorization rate of pollution from machines with a sustainable transition to generating a revolution in society and new electric vehicles. Environmental strategies can adopt sustainable mobility by enhancing rural, urban, and commuter public transport systems with electric automobiles and creating massive low emission zones (Coccia 2020; Espejo et al., 2020; Rume and Islam, 2020).

High levels of biodiversity are found in forests, cutting down forests to construct more roads, creating fields for cattle grazing, infrastructure, and agricultural investments increase exposure to vectors harboring diseases that are communicable to humans because wildlife is exposed to humans at the edges of their habitat. Different policies will preserve and make forests, and wildlife more valuable, drastically reduce deforestation in tropical areas and control future pandemics emergence (United Nations Environment Program 2017). The need to investigate and tackle the health effects of global climate change despite the potential for climate change to undermine the global health advantages of recent years is high (Karan et al., 2020). Pathogens of animal origin cause more than two-thirds of emerging diseases and almost all known pandemics and have been linked to destructive human activities like deforestation, climate change, and the wildlife trade (Keatts et al., 2021).

An intergovernmental partnership should be established to reduce the risk of spillover (Brookes et al., 2015) and should be adequately funded (Ellwanger et al. 2019). The climate-related health risks could be solved by effective decision-making and preparedness for pandemics (Hess et al., 2020). These strategies will help reduce mortality, stress, and morbidity, creating a vigorous health system response to prevent future pandemics (Hess et al., 2020).

Launching sustainable research and diagnostic technologies such as outbreak predictions, environmental scanning, intelligence methods, predictive modeling, foresight programs, efficient laboratory equipment, and web-based surveillance tools to improve actions that will detect pathogens early enough and help prevent future pandemics (Kelly-Cirino et al., 2019). The absence of more fundamental study of new potential human pathogens, their epidemiology, and further rapid and molecular identification of every new serious future pathogen will continue to allow future pandemics to hit humanity surprisingly. However, added investments in new technologies, particularly in communication and bioinformatics, could motivate the invention of "game changers" in disease speedy response, surveillance, and control.

Training the immune system to identify and fight pathogens through vaccination is the surest means of calming future pandemics and their associated risks; managing infectious disease outbreaks (Yassi et al., 2021), and identifying priority research areas and funding for a faster, effective, safe vaccine since a faster vaccine development led to rapid control of disease outbreaks (Excler et al., 2021). Therefore, timely expenditure on accelerated vaccine/drug research and development, production, allocation, distribution, and administration should be efficiently monitored to confer long-lasting protection against novel pathogens and their mutants. Increasing awareness on animal handling, sanitation, disease transmission, and sustainable wildlife management and support for hinterland inhabitants who mostly rely on wildlife for food will reduce zoonotic diseases (Dobson et al., 2020).

Epidemiologists, health care personnel, biologists, researchers, and emergency managers should be trained on infectious disease prevention to avail their expertise and capability in different sectors and fields to support government decisions and policies (Rose, 2020). This training will help them acquire new scientific knowledge and create stable partnerships to accelerate the learning process of preventing future pandemic crises and educating policymakers (Obrenovic et al., 2020) and other stakeholders regarding modeling processes, risks of pandemic outbreaks, and interpretation of findings. Subjects on epidemiology and emerging diseases and pandemics should be introduced in the curriculum in our universities, while experts on infectious diseases should be encouraged to enable them to work effectively.

## 5. Conclusion and prospects

The COVID-19 has stretched and has severely increased crises in the public health sector. However, most recent pandemics have been linked to destructive human activities like deforestation, climate change, and the wildlife trade. Therefore, coordination at the global level and investments to prevent tropical deforestation and limit wildlife trade could help control COVID-19 impacts and protect against future pandemics. Moreover, since COVID-19 is new, adequate risk management strategies using it as a model to mitigate future public health challenges are essential to ensure the sustainability of humans. Furthermore, substantial control of such anthropogenic activities will reduce the frequency of mutation, reduce pathogenic reservoirs, and reduce the emergence of other infectious diseases. Research on the importance of human-animal interaction is needed, including verifying the social buffering concept and developing mechanisms that can be used across animal species.

Besides, establishing new sustainable research and diagnostic technologies such as outbreak predictions, environmental scanning, intelligence methods, predictive modeling, foresight programs, efficient laboratory equipment, and web-based surveillance tools to improve the



early detection of pathogens will help prevent future pandemics. This requires an acceptable regulatory framework that allows for accurate and high-quality tests and applying new findings and massive responses to emerging infectious diseases.

Additionally, educating policymakers and other stakeholders on modeling processes, risks of pandemic outbreaks, and interpretation of findings and proactive measures to minimize possible health risks. Assessments of viral risks and environmental effects should be undertaken to forestall the pandemic's potential impacts on human health and ecosystems. Additionally, educating policymakers and other stakeholders on modeling processes, risks of pandemic outbreaks, and interpretation of findings and proactive measures to minimize possible health risks. Finally, active community participation in the governance response process for the epidemiologic management of the population coupled with suitable public health prevention and control measures.

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