A review on role of nitrous oxide nanoparticles, potential vaccine targets, drug, health care and artificial intelligence to combat COVID-19

S. Manigandan¹ · T. R. Praveenkumar² · Kathirvel Brindhadevi³

Received: 25 March 2021 / Accepted: 7 June 2021 / Published online: 16 June 2021
© King Abdulaziz City for Science and Technology 2021

Abstract

The lives of human individuals and groups around the globe have changed drastically due to the emergence of novel corona virus in late 2019. The significant part of CoV-19 from the global point is transmission rate, and therefore, it is mandatory to identify and isolate the affected persons even with the mild infection. To stop the rapid transmission of virus to drastic manner, it is essential to follow the hygienic practices, identification of potential vaccines and proper health care management systems to combat the novel virus. Despite the serious mortality rates and high confirmed cases, at present, there is no proven treatment and vaccine to treat the pandemic coronavirus. The current review prioritizes the recent trends in the health care sector, vaccine development pipeline and artificial intelligence role to combat CoV-2. Due to the unprecedented situation, the health care professionals was under high working stress and they were pushed to make serious decisions on time. Several health care workers pose directly threat to the occupational health risk. Besides, the industry is also experiencing a decrease in the outpatient footfalls along with the reduction of international patients. Furthermore, the services such as hypertension, diabetes, cancer and cardiovascular affected by 53%, 49%, 42% and 31%, respectively, due to the pandemic. Vaccines and treatments are the urgent need and have been extensively on progress worldwide. Despite the new technologies, the effectiveness of the old antiviral, such as Chloroquine and hydroxychloroquine, Lopinavir–Ritonavir, Nafamostat and Camostat, and Remdesivir COVID-19, was reviewed. The reviews on different vaccinations were effective in the understanding the efficiency of drugs in reducing the symptoms of COVID-19. Although vaccination and social distancing can reduce the infection, the role of the Artificial intelligence technology will enable the highest reduction of the COVID-19 infection by reducing the time and increasing the reliability.

Keywords COVID-19 · Health care · Nitrous oxide nanoparticles, clinical trial · SARS-CoV-2 · Coronavirus

Introduction

The Global health systems involve various networks and organizations of various hierarchies to provide worldwide health improvement, reduction of disparities, and protection against global threats that disregard national borders.

The most eminent agency associated with the Global health is the World Health Organization (WHO) (Andersen et al. 2020). The Global health sector has successfully brought in various interventions and solutions for various infectious diseases around the world such as Zika, Chikungunya, Ebola, Nipah, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Influenza. Though it has brought in a stringent system to these diseases, which has decreased the mortality rate and increased the life expectancy rate throughout the world, there are various sectors that are still a challenge for the sector. One of the very important challenges involves preparing for pandemics (Chen 2020). The emergence of the 2019 novel Corona virus that started its transmission initially due to human–animal interface activities has posted such a threat to the people worldwide (Zhou 2020). As on now June 30,

✉ T. R. Praveenkumar
pravirami@gmail.com

¹ Department of Aeronautical Engineering, Sathyabama Institute of Science and Technology, Chennai, India

² Department of Construction Technology and Management, Wollega University, Nekemte, Ethiopia

³ Institute of Research and Development, Duy Tan University, Da Nang 550000, Viet Nam

2020, the USA was recorded the highest confirmed cases with higher number of mortality rates despite the several measures from the government. Flattening the COVID-19 curve is the most prominent thing every country is looking for. The few countries already achieved that milestone, Taiwan, New Zealand, Germany, Finland, Belgium and China. The scientists around the globe are in urge to develop the efficient vaccines to combat in COVID-19 without any side effects. The guidance for development of new vaccines were given by food and drug administration of USA and several other agencies to several pharmaceutical companies and scientists signifies the guidelines for manufacturing process and clinical trials of a potential vaccine. Researchers around the globe were in collaboration with several companies in development of potential vaccines to develop the effective vaccines to combat the novel virus. The effective way of minimizing the novel virus infection is by means by potential vaccines. The scientific expertise of major developed countries can be explored to develop the potential vaccination in efficient manner. Vaccinations include Ribo nucleic acid proteins and other viral vector vaccinations were being developed by pharmaceutical companies.

Artificial intelligence is a technology wide used in recent days to combat the ongoing pandemic. The AI gained profound attention in recent days due to its reliability and accuracy compared to the conventional methods. For instance, AI empowered to predict the positive infection by comparing the computed topography (CT) images. Furthermore, they were employed to analysis the infection region, clinical assessment and diagnosis based on the data provided. Here, we discuss few factors based on the short progress and the advancements in the AI technology. Health care professionals are much dedicated to react quickly to the raise in number of coronavirus cases. Many officials are come into huge risk of infection during the combat. Securing the health care workers was huge responsibility to the government bodies by regulating many safety measures and special procedures. Role of the AI on protecting the health care workers was immense. AI empowers the workers to work away from direct contact with the patients. Direct exposure to infected patients possesses the high risk of getting occupational infection. Adequately technology and the personal protective equipment reduce the risk and save the health professionals in a high margin. The main objectives of the current review to enlighten the current trends in AI technology to combat COVID-19. Further detail review has been carried out on diagnosis, drug discovery and protection of health care workers. In addition to above, the potential vaccines were reviewed.

Fig. 1 Transmission of COVID-19 to the susceptible individual

Nature of SARS-CoV-2 (COVID-19)

Corona Viruses include a large family of Viruses found in nature. They belong to the Family Coronaviridae and order Nidovirales possessing single stranded, positive sense RNA genome. The technical name of corona virus is SARS-CoV-2. Corona Viruses are named for their crown like spikes protruding from their surfaces. The most common symptoms are fever, dry cough, tiredness, difficulty in breathing and chest pain. Based on the study by UK Kings College London, there is a possibility of six different types of strains cause's different type's symptoms such as Flu (with and without fever), fatigue, and gastrointestinal, abdominal and respiratory issues. The common things between all strains are breathing difficulties. Incubation period refers to the time between being exposed to the disease and when the actual symptoms start to show up. Knowing the incubation period of the disease is really helpful to take the necessary steps such as, active monitoring, surveillance, control and modeling (Wu 2020). This time is critical for the prevention of the diseases and allows the health officials to take decisions regarding quarantine or observation of people who may have been exposed to the virus. The novel coronavirus has an incubation period of 2 to 14 days, according to the Centers for Disease Control and Prevention (CDC), with symptoms appearing about 5 days after infection in most cases (Ma 2020). Fatality rate refers to the proportion of deaths due to the disease as compared to the people who have been

diagnosed with the same (Manigandan, 2020; Manigandan et al. 2021). The fatality rate shows the severity of the disease. The WHO estimates the fatality rate of novel corona virus to be about 3%. Figure 1 shows the possible transmission modes of the infection. R-Naught is a mathematical value, which refers to the reproduction rate of the disease. R_0 conveys in average how many persons will get infected because of one infected person, as long as no one has been vaccinated against it or is already immune to the disease (Ceylan 2020).

A disease R_0 value applies only when:

- No one has been vaccinated.
- No one has been immune to it yet.

There is no way to control the spread of the disease. Accordingly, the R-Naught of the novel Corona virus is predicted to be between 2 and 4, which means an infected person may infect 2–4 healthy people (Liu et al. 2020). On the other hand, due to the lack of data and short onset time, prediction of Fig. 2 presented the COVID-19 cases as on June 29, 2020 for top five nations.

Impact of COVID-19 on health care sector

The shutdown of world economy due to COVID-19 pandemic has created a health crisis across the globe, and unsurprisingly, there exists a correlation between the global economy and the health care systems. Health care industry

across the globe had not prepared well before for this pandemic, urgent requirement of resources impacts the global population. Changes in lifestyle and population aging create more burdens to the health care systems in addition to the pandemics. A center for disease control in china analyzed that the infectious diseases were less concerned as compared with the chronic health diseases in aged group population (China Faces The Challenge Of Chronic Disease 2020). Estimation showed that the people affected by diabetes will be around 11% of globe population in the year 2023 and the highest share by Europe and Japan. The population subjected to chronic diseases will grow up by 50% in the year 2045 with China, India and America sealing the top spots. The pandemic will affect the mental health of the workforce and it creates inability of the health care workers to treat the patients with chronic diseases, creating a backlog in the health care system. The physical and mental health of public will undoubtedly be affected due to lockdown procedures and economic fall down (Allen 2020).

According to the recent survey conducted by researchers from Department of Epidemiology and Biostatistics, School of Public Health, Peking University in 155 countries, COVID-19 pandemic has worst affected the treatment services for non-communicable diseases (NCD) and most affected the underdeveloped nations. The risk factor for the people affected by COVID-19 with non-communicable diseases was very high as compared with the healthy human beings (Wu 2020). From the survey, it was highlighted that the treatment services needed for persons with non-communicable diseases were not availed due to COVID-19 pandemic and

Fig. 2 COVID-19 daily confirmed cases (Ourworlddata)

the need to frame innovative policies to treat persons with NCDs and other illnesses was substantiated. Health services were totally disrupted in most of the countries as per the recent survey. Around 50% of hypertension patients, 49% of diabetes patients, 30% of heart-related patients, and 40% of carcinoma patients had not received proper treatment due to the pandemic situation.

In most of the countries, the health care workers assigned for NCDs have been shifted to help the patients affected by COVID-19. Almost half of the globe had delayed the onset of public screening programs and it adheres with the guidelines of WHO to reduce the non-emergency services to tackle the COVID-19 pandemic. The reasons for the reduction in treatment services include minimization of transport systems and cancelation of appointments due to shifting of health workers to support COVID-19 pandemic. In fact, there is a direct relation between the discontinuance of treatment services for NCDs and the emergence of COVID-19 outbreak across different nations. The reduction in the treatment services occurred when the transmission of the virus in people has moved to community transmission level. Around 65% of the countries listed NCDs in the response plan along with COVID-19 preparation plans (Noncommunicable Diseases—NCDs | Knowledge for policy 2020). The heart-related diseases, diabetes, lung diseases and carcinomic diseases were primarily included in the response plan, whereas the teeth-related infections and programs for tobacco usage counseling services were not concentrated widely in the response plans. Proper management through vaccination is required to tackle the NCDs and it should be on prime focus to reduce the mortality rate.

The private health sector is currently facing drastic drop in outpatient footfalls, foreign patients and other surgeries. This sector currently needs to hire more health workers, machines and other safety devices to protect the chronic patients with 100% effectiveness to handle the current pandemic. The industry is currently experiencing severe loss and this situation is expected to prevail for a year, thus, affects the cash flow in business.

Currently, the primary goal of every nation is to contain the transmission of the virus and reduction of social spread and limit the mortality rate by creating the appropriate awareness and warning with sufficient data. Awareness about sanitation practices will have an effective impact on the current situation for a longer duration but for a while, it increases the public health system burden dramatically. However, the delay in care of patients subjected to other ailments for a shorter duration creates a longer term impact on the health care system. The primary health care access for the public has been obstructed worse due to the pandemic situation prevailing over the globe for the past few months.

If the situation prevails for a longer duration and in order for the hospitals to function effectively, the personal

protective equipments are necessary for a longer duration. With the knowledge acclaimed from the outbreak of SARS and MERS, several nations stockpile the antiviral medicine and personal protective equipments including masks, gloves, sanitizer, etc. (Swaminathan 2007). WHO and other governmental guidelines were framed to control the pandemic within the health care system settings. The strategies include rigorous sanitation practices and awareness about the use of protective equipments and antibacterial medications.

The alternative strategy followed by several nations to treat the people suffering from chronic diseases is to give telemedicine rather in person contact. This reduction of in person contact by the doctors worsely affects the pregnant women. The prenatal care should be of more importance to check the baby's health throughout the delivery period. Most of the parents have the fear that what would happen if they encounter with COVID-19 and also the experience of birthing during this period. The persons with non-communicable diseases are at high risk and becoming seriously affected, but most of them do not have access to healthcare for their treatment. It is necessary to prepare a response plan for people with NCDs in an innovative manner to handle them effectively and steps need to be taken to strengthen the health care system in future to tackle any sort of circumstances.

Potential drugs for the treatment of COVID-19

Chloroquine and hydroxychloroquine against COVID-19

Chloroquine has been in use from 1944 and extensively used to treat malaria and autoimmune disorders. In general, chloroquine has the capability to handle several intracellular micro organisms. Experimental clinical studies predicted that the antimalarial drug has a potential to treat COVID-19 patients. In malarial treatment, it releases the toxic heme, which kills the parasite. Chloroquine has the capacity to reduce the viral infection by increasing the endosomal pH and having contact with glycosylation (Singh et al. 2020). Due to the global emergency, several urgent trials had been conducted worldwide to see the potential of chloroquine. Initially, 100 Chinese patients were involved in the trial and it was observed that the symptoms were reduced without critical side effects during the chloroquine treatment; this was the initial breakthrough of chloroquine on COVID-19 (Gao et al. 2020). Another study was conducted in France ($n = 36$) to observe the effect of chloroquine with azithromycin. The combination was very effective in virological naso clearance (Gautret 2020). 500 mg Chloroquine can be used for patients of age 18–65 two times a day continuously for 7 days. On contrary, there were no findings available for the

effects of Chloroquine on children. The use of Chloroquine was recommended due to its low cost and availability. Furthermore, the recorded side effects due to the consumption of medicine were less (Kapoor and Kapoor 2020). However, a notable study from New York revealed that chloroquine did not offer any advantage in the reduction of the mortality rate after testing 346 critically ill patients (Geleris 2020). In the other end, the Food and Drug Administration has banned the chloroquine on June, 2020 due to the risk of heart problems. Based on the clinical trials the determination has been made, the use of chloroquine can lead to lymph disorder, kidney failures, liver failure and other safety issues.

Lopinavir–ritonavir

The combination of Lopinavir–Ritonavir medication is generally used for controlling the HIV infection by building the immune system and decreasing the infection in the body. Initially, the infected patients are treated with 400 mg and 100 mg of lopinavir and ritonavir twice a day. The patients are treated for 14 days. It was found that lopinavir and ritonavir have reduced the symptoms from severe to mild/moderate. Furthermore, there were no side effects observed. Besides, the usage of ribavirin along with lopinavir and ritonavir has the ability to shortening the virus shedding and critical symptoms (Hung 2020). Another crucial study was conducted on 99 patients and compared with 100 standard patients to observe the effect of lopinavir and ritonavir (Cao 2020). From the studies, it was predicted the lopinavir and ritonavir did not show any advantage to the COVID-19 patients. On the other hand, 13% of the patients suffered from side effects of the treatment. Besides, the gastrointestinal adverse effects were comparatively low than the standard group. From the results, it was evident that the usage of lopinavir and ritonavir did not provide any benefit to the COVID-19-infected patients. In addition, the side effects such as nausea, diarrhea and liver damage are possible.

Nafamostat and camostat

Nafamostat and camostat were approved by Japan for use against Pancreatitis. There have been some trials to observe the positive impact of serine protease against COVID-19. After some crucial trials, there was no trace of suppression

in viral infection. Besides, nafamostat mesylate and camostat mesylate need to be tested further to understand their effects on SARS-CoV-2 infection in human lungs (Hoffmann et al. 2020). Moreover, another study predicted that Camostat and Nafamostat would inhibit prothrombin. However, the usage of Nafamostat was not safe due to its severe side effects such as cardiac arrest, agranulocytosis and anaphylaxis (Kailas2020).

Remdesivir

A nucleotide analogue, Remdesivir drug, is viewed as the most potential treatment for SARS-CoV-2infection. A notable study reported the improvement in patients after remdesivir therapy. Totally, 53 patients were treated with remdesivir. The patients were administered single dosage per day (200 mg). Among the treated, 36 reported improvement in the health condition (Grein 2020).

Vaccines and clinical treatments on pipeline

Researchers and the pharmacy industries are scrambling to develop a cure for the COVID-19 infection. Approximately, 583 companies worldwide are involved in the vaccine development. DNA and mRNA vaccines are believed to be a potential response to the novel SARS-CoV-2pathogens. Table 1 shows the list of DNA and mRNA vaccines under development. Although there are several clinical trials happening on the older antiviral, the researchers are keen in developing a true new technology to combat COVID-19. Table 2 shows the list of vaccines and treatment under pipeline. For better understanding, this study focuses on the drugs in phase II and phase III clinical trials (COVID-19 2020).

Vaccines typically train the immune system to fight against the infectious virus. Proper prevention vaccines will immune the people in advance to protect themselves from the viral infections. With regard to COVID-19 vaccines, many community are working hard to find the potential antibody to combat the ongoing pandemic. Around the world, there are more than 100 projects from different parts world working. Despite the many, only few reported the positive results in phase I and II. Based on the phase I

Table 1 Active trails of DNA and mRNA (COVID-19 2020)

Developer	Product category	Development stage
Inovio Pharmaceuticals/Beijing Advaccine Biotechnology/VGX Inc./Richter-Helm BioLogics/Ology Bioservices	DNA-based	Phase I
Moderna NIAID/Lonza	RNA-based vaccine	Phase II
BioNTech/Fosun Pharma/Pfizer	RNA-based vaccine	Phase I
Imperial College London/VacEquity Global Health	RNA-based vaccine	Phase I

Table 2 Treatment and vaccine tracker (COVID-19 2020; COVID-19 vaccine tracker | RAPS. 2020)

Developer	Type	Development stage
Moderna NIAID	mRNA = 1273	Phase II
CanSino Biological Inc, Beijing Institute of Biotechnology	Ad5-nCoV	Phase II
University of Oxford, Astra Zeneca https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/	AZD1222/ChAdOx1-S	Phase II
Genexine	GX-19	Phase I/II
Inovio pharmaceuticals	INO-4800	Phase I/II
Sinopharm, Beijing Institute of Biological Products	Inactivated vaccine	
Wuhan Institute of Biological Products	Inactivated vaccine	
BioNTech, Fosun Pharma, Pfizer	BNT 162	
University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital	Bacillus Calmette–Guerin (BCG) live-attenuated vaccine	Phase II

and phase II results, eight candidates showed the profound potential in the clinical trials. Here is a short look of some of key projects such as Moderna, Inovio, Oxford-AstraZeneca, J&J-Sanofi and Covaxin. Moderna is an mRNA vaccine currently in phase III (COVID-19 vaccine tracker | RAPS 2020). It basically generates the antibodies and T cells to work against the SARS-CoV-2 infection. As per the current progress, they expected to launch before the year end. The Moderna supported by the US government. The expected launch price was \$50–\$60 with the required dosage of two. Another key potential vaccine the whole world closely watching is Oxford-AstraZeneca. Oxford-AstraZeneca is also in phase III state. Similar to Moderna, Oxford-AstraZeneca also generates antibodies and T-Cells. The positive thing of Oxford vaccine is its cost and number of dosage. As per the early estimation, the cost is below \$13 with single dose. BioNTech-Pfizer is a German vaccine. Similar to the above, BioNTech also in phase III in development of potential vaccine. The expected price is \$3–\$4 per dose. Based on the current progress, the Pfizer say two dose is required for an individual. However, the exact number of dose will be finalized once the sufficient data were obtained. The expected date of all three were end of this year or mid of 2021. Inovio developed a DNA vaccine with support from Bill and Melinda gates foundation. Currently, three are in the phase II/III as on July, 2020. The other potential vaccines are Bharat Biotech—Covaxin, India. The Covaxin helps the body to detect the inactivated virus and urge to respond to the CoV-2. Since it is in the phase I, the expected launch date is unknown. As per the ICMR (Indian Council of Medical Research), the phase I/II human trials will be started by July, 2020. In initial trials, 50 volunteers between 18 and 55 age were responded without major side effects.

Role of nitrous oxide (NO) nanoparticles to combat against COVID-19

Virus usually constitutes variable size ranges from 10 to 850 nm. NO is known to combat various fungi, bacteria, virus and tumor cells. Nitrous oxide combined with nanoparticles can be used for various applications. NO can act as an antimicrobial agent because of its anti fungal and antibacterial properties. In addition to those properties, it can able to modulate foreign agents. NO had considered to be a vital agent to treat corona virus and other lung-related ailments.

NO can be administered with some other medicines can be effectively used to cure MERS-CoV affected patients and showed positive impacts with very less side effects (Pieretti et al. 2021; Akaike and Maeda 2000). Inhalation of NO treatment has been assessed for COVID patients in two nations, United States of America and China. Previously, NO was effectively used to treat lung-related ailments caused by certain virus. The studies found that NO compounds have potential to combat SARS-CoV replication. Nitrous oxide donor S-nitroso-N-acetyl penicillamine was effective in inhibition of SRS-CoV replication mechanism. Several researchers tried to assess the effects of NO against SARS-CoV-2 and NO donors were considered to important medical treatment. NO can be used as an alternative to tackle the current pandemic. Ultraviolet radiation promotes the NO generation and it is stored in skin and releases into blood, thereby reducing the blood pressure.

Fig. 3 Applications of the AI

Role of artificial intelligence

The AI technology plays a crucial role in addressing the patterns of the SARS-CoV-2 crisis. Machine learning can be applied to the SARS-CoV-2, to determine how the infection is spreading and the pipeline for the vaccines and treatment procedures. The main objective of the AI on the COVID-19 pandemic was, early detection of the infection before shedding, monitoring the infected and treating them, tracing the individuals how they came in contact and prediction of mortality and the confirmed cases. Furthermore, the AI technology can be linked with the computed topography (CT) to find the positive SARS-CoV-2 cases by image featuring (Vaishya et al. 2020). Figure 3 shows the various applications of the AI technology. Li et al. utilized the AI technology with chest CT in predicting the infection. The 4356 chest CT exams were collected from 3332 patients to develop the frame work and deep learning model (Li 2020). Becky McCall utilized the AI technology to protect the health care workers amid the serious spread. Application of the AI can be possible to protect the next outbreak of infection (McCall 2020).

The implementation of the AI in the medical fields was not extensively tested. Initially, the AI was used to diagnosis

based on the X-ray and CT-scan. The AI technology helps the professional to operate the imaging procedure. Due to the long processing time of the radiology scans, the AI technology plays a key role. On the contrary, the AI requires plenty of data. By uploading thousands of data, the AI can diagnose the disease without radiologist support. With regard to prevention, AI monitors the CCTV feeds to identify the patients who was not wearing mark and not following the social distance guidelines. In addition to above, the AI used in the discovery of new drugs. AI allowed making plenty of trials and choosing the op optimized one. For instance, from the lakh of molecules, the optimum 30 can be optimized easily. Instead of testing 1 lakh, 30 molecules sounds like saving more time with least expenditure. The decision-making process were also viable and compromising using AI technology. The types of the machine learning methods are image processing method, 3D CNN model image classification model and Noisy or Bayesian function. These basic machine learning methods used to aid the SARS-CoV-2 AI response for the diagnosis and treatment (Vaishya et al. 2020).

Conclusion

In conclusion, the COVID-19 is a challenging tasks for most of the researchers and the pharmaceutical industries. To handle the situation effectively, awareness about hygiene practices among the public, is needed. Alternative strategies need to be framed to effectively handle the NCD patients in an innovative manner. Despite the several clinical trials, no profound impact was observed on the old antiviral such as Chloroquine and hydroxychloroquine, Lopinavir–Ritonavir, Nafamostat and camostat, and Remdesivir. To combat the COVID-19, vaccination is the only solution. Among the 174 vaccine developers, as of now, only 12 are under the phase II and phase III developmental stages. Development of the AI tool can be promising for the identification of the infection before the outbreak with the optimized algorithm. In addition to the prediction of the infection, the AI can be used as the health monitoring tool. However, a better algorithm with the least uncertainty can only be possible by maintaining the COVID-19 data accessible for the entire world. This would help to develop a reliable AI and a deep learning model.

Funding No funding received.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

- Akaike T, Maeda H (2000) Nitric oxide and virus infection. *Immunology* 101:300–308. <https://doi.org/10.1046/j.1365-2567.2000.00142.x>
- Allen S (2020) Global health care outlook Laying a foundation for the future. [Online]. Available: www.linkedin.com/in/dr-stephanie-allen-gaica-7a841a4/. Accessed 30 Jun 2020
- Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF (2020) The proximal origin of SARS-CoV-2. *Nat Med*. <https://doi.org/10.1038/s41591-020-0820-9>
- Cao B et al (2020) A trial of lopinavir-ritonavir in adults hospitalized with severe covid-19. *N Engl J Med*. <https://doi.org/10.1056/NEJMoa2001282>
- Ceylan Z (2020) Estimation of COVID-19 prevalence in Italy, Spain, and France. *Sci Total Environ*. <https://doi.org/10.1016/j.scitotenv.2020.138817>
- Chen H et al (2020) Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. [https://doi.org/10.1016/S0140-6736\(20\)30360-3](https://doi.org/10.1016/S0140-6736(20)30360-3)
- China Faces The Challenge Of Chronic Disease | Asian Scientist Magazine | Science, technology and medical news updates from Asia. <https://www.asianscientist.com/2019/07/health/china-chronic-diseases-death/>. Accessed 30 Jun 2020
- COVID-19. https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/. Accessed 30 Jun 2020
- COVID-19 vaccine tracker | RAPS. <https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker>. Accessed 30 Jun 2020
- Gao J, Tian Z, Yang X (2020) Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. <https://doi.org/10.5582/BST.2020.01047>
- Gautret P et al (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. <https://doi.org/10.1016/j.ijantimicag.2020.105949>
- Geleris J et al (2020) Observational study of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med*. <https://doi.org/10.1056/nejmoa2012410>
- Grein J et al (2020) Compassionate use of remdesivir for patients with severe Covid-19. *N Engl J Med*. <https://doi.org/10.1056/NEJMoA2007016>
- Hoffmann M, Schroeder S, Kleine-Weber H, Müller MA, Drosten C, Pöhlmann S (2020) Nafamostatmesylate blocks activation of SARS-CoV-2: new treatment option for COVID-19. *Antimicrob Agents Chemother*. <https://doi.org/10.1128/AAC.00754-20>
- Hung IFN et al (2020) Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomized, phase 2 trial. *Lancet*. [https://doi.org/10.1016/S0140-6736\(20\)31042-4](https://doi.org/10.1016/S0140-6736(20)31042-4)
- Kailas S et al (2020) Homology modeling and docking studies of TMPRSS2 with experimentally known inhibitors camostatmesylate, nafamostat and bromhexine hydrochloride to control SARS-Coronavirus-2. *chemRxiv*. <https://doi.org/10.26434/chemrxiv.12162360.v1>
- Kapoor KM, Kapoor A (2020) Role of chloroquine and hydroxychloroquine in the treatment of COVID-19 infection—a systematic literature review. *medRxiv*. <https://doi.org/10.1101/2020.03.24.20042366>
- Li L et al (2020) Artificial intelligence distinguishes COVID-19 from community acquired pneumonia on chest CT. *Radiology*. <https://doi.org/10.1148/radiol.2020200905>
- Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J (2020) The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med*. <https://doi.org/10.1093/jtm/taaa021>
- Ma Y et al (2020) Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China. *Sci Total Environ*. <https://doi.org/10.1016/j.scitotenv.2020.138226>
- Manigandan S et al (2020) A systematic review on recent trends in transmission, diagnosis, prevention and imaging features of COVID-19. *Process Biochem* 98:233–240. <https://doi.org/10.1016/j.procbio.2020.08.016>
- Manigandan S, Thaloor Ramesh PK, Chi NTL, Brindhadevi K (2021) Early detection of SARS-CoV-2 without human intervention to combat COVID-19 using drone technology. *Aircr Eng Aerosp Technol* 93(1):85–88. <https://doi.org/10.1108/AEAT-06-2020-0120>
- McCall B (2020) COVID-19 and artificial intelligence: protecting health care workers and curbing the spread. *Lancet Digit Heal*. [https://doi.org/10.1016/s2589-7500\(20\)30054-6](https://doi.org/10.1016/s2589-7500(20)30054-6)
- Noncommunicable Diseases—NCDs | Knowledge for policy. https://ec.europa.eu/knowledge4policy/foresight/topic/shifting-health-challenges/non-communicable-diseases-ncds_en. (Accessed Jun 30, 2020).
- Pieretti JC, Rubilar O, Weller RB, Tortella GR, Seabra AB (2021) Nitric oxide (NO) and nanoparticles—potential small tools for the war against COVID-19 and other human coronavirus infections. *Virus Res* 291:198202
- Singh AK, Singh A, Shaikh A, Singh R, Misra A (2020) Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: a systematic search and a narrative review with a special reference to India and other developing countries. *Diabetes Metab Syndr Clin Res Rev*. <https://doi.org/10.1016/j.dsx.2020.03.011>
- Swaminathan A et al (2007) Personal protective equipment and antiviral drug use during hospitalization for suspected avian or pandemic influenza. *Emerg Infect Dis*. <https://doi.org/10.3201/eid1310.070033>
- Vaishya R, Javaid M, Khan IH, Haleem A (2020) Artificial Intelligence (AI) applications for COVID-19 pandemic. *Diabetes Metab Syndr Clin Res Rev*. <https://doi.org/10.1016/j.dsx.2020.04.012>
- Wu Y et al (2020) Effects of temperature and humidity on the daily new cases and new deaths of COVID-19 in 166 countries. *Sci Total Environ*. <https://doi.org/10.1016/j.scitotenv.2020.139051>
- Zhou P et al (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. <https://doi.org/10.1038/s41586-020-2012-7>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.