

## The New Technologies in the Pandemic Era

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The pandemic of the new coronavirus affected people's lives by an unprecedented scale. Due to the need for isolation and the treatments, drugs, and vaccines, the pandemic amplified the digital health technologies, such as Artificial Intelligence (AI), Big Data Analytics (BDA), Blockchain, Telecommunication Technology (TT) as well as High-Performance Computing (HPC) and other technologies, to historic levels. These technologies are being used to mitigate, facilitate pandemic strategies, and find treatments and vaccines. This paper aims to reach articles about new technologies applied to COVID-19 published in the main database (PubMed/Medline, Elsevier Science Direct, Scopus, Isi Web of Science, Embase, Excerpta Medica, UptoDate, Lilacs, Novel Coronavirus Resource Directory from Elsevier), in the high-impact international scientific Journals (Scimago Journal and Country Rank - SJR - and Journal Citation Reports - JCR), such as The Lancet, Science, Nature, The New England Journal of Medicine, Physiological Reviews, Journal of the American Medical Association, Plos One, Journal of Clinical Investigation, and in the data from Center for Disease Control (CDC), National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) and World Health Organization (WHO). We prior selected meta-analysis, systematic reviews, article reviews, and original articles in this order. We reviewed 252 articles and used 140 from March to June 2020, using the terms coronavirus, SARS-CoV-2, novel coronavirus, Wuhan coronavirus, severe acute respiratory syndrome, 2019-nCoV, 2019 novel coronavirus, n-CoV-2, covid, n-SARS-2, COVID-19, corona virus, coronaviruses, New Technologies, Artificial Intelligence, Telemedicine, Telecommunication Technologies, AI, Big Data, BDA, TT, High-Performance Computing, Deep Learning, Neural Network, Blockchain, with the tools MeSH (Medical Subject Headings), AND, OR, and the characters [,"; /, to ensure the best review topics. We concluded that this pandemic lastly consolidates the new technologies era and will change the whole way of the social life of human beings. Also, a big jump in medicine will happen on procedures, protocols, drug designs, attendances, encompassing all health areas, as well as in social and business behaviors. **Keywords:** COVID-19. SARS-CoV-2. New Technologies. AI. Big Data. BDA. Telecommunication Technologies.

### Introduction

The COVID-19 pandemic is causing serious disturbances in human society and unprecedented health and economic crisis. At the same time, several new technologies are being applied to the novel pandemic of coronavirus in a global effort to mitigate the consequences of the disease, to optimize the efforts against COVID-19, and to find a drug or vaccine as quickly as possible to treat and cure people worldwide. Healthcare fields were fast to adopt digital solutions and the most advanced technology tools in response to the COVID-19 pandemic. Many of the solutions

implemented now could be solidified soon, contributing to the meaning of new digital-based models of care. These technologies mainly include Artificial Intelligence (AI), Telecommunication Technology (TT), Big Data Analytics (BDA), 3D Printing Technology (3DPT), High-Performance Computing (HPC), among others. Due to the considerable studies on technological innovations in the combat and control of the COVID-19 pandemic, we decided to summarize them in Tables (Table 1-6) and Figures (1-28) and describe the main technologies and their applications to mitigate the pandemic and help in the solutions against COVID-19.

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### General Use of New Technologies Against COVID-19

New technologies very often are capable of providing solutions for our daily lives during a crisis [1, 16, 29, 30]. They have the potential to

**Table 1.** New Technologies and the applications in COVID-19 pandemic.

Technology	Description	Applications (Examples)
Artificial Intelligence (AI)	<p>Artificial intelligence can be a powerful instrument when it comes to the assessment of risks of infection and screening of the population, which comes in handy in pandemic times. It works similarly to machine learning, computer vision, and natural language processing, instructing computers to use models based on big data for recognizing, explaining, and predicting patterns. Currently, the use of this technology is somewhat restricted due to lack of data, and because sometimes the data can be noisy and outlier [1,2].</p>	<p>It can work detecting viruses, individuals with fever, and suspected symptoms of COVID-19 through the integration of thermal imaging, AI, Computer vision, and cloud computing, and advice accordingly for appropriate treatment. Its use can bring down the time for genetic detection to minutes. [2] It can provide real-time coverage of the COVID-19 outbreak (great importance for epidemiological information) [3]. It can aid in keeping this virus within reasonable limits, and in designing new molecules in silico [4]. For automated detection and monitoring of COVID-19 patients over time, a deep learning-based analysis system of thoracic CT images has been built [5, 6]. Machine learning-based screening of SARS-CoV-2 assay designs using a CRISPR-based virus detection system was demonstrated with high sensitivity and speed [7]. For large-scale screening of COVID-19 patients, neural network classifiers were developed to work based on their distinct respiratory patterns [8]. It can be used with deep learning and neural network and radiological images (CT and x-Ray) [9,10] Lastly, Artificial intelligence can also be used to predict the immunogenic landscape of SARS-CoV-2.</p>
Computer Vision	<p>Computer vision is an interdisciplinary field that is devoted to using computers to develop a high-level understanding by interpreting digital images and the information present in them. It has made substantial progress in the last few years, mainly due to the success of deep learning, a sub-field of machine learning [11]</p>	<p>Prevention and control, when applied to CT and x-Ray images [11]</p>
Big Data	<p>Big data is an analytic technique using technology that can store information about a large number of patients infected by this virus. It can be quite useful to track and control the worldwide spread of COVID 19 since this technology provides the basis for faster (almost real-time) evaluation and decision making. It is helping save lives and quickly identifying effective therapies [1,2].</p>	<p>Storage capacity for extensive public data is provided in a format that lends itself efficiently for analysis, and as a result, appropriate measures can be taken towards the prevention of disease transmission, movement, health monitoring, and prevention system. Big data can be highly useful for analyzing and forecasting the reach and impact of coronavirus. COVID-19 trackers are able to gather nearly real-time data from sources around the world and subsequently equip scientists, doctors, epidemiologists, and policymakers with up-to-date information, which can be very helpful to make better decisions in order to neutralize the effects of the virus [1, 2]. It can be used in association with AIs: whilst Big Data enables data analysis and interpretation, the AI uncovers hidden trends and patterns, which can be used to build predictive models.</p>

Technology	Description	Applications
Telemedicine	<p>Telehealth or Telemedicine is the distribution of health-related services and information via electronic information and telecommunication technologies [12]. It allows long-distance patient and clinician contact, care, advice, reminders, education, intervention, monitoring, and remote admissions [13, 14].</p>	<p>A patient can have a consultation from well-trained professionals on their medical conditions through video calls, avoiding the need for a hospital visit and thus helping the social distancing and man-to-man contact and disease transmission. However, these remote consultations are now possible by using better telecom infrastructure with Virtual reality and Augmented reality: - Medical Care Appointments (SMAs) [15].</p>
Blockchain	<p>Blockchain has recently come to light as a key technology in the field of epidemic management. It is able to provide robust, transparent, and cheap means of assisting effective decision-making and, as a result, could lead to faster responses during emergencies of this kind. Blockchain has the potential to be an integral part of the global response to COVID-19 by tracking the transmission of the virus, managing insurance payments, and maintaining the sustainability of medical supply chains and donation tracking pathways [16].</p>	<p>Algorithms can facilitate the offer of real-time data to all the strategic partners, as well as traceability in the process of disease control, and support in the effective management of the supply chain [2].</p>
5G + Smart Applications	<p>5G networks are digital cellular networks, in which the service area covered by providers is divided into small geographical areas called cells. Analog signals representing sounds and images are digitized in the telephone, converted by an analog-to-digital converter, and transmitted as a stream of bits. All the 5G wireless devices in a cell communicate by radio waves with a local antenna array and low power automated transceiver (transmitter and receiver) in the cell, over frequency channels assigned by the transceiver from a pool of frequencies that are reused in other cells. The local antennas are connected with the telephone network and the Internet by a high-bandwidth optical fiber or wireless backhaul connection. As in other cell networks, a mobile device crossing from one cell to another is automatically "handed off" seamlessly to the new cell. 5G can support up to a million devices per square kilometer, while 4G supports only up to 100,000 devices per square kilometer [17, 18]. The new 5G wireless devices also have 4G LTE capability, as the new networks use 4G for initially establishing the connection with the cell, as well as in locations where 5G access is not available [19].</p>	<p>The high-speed network allows real-time data of video and audio quality for patient data analysis, telemedicine, medical and surgical intervention</p>

Technology	Description	Applications
Internet of Things (IoT)	Internet of Things is an automated solution that has resulted in tremendous growth in automated manufacturing, management of assets, etc. It comprises of collection, transfer, analytics, and storage of data. Collection of data is done with the help of sensors incorporated in mobile phones, robots, etc. The data collected is then sent for analytics and decision making to the central cloud server [1, 2].	All devices are connected to the internet in the hospital and strategic locations. Thus, these connected devices help to inform the medical staff of any errors and changes of requirements during the treatment process (similar to the factories of the future). IoT is proving to be very helpful in the fight against COVID-19. For instance, drones are in use for surveillance in order to ensure the implementation of quarantine and mask-wearing. This technology can be used for tracing the origin of an outbreak. It can be helpful to the epidemiologists for searching patient zero and also in identifying the persons coming in contact with the patients. The compliance of quarantine by the patients can be ensured. The patients who breach the quarantine can be tracked down. Moreover, this technology can be beneficial in providing relief to the medical staff by remote monitoring of in-home patients [1, 2].
Drones	An unmanned aerial vehicle (UAV) (or uncrewed aerial vehicle [20], commonly known as a drone) is an aircraft without a human pilot onboard and a type of unmanned vehicle. UAVs are a component of an unmanned aircraft system (UAS); which includes a UAV, a ground-based controller, and a system of communications between the two. The flight of UAVs may operate with various degrees of autonomy: either under remote control by a human operator, autonomously by onboard computers [21] or piloted by an autonomous robot [22].	These unmanned vehicles controlled by remote location can undertake jobs of logistics provider and area surveillance and can also be used for disinfecting remote locations
Robotics	Robotics is an interdisciplinary research area at the interface of computer science and engineering [23]. Robotics involves the design, construction, operation, and use of robots. The goal of robotics is to design intelligent machines that can help and assist humans in their day-to-day lives and keep everyone safe. Robotics draws on the achievement of information engineering, computer, engineering, mechanical, engineering, electronic, engineering, and others.	Undertakes repetitive jobs with precision and reliability in the hazardous environment of infectious disease in and around the hospitals and can make an intelligent decision with inputs from the population data analyzed through AI.
Modern enterprise video communications platform	Communication technologies that provide videotelephony and online chat services through a cloud-based peer-to-peer software platform and are used for teleconferencing, telecommuting, distance education, and social relations [24, 25].	The application of the software helps in holding video and audio communications, chats, and webinars easily and quickly through large numbers of communication devices.

Technology	Description	Applications
Smartphone apps	<p>A mobile application, also known as an app, is a computer program or software application designed to run on a mobile device such as a phone, tablet, or watch. Apps were originally intended for productivity assistance such as email, calendar, and contact databases, but the public demand for apps caused rapid expansion into other areas such as mobile games, factory automation, GPS and location-based services, order-tracking, and ticket purchases so that there are now millions of apps available. Apps are generally downloaded from application distribution platforms which are operated by the owner of the mobile operating system, such as the App Store (iOS) or Google Play Store. Some apps are free, and others have a price, with the profit being split between the application's creator and the distribution platform. Mobile applications often stand in contrast to desktop applications which are designed to run on desktop computers, and web applications that run in mobile web browsers rather than directly on the mobile device [26].</p>	<p>Uses a high-speed network and helps to track strategic locations, infected patients, and registering the data and modeling of disease outcomes as per the application software and other technologies can also be integrated with the software.</p>
Virtual reality	<p>Virtual reality (VR) is a digital technology that provides a simulated experience that is almost the same or different from the working world. Its applications include video games, 3D games, educational training, medical training, military training, etc. The environment provided by this technology presents the benefits of great comfort, creativity, and productivity. People can work together in real-time through intuitive whiteboards, the simulations can be visited, and the content can be recorded [1, 2].</p>	<p>In the times of the COVID-19 outbreak, the technology of virtual reality offers a great option for video calls. The most significant benefit of this medium is its ability to make people feel like they are together in the same space without the need for traveling. The extra benefit is that people can entirely focus on the task at hand without any distractions at all. VR improves efficiency, upgrades the working in a group, reduces travel costs, reduces absenteeism, and lowers the impact of the environment. So, in this time of COVID-19 disease, VR has been an excellent tool for communication and collaboration [1, 2].</p>
Holography	<p>Holography is 3D photography. It presents 3D views with changing perspectives. It is a contrast to photography; it records both the phase and the complex amplitude of the wave which comes from the object. The record is called the hologram. It is like a window that has memory. The hologram can reconstruct an accurate 3D image of the original object. It provides corporations with an alternative to virtualize their events without the need for webcasting. With the use of this, the businesses can launch products, add new clients, and build their brands [1,2].</p>	<p>The digital technology of holography has paved a new way to conduct conferences and live events. It ensures the reduced exposure of the speakers, employees, and clients to COVID-19. It feels like speakers are living from their homes or offices virtually on a real event stage regarding COVID-19. Thousands of people can attend this live streaming at the same time. Holography has now the ability to offer ultra-realism. In this time of COVID 19 outbreak, when the workers are bound to stay at home, this technology of streaming holographic events is becoming readily acceptable [1, 2].</p>

Technology	Description	Applications
Cloud computing	<p>Cloud computing is a digital technology that involves the delivery of computer system resources over the internet such as servers, storage, databases, networking, intelligence, etc. This technology provides faster innovation and resources which are flexible. It results in reduced operating cost and increased efficiency of running the infrastructure [1, 2].</p>	<p>In the present times of social isolation amid the COVID-19 outbreak, people have been able to continue their digital lives with the help of applications like Zoom video, Slack, Netflix through services such as Amazon Web Services, Microsoft Azure, and Google Cloud. Cloud computing can be helpful to fight against COVID-19 in several ways. For instance, introduced especially designed Salesforce Care solution for healthcare providers who receive a large number of requests due to COVID-19 [1, 2]. All necessary information is stored at a computing platform and made available, to enable an enormous amount of computing power to the users with the help of the internet and helps in making real-time decisions in disease modeling. The software can be employed with blockchain and other tools to model requirements of critical facilities at a different level, from the hospital to the nation. Use official epidemiological data and predict the possible outcomes of the COVID-19 pandemic using based RNNs on (Recurrent Neural Networks).</p>
Autonomous robot	<p>An autonomous robot is used to carry out the tasks without the influence of any external agency. It can be employed to collect information about the environment. It can be used for a very long period without help. It is considered as a sub technology of robotics and artificial intelligence. It can ignore the situations which may be dangerous for human beings [1, 2].</p>	<p>During the present times of lockdown in the COVID-19 pandemic, an autonomous police robot can be deployed for patrolling the areas to confirm that the people are following the orders of lockdown. The autonomous police robots may also be deployed in the hospitals in order to help the medical staff to perform their duties without any disruption. It can be very helpful to enhance the performance of the medical staff and in turn, to contain the spread of the COVID-19 [1, 2].</p>
3D Scanning	<p>3D scanning is used to convert the physical part into CAD digital data. This technology is successful for the reverse engineering processes. In medicine, this technology is used for scanning the human body and its part as per precise dimension. 3D scanning output is used for the analysis of real-world objects for collecting data about its shape and appearance. The 3D model can then be constructed with the use of collected data. This data can be used for a large number of applications. 3D scanners are also useful in developing video games and movies [1, 2].</p>	<p>3D scanning is a non-contact technique that helps the thoracic chest scanning for COVID-19. Also, a useful tool to detect and quantify COVID 19 virus. Virtual reality, motion capture, robotic mapping, and industrial design are some of the other applications of this technology [1, 2]. Undertakes manufacture of personalized devices for healthcare workers and patients, using 3D printing technology for the COVID-19, whenever required.</p>
3D Printing	<p>3D printing is already emerging in the medical field for the manufacturing of customized part from the input of CAD digital file. This can quickly revise the previous version of the product in lesser time and cost. It helps in the design and development of ventilator parts as per the required shortage. Thus, fulfills the need for the global supply chain by manufacturing required precaution parts [1, 2].</p>	<p>3D printing technology can be used in some critical applications to contain the spread of COVID-19 disease. A face mask to be produced with the use of this technology is already under development. This face mask can be employed to test a large number of persons for COVID-19 in 30 min. The use of surgical masks and N95 respirators is not suitable for the environment, and it can prove to be detrimental to the ecosystem. On the other side, it is claimed that the newly developed NanoHack 3D-printed mask is recyclable and can be reused [1, 2].</p>

Technology	Description	Applications
Biosensor	<p>Biosensors are used for the conversion of the biological signal into an electrical signal. Some of the essential types of biosensors are optical, thermal, piezoelectric, and electrochemical biosensors. They find applications in a wide variety of fields such as medical science, the food industry, the marine sector, etc. They are stable and sensitive. In the case of biological wars, the biosensors can be employed for the support of the military. This technology of biosensor, which is entirely new to the market used effectively as a wireless device in an environment of the multi-patient hospital [1, 2].</p>	<p>In the present time of pandemic COVID-19, the biosensors are capable of providing devices that can be easy to employ, sensitive, cost-saving and can provide high accuracy. A glucose monitor is a perfect example of the biosensor which is used in clinical analysis and diagnosis of the disease. A single-use wireless biosensor patch IAX is under development. This biosensor patch can be employed for the early detection and then the monitoring of the symptoms of COVID-19. The real-time recording of the temperature, ECG trace, respiration rate, etc. will be performed by this patch [1, 2].</p> <p>- Lab on a chip (microfluidics) is promised technology for diagnostic COVID-19 [27].</p>
Nanotechnology	<p>Nanotechnology is a multidisciplinary field that makes use of nano-sized particles and devices for various applications, including diagnostics, targeted drug delivery, and the production of new therapeutic materials. Nanoparticles such as gold and silver have been used in biomedical and diagnostic applications, for the detection of viral particles for instance. Nanotechnology has been shown to help in treating viral infection by means of various mechanisms. Nanoparticles can act as antiviral drug delivery systems; they can interact and bind to a virus and thereby prevent it from attaching and entering the host cell; they can be designed to exhibit antiviral effects. Altogether, the use of nanotechnology in the development of new medicines has been recognized as a key enabling technology, capable of providing new and innovative medical solutions to address unmet medical needs [16].</p>	<p>Nanomedicine has already been used in drug delivery. In the case of an RNA-based vaccine, which consists of messenger RNA (ribonucleic acid) strands, lipid nanoparticles have been used to pack the RNA molecule and deliver it within the body. While no RNA vaccine has ever been licensed, a US-based biotechnology company specializing in messenger RNA therapeutics recently announced that its mRNA-based vaccine candidate (mRNA-1273) for the novel coronavirus disease (COVID-19) had just entered Phase 1 study. Novavax, meanwhile, also recently initiated the development of a vaccine candidate for COVID-19, using its proprietary recombinant nanoparticle vaccine technology [16].</p>
Virtual screening	<p>New programs with <i>in silico</i> methods.</p>	<p>Identification of novel drug candidates and repurposing of known drugs [28].</p>

help people perform daily life work during the lockdown [31, 32] and bring benefits for mitigating effects of COVID-19 pandemic such as:

- Planning of activities regarding COVID-19;
- Providing a better experience without imposing the risks to healthcare and other workers;
- Manufacturing of items for precautionary measures related to SARS-CoV-2;
- In-time provisioning of medical items using smart supply chain;
- Using robotic based treatment for infected patients aiming at reducing risks and increasing workplace safety for health professionals;
- Using virtual and augmented reality for training purpose;
- Promoting a flexible working environment for treatment.
- Detecting of images from computerized tomography (CT) lung scans and faster RT-PCR correlation;
- Monitoring, in real-time, changes in body temperature through the use of wearable sensors;
- Providing an open-source data platform to track the spread of the disease;
- Predicting the number of potential new cases by area and which types of populations will be most at risk, as well as to evaluate and optimize strategies for controlling the spread of the epidemic;
- Detecting fake news about COVID-19 using applying machine-learning techniques, following words that are excessive or alarming, and recognize which online sources are considered eligible to believing or not.

Ting and colleagues [33] described the potential application of inter-related digital technologies for tackling COVID-19 (Table 2) by monitoring, surveillance, detection and prevention of the disease through IoT, BDA, AI, and deep learning; and mitigation of the impact on the healthcare

sector indirectly related to COVID-19 through telemedicine and education.

They concluded that the successful use of digital technology to mitigate the major public health challenge in 2020 will probably positively influence the public and government of such technologies for other areas in the future. As well, according to Brohi and colleagues [34], Artificial Intelligence (AI), 3D Printing Technology (3DPT), Big Data Analytics (BDA), High-Performance Computing (HPC), and Telecommunication Technology (TT) are the five state-of-the-art technologies that could assist the scientists and researchers in mitigating and eliminating COVID-19 (Figure 1).

### **Artificial Intelligence (AI)**

Different studies describing the use of Artificial Intelligences against COVID-19 and the issues in that regard are presented below, as well as state-of-the-art studies on AI techniques (Table 3). According to Brohi and colleagues [34], AI applications that rely on deep machine learning and neural network models are being used as a tool to help with prediction and detection of COVID-19, such as detecting COVID-19 through chest scans with remote monitoring and controlling, predicting COVID-19 threats, combating fake news, handling AI-based Apps with geolocation to follow individuals and inform communities via real-time interaction on limitations, advice, and guidelines to avoid COVID-19 hotspots, as well as in using drug discovery platforms to recognize molecules with possible effects against SARS-CoV-2, developing robots as support systems to disinfect hospitals, restaurants, public transport hubs, and possible COVID-19 locations without human intercommunication with infectious objects. Vaishya and colleagues [50] also described the quick analysis of irregular symptoms and alert patients and healthcare authorities that AI can do. Ai and colleagues [51] similarly reported that AI can give updated information in real-time that is helpful in the prevention of COVID-19, since



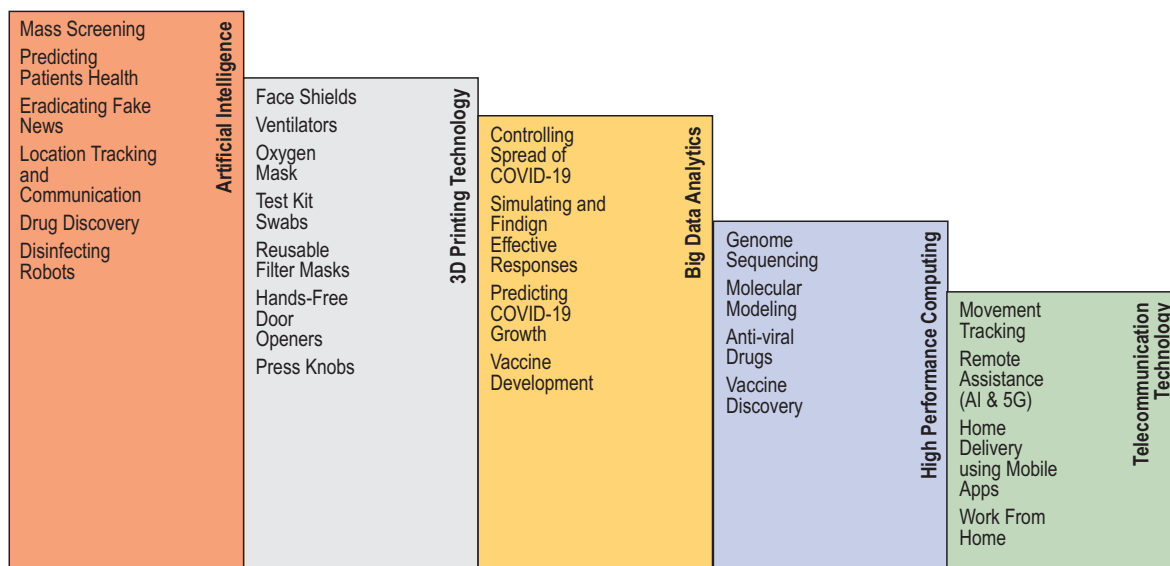
**Table 2.** Digital technologies and their impact on public-health strategies.

Digital Technologies				
Public-health measures	IoT	Big Data	AI	Blockchain
Monitoring, surveillance, detection and prevention of COVID-19 (directly related to COVID-19)	+++	+++	++	+
Examples	Real-time tracking and live updates in various online databases in the USA, UK and China	Modeling of disease activity, potential growth and areas of spread	Detection of COVID-19 from chest imaging (x-Ray) (Beijing Hospital)	Manufacturing and distribution of COVID-19 vaccines once they are available
	Live tracking of the at-risk vicinity in Korea (Coronamap. live; Wuhanvirus.kr)	Modeling of the preparedness and vulnerability of countries in fighting a disease outbreak	Prognostication of disease progression via clinical data, imaging and AI	Insurance claims from COVID-related illness and death
Mitigation of impact (indirectly related to COVID-19)	+++	++	+++	++
Examples	Virtual clinics (PingAn, China)	Business modeling on pharmaceutical supplies for various medications	AI to automatically diagnose medical conditions unrelated to COVID-19 (Zhongshan Ophthalmic Eye Center, China)	Distribution of patients' regular medication to the local pharmacy or patients' doorstep
	Public information dissemination via WhatsApp in Singaporea	Modeling of the utility of operating theaters and clinics with manpower projections	Medical 'chat bots' to address public inquiries on COVID-19	-

+++; high; ++; regular; +; low.

Credit/Source: Ting and colleagues [33].

**Figure 1.** Key applications of state-of-the-art technologies to mitigate and eliminate COVID-19.



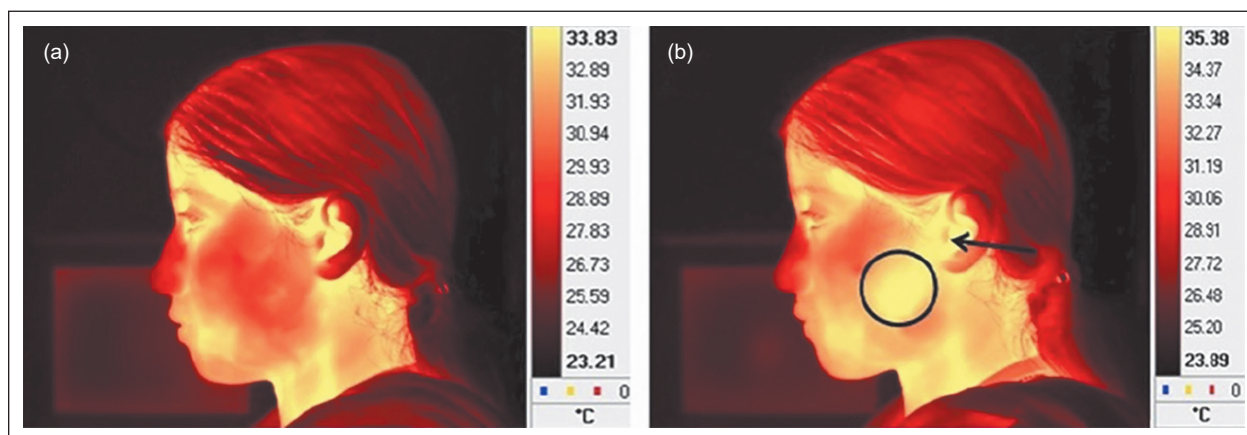
Credit/Source: Brohi and colleagues [34].

**Table 3.** State-of-the-art studies on AI applications for COVID-19.

Subject	Contributions	References
Detection and diagnosis	A CNN-based DeTraC framework is proposed. In particular, the transfer learning concept is used to utilize wellperformed deep models. For the pre-trained ResNet18 model, the DeTraC method achieves competitive performance, accuracy of 95.12%, sensitivity of 97.91%, and specificity of 91.87%.	[35]
	A deep CNN model for classification of COVID-19 and the dataset is designed by collecting 13, 975 chest X-ray images across 13, 870 patients. The proposed CNN model can achieve the test accuracy of 93.3%.	[36]
	Using chest CT images, 63 quantitative features of COVID-19 are analyzed by an RF model. The proposed method can obtain promising results, e.g., accuracy of 0.875 and AUC score of 0.91.	[37]
	The AI4COVID-19 framework is proposed to consider domain knowledge of medical experts. The input data is cough/sound signals, which may be recorded by smartphones. The performance is very promising, the classification accuracy of 97.91% (93.56%) is obtained for cough (COVID-19) detection.	[38]
Identifying, tracking, prevention and control, and predicting the outbreak	A time-dependent SIR model is proposed to dynamically adjust the control parameters according to the outbreak policies. The model is also extended to consider undetectable infected cases.	[39]
	A modified autoencoder framework is investigated to model the transmission dynamics of COVID-19. Using the empirical data from the WHO, the model can achieve an average error of less than 2.5%. An interesting observation is that a faster intervention can significantly reduce the numbers of infected and dead cases.	[40]
	Infrared thermography was also recommended as an early detection strategy for infected people, especially in crowds like passengers on an airport (Figure 2).	[41, 42]
Infodemiology and infoveillance	Data is collected from Sina Weibo, Baidu search engine, and Ali e-commerce 29 marketplace to evaluate public concerns/behaviors and risk perception to the COVID-19 outbreak. The result shows that fast reaction to quickly classify rumors and misinformation can well mitigate impacts of irrational behaviors.	[43]
	Applications of computer visions for combating the COVID-19 pandemic are presented. Potential use cases (e.g., risk assessment and diagnosis) and challenges (e.g., data collection and model sharing) are also discussed.	[44]
	An AI-driven system, namely $\alpha$ -satellite, is proposed to estimate the risk of COVID-19 in an hierarchical manner. Data is collected from heterogeneous sources, e.g., WHO, demographic and mobility data, and social platforms.	[45]
Biomedicine and pharmacotherapy	A pre-trained deep learning model is utilized to train a dataset of 4, 895 commercially available drugs. After learning and manual refinement, 10 drugs are selected as potential COVID-19 inhibitors.	[46]
	For drug repurposing, a data-driven approach is examined over 6, 000 candidate drugs. The key finding is that the inhibitor CVL218 is very promising and has a safety profile in monkeys and rats.	[47]
	A deep generative model, namely CogMol, is proposed to find potential molecules that can bind three relevant protein structures of coronavirus. Also, in silico screening experiments are conducted to assess the toxicity of the generated molecules.	[48]

Credit/Source: Pham and colleagues [49].

**Figure 2.** Temperature screening in process using thermal images of a subject talking on a hand-held mobile phone; (a) after 1 min and (b) after 15 min of talking. After 15 min of talking the temperature of the encircled region increased from 30.56 to 35.15 C, whereas the temperature of the ear region (indicated by an arrow) increased from 33.35 to 34.82C. Similar system can be used for fever screening.



Credit/Source: Ulhaq and colleagues [11].

it can predict the probable sites of infection, the necessity for beds, and healthcare professionals during this emergency. It recognizes features, causes, and reasons for the spread of infection helping the process of early detection, diagnosis, and decision-making. In the near future, AI will perform an essential role in affording more predictive and preventive healthcare [51, 53-54]. Moreover, AI aids in developing vaccines and treatments faster than usual and is also helpful for clinical trials [55-60]. It also reduces the workload of healthcare workers [61, 62] and adopts digital approaches with decision science [51, 63, 64].

McCall [65] pointed out some companies that it is using AI for predicting the news of the outbreak (Blue Dot, a Canadian company); and potential drugs (BenevolentAI and Imperial College London); designing new molecules that can halt viral replication (Insilico Medicine); and use imaging methods (Infervision's AI).

Unfortunately, patient-level COVID-19 data is not publicly available. However, Cosgriff and colleagues [66] described the Medical Information Mart for Intensive Care (MIMIC), which has been a model of publicly-available, anonymized electronic health record data sharing since 1996 that represents

the most studied critical care cohort in the world, allowing clinicians and computer scientists to address research questions and build predictive models [67]. Sun and colleagues [3] described the online platform that provides real-time coverage of the COVID-19 outbreak in China, obtained by using crowdsourced reports from DXY.cn [68], a social network for Chinese physicians, health-care professionals, pharmacies, and health-care facilities established in 2000, by the reports linked to an online source, concluded that the news reports and social media can “help reconstruct the progression of an outbreak and provide detailed patient-level data in the context of a health emergency”.

In a review study, Alimadadi and colleagues [5] report the large-scale data of COVID-19 patients that can be combined and analyzed by advanced machine learning algorithms to a better comprehension of the pattern of viral spread, further enhance diagnostic agility and precision, develop new efficient therapeutic procedures, and potentially recognize the most susceptible people based on personalized genetic and physiological properties. They presented some examples that represent a good model of the application of AI: the Allen Institute for AI in partnership with leading

research groups issued an open-source, weekly updated COVID-19 Open Research Dataset [69], which continuously documents COVID-19-related scholarly articles to accelerate novel research projects urgently requiring real-time data; the survival prediction of severe COVID-19 patients [47, 61]; the discovering potential drug candidates against COVID-19 [47, 61]; biochemistry (e.g., ACE2 expression level) and clinical data (e.g., age, respiratory pattern, viral load, and survival) of COVID-19 patients with underlying medical conditions can be analyzed by machine learning approaches to not only identify any reliable features (e.g., ACE2) for risk prediction but also further perform risk classification and prediction for a balanced preparation of ongoing disease treatment and COVID-19 defense.

However, as well as other studies, Alimadadi and colleagues [5], see a current hurdle in the availability of COVID-19-related clinical data, which would need to be managed and processed into easily accessible databases. The creation of integrating COVID-19-related clinical data such as the UK Biobank, with pre-existing data of patients, could potentialize the efforts towards a faster and feasible approach for meaningful data-mining by bioinformaticians and computational scientists. A centralized compilation of global COVID-19 patient data will be helpful for future artificial intelligence and machine learning researches to promote predictive, diagnostic, and therapeutic approaches against COVID-19 and alike pandemics in the future.

Blasiak and colleagues [70] described the use of IDentif.AI, a platform that quickly optimizes infectious disease (ID) combination therapy design applying artificial intelligence (AI). The platform IDentif.AI was realized on a 12-drug candidate therapy search set representing over 530,000 possible drug combinations. The combination therapy against SARS-CoV-2 was composed of remdesivir, ritonavir, and lopinavir, which the results proposed that the combination was a 6.5-fold improvement in efficacy than remdesivir alone. Also, IDentif.AI showed

hydroxychloroquine and azithromycin to be relatively inefficient. The platform analysis was also capable to confirm clinical trial results to date without requiring any data from these trials. So, the IDentif.AI platform suggests that it may apply to the speedy development of optimal drugs for this current pandemic and future outbreaks. Ramdas and colleagues [15] presented a virtual platform for remote shared care delivery that has the potential to enhance provider capacity while mitigating transmission risks and enabling privacy in COVID-19 pandemic: identity can be withheld, voices disguised, and patient video made visible only to the clinician. This technology such as shared medical appointments (SMAs) has been used since 1999 in the US and could be very important in the pandemic especially to mitigate the transmission of COVID-19.

Thorlund and colleagues [71] developed a network of COVID-19 interventional clinical trials (completed, ongoing, and planned) by the data from the International Clinical Trials Registry Platform, including those from the Chinese Clinical Trial Registry, ClinicalTrials.gov, Clinical Research Information Service - Republic of Korea, EU Clinical Trials Register, ISRCTN, Iranian Registry of Clinical Trials, Japan Primary Registries Network, and German Clinical Trials Register. They also developed an artificial intelligence (AI)-based method for data searches to identify potential clinical studies not captured in trial registries, and used a content aggregator service, such as LitCovid, to ensure their data acquisition strategy was complete. Trials for COVID-19 were then “mapped according to geographical, trial, patient, and intervention characteristics when these data are available. Syntheses of these trials are urgently needed to assist clinicians, researchers, and policymakers to make evidence-informed decisions to minimize the morbidity and mortality due to COVID-19”.

About chest images, COVID-19, and pneumonia of different natures share similar CT characteristics, which contributes to the challenges in distinguishing between them with accuracy.

Bai and colleagues [72] used AI to compare if AI assistance improved radiologists' performance in identifying COVID-19 and non-COVID-19 pneumonia on chest CT. Their AI model achieved a test accuracy of 96% (95% CI: 90-98%), sensitivity 95% (95% CI: 83-100%), and specificity of 96% (95% CI: 88-99%) with Receiver Operating Characteristic (ROC) AUC of 0.95 and Precision-Recall (PR) AUC of 0.90, concluding that the AI aided the radiologists to distinguish the chest CT with COVID-19 pneumonia from non-COVID-19 pneumonia (Figures 3).

Singh and colleagues [73] classified COVID-19-infected patients from chest CT images using multi-objective differential evolution (MODE), a novel deep learning model, and convolutional neural networks (CNN) for classification of human beings based upon whether they are affected by COVID-19 or not. A multiobjective fitness function is designed to classify COVID-19-infected patients by considering sensitivity and specificity. For that, they compared their model with other studies (Table 4).

From an extensive review, it has been found that the chest CT images can be helpful in the early classification of COVID-19-infected patients. They did extensive experiments that reveal the proposed model "outperforms competitive models, i.e., adaptive neuro-fuzzy inference systems (ANFIS), artificial neural networks (ANN), and convolutional neural networks (CNN) CNN models in terms of accuracy, F-measure, sensitivity, specificity, and Kappa statistics by 1.9789%, 2.0928%, 1.8262%, 1.6827%, and 1.9276%, respectively". Therefore, the proposed model is useful for real-time COVID-19 disease classification from chest CT images, according to Singh and colleagues [73].

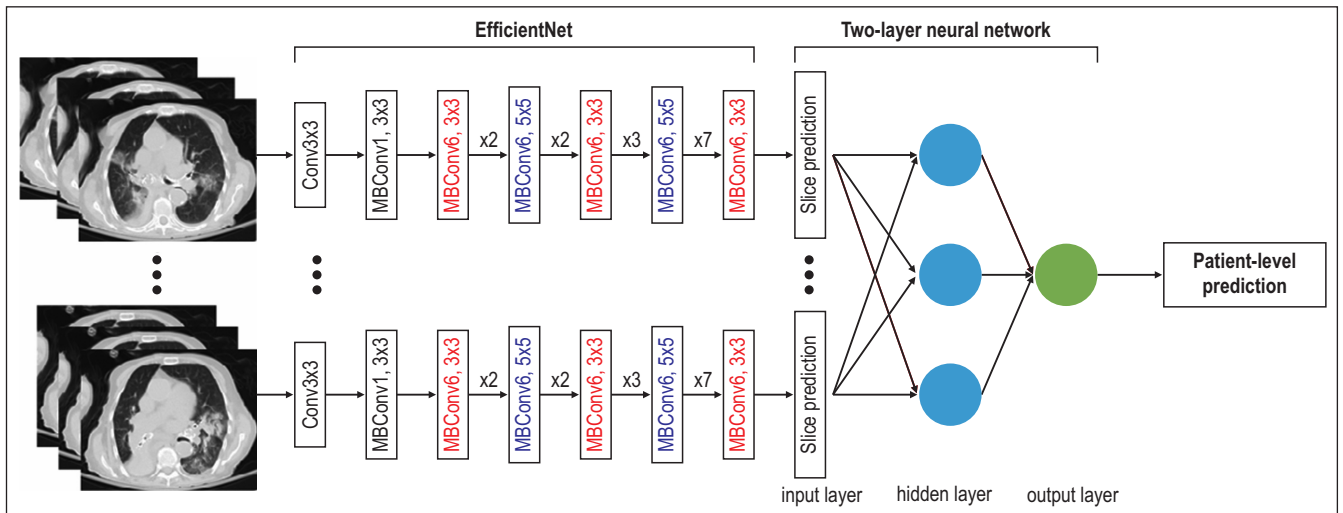
About chest CTs, Laghi [83] disagrees with some of the optimistic expectations about the diagnostic value of a particular algorithm applied to lung CT images as outlined by McCall because this is not yet supported by scientific evidence. According to Laghi, the little evidence that has been reported shows that approximately 50% of patients with COVID-19 infection have a

normal CT scan if scanned early after the onset of symptoms [84]. This evidence is the main reason why the American College of Radiology does not consider CT imaging as a useful screening test in asymptomatic individuals [85]. On the other hand, he deeply believes that AI can and should be used to support the work of a radiologist and that "the objective quantification of the disease, expressed as a percentage of the pulmonary parenchyma involved, is currently the most interesting application of AI in COVID-19 infection, which allows monitoring the course of the disease" [86].

There are many studies using chest CT and AI. Although chest CT is an effective imaging technique for lung-related disease diagnosis, chest x-Ray is more widely available, has a lower cost, and lower ionizing radiation when compared to CT (Table 5). So, deep learning, one of the most successful AI techniques, is an effective means to assist radiologists to analyze the vast amount of chest x-Ray images, which can be critical for efficient and reliable COVID-19 screening (Figure 4). Zhang and colleagues' study [87] developed a new deep anomaly detection model for fast, reliable screening of 100 chest x-Ray images of 70 patients confirmed with COVID-19 and 1,431 additional chest X-ray images with other pneumonia (Figures 5 and 6).

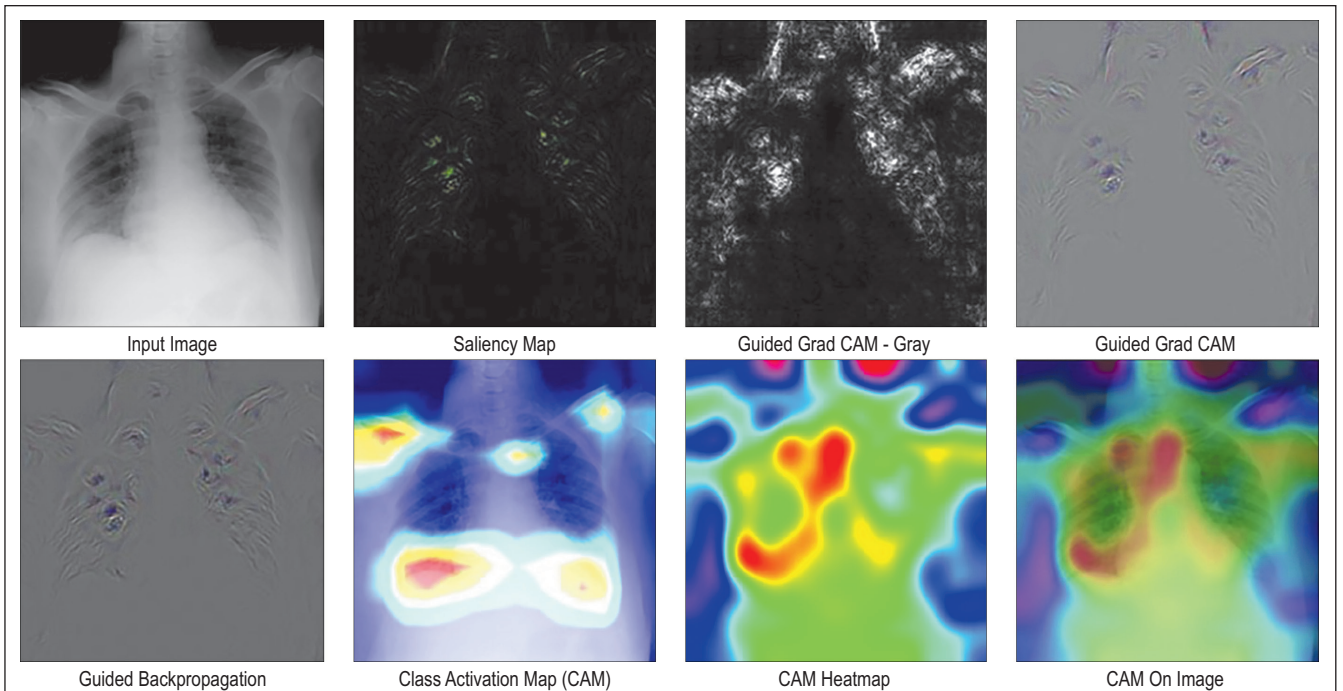
The initial experimental results show 96% sensitivity and 70.65% specificity. Shi and colleagues [88] obtained a sensitivity of 90.70% and specificity of 83.30% on a large-scale CT dataset, including 1,658 patients with COVID-19 and 1,027 with non-COVID-19 pneumonia. In this study, the model obtained the sensitivity of 90.00%, specificity of 87.84% (when  $T = 0.25$ ) or the sensitivity of 96.00%, specificity of 70.65% (when  $T = 0.15$ ) on the x-Ray dataset that contained 100 images from 70 COVID-19 subjects and 1,431 images from 1,008 non-COVID-19 pneumonia subjects. When compared to the CT-based screening method, Zhang and colleagues' x-Ray-based model performed relative performance. More importantly, the model only learns from 70 COVID-19 patients, which is less than 5 percent

**Figure 3.** COVID-19 classification neural network model.



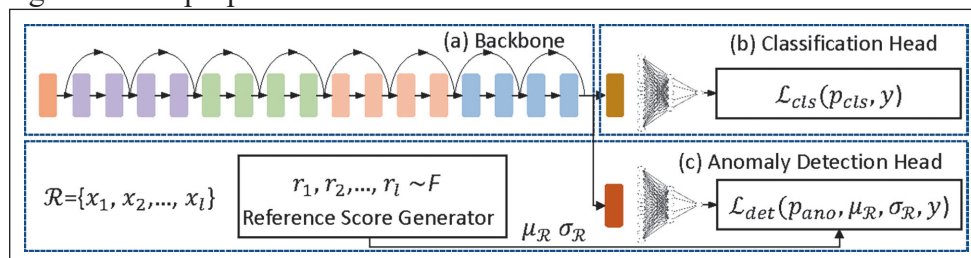
Credit/Source: Bai and colleagues [72].

**Figure 4.** Visualizations shown by using different saliency maps that provide additional insights diagnosis. Adapted from Ghoshal and Tucker [93].



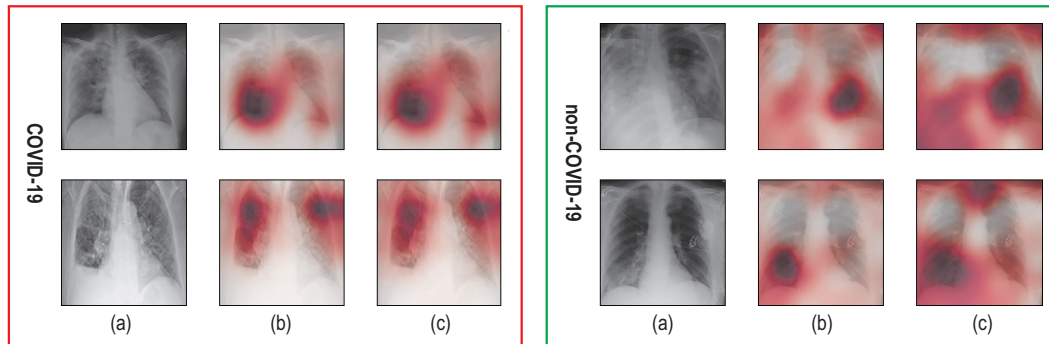
Credit/Source: Ulhaq and colleagues [11].

**Figure 5.** Diagram of the proposed model.



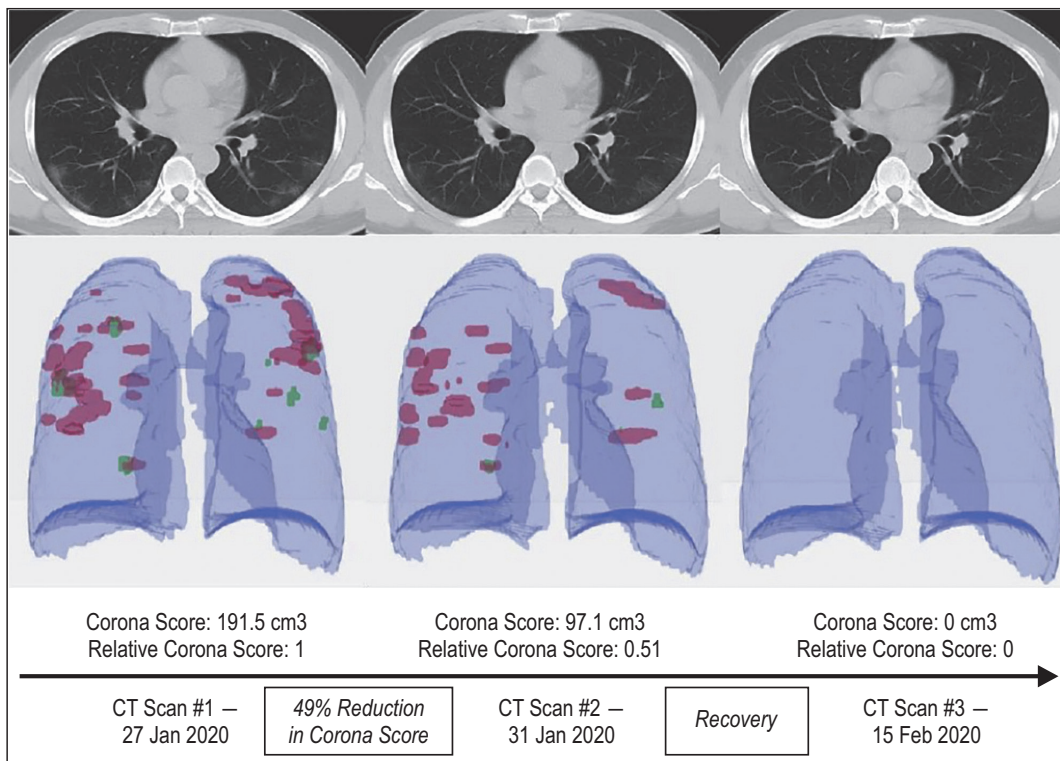
Credit/Source: Zhang and colleagues [87].

**Figure 6.** Visualization of the patients’ chest X-Ray images (a) and the corresponding Grad-CAMs obtained by this model; (b) is the Grad-CAMs obtained by the classification head and (c) in the Grad-CAMs obtained by the anomaly detection head.



Credit/Source: Zhang and colleagues [87].

**Figure 7.** Corona score that is calculated by measurements of infected areas and severity of disease from CT images. It can be used for identifying patients that are critically ill so that they get immediate medical attention. Image adapted from Gozes and colleagues [61].



Credit/Source: Ulhaq and colleagues [11].

of Shi’s study [88]. Hence, the proposed model that utilizes chest x-Rays can be recognized as an effective computer-aided diagnosis (CAD) tool for low-cost and fast COVID-19 screening [87].

According to Pham and colleagues [49], the AI is applicable in this pandemic in the detection

and diagnosis, identification, prediction, as well as pharmacotherapy, among other areas of healthcare. They observed that the AI-based framework is highly suitable for mitigating the impact and effect of the COVID-19 pandemic as an amount of credible COVID-19 data is becoming available.

**Table 4.** Studies of chest CT and AI (Figure 7).

Studies	Results
Li and colleagues [74]	The authors developed a deep learning model (COVNet) to extract visual features from chest CT for detection of COVID-19. They used visual features to distinguish between community acquired pneumonia and other nonpneumonia lung diseases. However, COVNet is unable to categorize the severity of this disease.
Gozes and colleagues [61]	The authors developed an artificial intelligence-based CT analysis tool for detecting and quantification of COVID-19. The system extracted slice of opacities in the lungs automatically. The developed system achieved 98.2% sensitivity and 92.2% specificity. The output of system provides quantitative opacity measure and 3D volume display for opacities. The system is robust against pixel spacing and slice thickness.
Shan and colleagues [75]	The authors developed a deep learning-based system named VB-net for automatic segmentation of all the lung and infection sites using chest CT.
Xu and colleagues [76]	The authors developed a prediction model to discriminate COVID-19 pneumonia and influenza-A viral pneumonia using deep learning techniques. The CNN model was used for prediction. The maximum accuracy obtained from prediction model was 86.7%.
Wang and colleagues [9]	The authors investigated the radiographic changes in CT images of infected patients. They developed a deep learning-based prediction model that utilizes the modified inception transfer learning technique. The features are extracted from CT images for prior diagnosis. The accuracy of 89.5% obtained from this method is better than Xu's model [76] and saved time for diagnosis.
Narin and colleagues [77]	The authors proposed an automatic deep convolution neural network– based transfer models for prediction of COVID-19 in chest X-ray images. They used InceptionV3, Inception-ResNetV2, and ResNet50 models for better prediction. The ResNet50 pre-trained model produced accuracy of 98%, which is higher than Xu and Wang studies [9, 76].
Sethy and colleagues [78]	The authors developed a deep learning model for detecting COVID-19 from X-ray images. They extracted deep features and transferred them to support vector machine for classification. The accuracy of 95.38% obtained from the proposed model, which is better than Xu and Wang studies [9, 76].
Chen and colleagues [79]	The authors found sensitivity of 100%, specificity of 93.55%, accuracy of 95.24%, from the platform UNet++ to extract valid areas in CT images (46,096 CT images) using 289 randomly selected CT images.
Song and colleagues [80]	The authors used neural networkDRENet + ResNet50 [81], with Feature Pyramid Network (FPN)+ Attention module, with 777 CT images and results of AUC of 0.99 and recall (sensitivity) of 0.93. Accuracy of 0.86 and F-Score 0.87.
Jin and colleagues [81]	The authors used 2D CNN based AI system, model name is not specified with 970 CT with accuracy of 94.98%, an area under the receiver operating characteristic curve (AUC) of 97.91%.
Zheng and colleagues [82]	The authors used Zheng [65] 3D deep convolutional neural Network to Detect COVID-19 (DeCoVNet) from CT volumes, obtained d 0.959 ROC AUC and 0.976 PR AUC.

So, AI studies are not executed at a large scale, but they are still helpful as they can provide rapid response and meaningful information to medical staff and policymakers. However, it is still a big challenge to design AI algorithms with the current quality and quantity of COVID-19 datasets. These issues should be resolved with time, but not without constant effort from the research communities and the help from official organizations with more reliable and high-quality data.

In order to create an algorithm or a platform for AI, it is crucial to have a deep understanding of the disease (pathogenesis, genetics, the behavior of the disease, transmissibility, risk groups) and to have collected credible data. AIs need high-quality input data in order to have good results in a pandemic. It is important to point out that, regarding imaging methods (CT and x-Ray), AI is a powerful tool for radiologists, but still, it is not completely reliable by itself.



**Table 5.** Representative work for X-Ray based COVID-19 diagnosis.

Study	Results
Guszt'av Ga'al and colleagues [89]	The authors used 247 images with the model Attention U-Net+ adversarial+ Contrast Limited Adaptive Histogram Equalization (CLAHE) [90] with a performance of DSC of 97.5% on the JSRT dataset.
Abbas and colleagues [35]	The authors used CNN features of pre-trained models on ImageNet and ResNet+ Decompose, Transfer, and Compose (DeTraC), for the classification of COVID-19 chest X-Ray images from Japanese Society of Radiological Technology (JSRT) + Cohen JP. COVID-19 image data collection with a performance of a high accuracy of 95.12% (with a sensitivity of 97.91%, a specificity of 91.87%, and a precision of 93.36%).
Narin and colleagues [77]	The authors used the model pre-trained ResNet50 with transfer learning with an accuracy of 97% for InceptionV3 and 87% of accuracy for Inception-ResNetV2 (Images from The open source GitHub repository shared by Dr. Joseph Cohen+ Chest X-Ray Images (Pneumonia) <a href="https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia">https://www.kaggle.com/paultimothymooney/chest-xray-pneumonia</a> ).
Wang and colleagues [36]	The authors used the model COVID-Net: lightweight residual projection expansion projection-extension (PEPX) design pattern, with 16,756 chest radiography images across 13,645 patient cases from COVIDx dataset, with a performance of 92.4% of accuracy on COVIDx dataset.
Asnaoui and colleagues [91]	The authors used the fine-tuned versions of VGG16, VGG19, DenseNet201, Inception-ResNet-V2, Inception-V3, Resnet50, MobileNet-V2 and Xception with 5856 images (4,273 pneumonia and 1,583 normal), with the following performance: Resnet50, MobileNet-V2 and Inception-Resnet-V2 show highly satisfactory performance with accuracy (more than 96%).
Sethy and colleagues [78]	The authors used Deepfeatures from Resnet50 + SVM classification and Data available in the repository of GitHub, Kaggle and Open-i as per their validated X-ray images with a following performance: resnet50 plus SVM achieved accuracy, FPR, F1 score, MCC and Kappa are 95.38%, 95.52%, 91.41% and 90.76%, respectively.
Apostolopoulos and colleagues [92]	The authors used various fine-tune models: VGG19, MobileNet, Inception, Inception Resnet V2, Xception (1427 X-Ray images) and the performance was: accuracy with Xception was the highest, 95.57, sensitivity of 0.08 and specificity of 99.99.
Ghoshal and Tucker [93]	The authors used dropweights based Bayesian Convolutional Neural Networks (BCNN) (total of 5,941 PA chest radiography images across 4 classes (Normal: 1,583, Bacterial Pneumonia: 2,786, non-COVID-19 Viral Pneumonia: 1,504, and COVID-19: 68) and a performance of 88.39% accuracy with BCNN.
Farooq and Hafeez [94]	The authors used 3-step technique to fine-tune a pre-trained ResNet-50 architecture to improve model performance (COVIDx dataset image) with an accuracy of 96.23% (on all the classes) on the COVIDx dataset.

### Big Data (Figure 8)

In Pham and colleagues' study, [49], they reviewed the emerging literature about Big Data and found that big data plays an important role in combating the COVID-19 pandemic through many promising applications, including outbreak prediction (Table 6) (Figures 9 and 10), the virus spread tracking, coronavirus diagnosis/treatment, and vaccine/drug discovery (Figure 11). Big data potentially allows outbreak prediction on the global scope using data analytic tools on large

datasets collected from available sources such as health organizations (e.g. WHO), and healthcare institutes [95, 96]. Big data has also appeared to be a hopeful solution for coronavirus spread tracking by linking intelligent tools such as ML and DL [97] for developing prediction models, which could be extremely useful for governments in controlling the potential COVID-19 outbreak in the future. Furthermore, big data has the potential to help COVID-19 diagnosis and treatment processes. The investigation results from the literature studies show that big data can improve

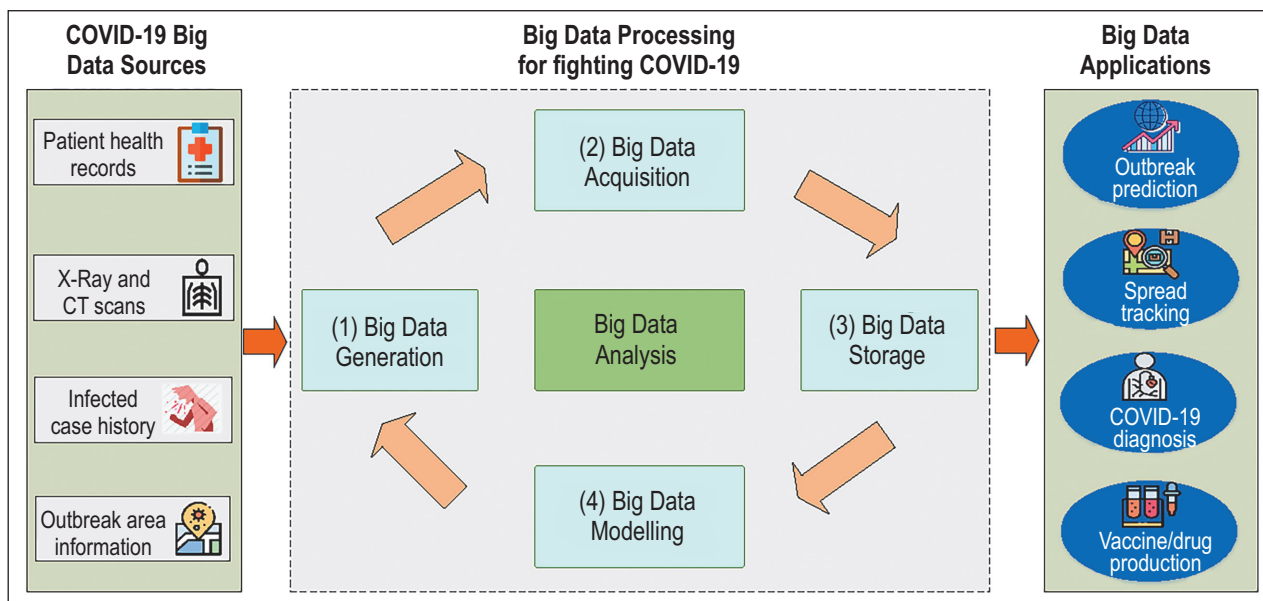
many medical procedures from early diagnosis, disease analysis, and prediction of treatment outcomes [98, 99]. Finally, data learning from big datasets also aids to discover potential targets for an effective vaccine against SARS-CoV-2 [100], and combining large-scale knowledge graphs, literature, and transcriptome data, helping to identify potential drug candidates against SARS-CoV-2 [101].

**BDA, AI, and TT**

According to Brohi and colleagues [34], the Big Data Analytics (BDA) systems integrated with AI and TT can be used to perceive swift insights and undertake proactive decisions to encounter COVID-19 by extracting and analyzing data from sources such as hospitals, clinics, insurance, immigration, and national databases, travel history, and location-tracking applications. BDA systems are capable to classify individuals and communities in many categories of risk. For example, high-risk patients, such as those that came from a country with a high rate of virus spread, can be tracked down to be quarantined quickly and undergo

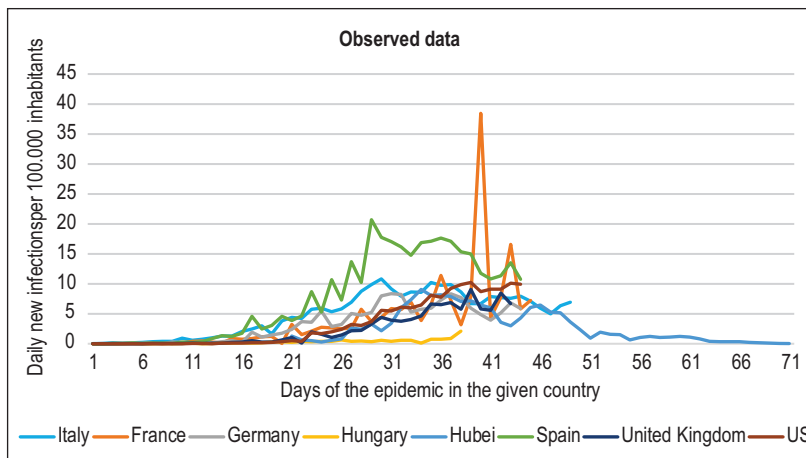
health screening. Similarly, the authorities can “urge the low and medium risk patients such as those who have recently visited COVID-19 high-risk countries or been in potential contact with COVID-19 positive patient but are asymptomatic, to practice self-isolation”. These types of interventions due to insights provided by BDA systems have the potential to reduce the weight on healthcare practitioners and control the spread of disease. Using BDA, authorities can conceive prescription models, simulate and investigate their impacts before implementation in real-life situations. Furthermore, real-time trackers such as the COVID-19 map of Johns Hopkins University, are examining enormous datasets and updating the number of deaths and cases. The information produced by the trackers could be applied to predict the COVID-19 curve and might allow insight for decisions regarding public safety and economic stability. BDA tools are also used by scientists worldwide to produce an anti-viral drug and vaccine in the combat against SARS-CoV-2. Some notable contributions and applications of BDA to mitigate COVID-19 are described in Wang and colleagues [116] and Balilla’s studies [117].

**Figure 8.** Big data and its applications for fighting COVID-19 pandemic.



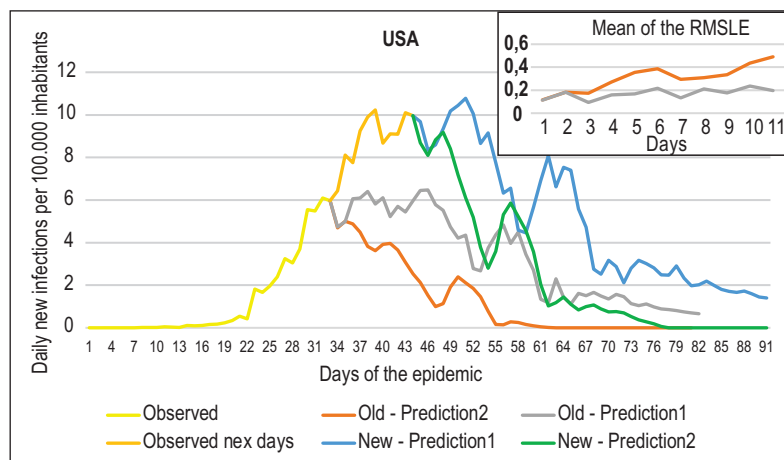
Credit/Source: Pham and colleagues [49].

**Figure 9.** The historical datasets from different countries (use of AI-based RNN).



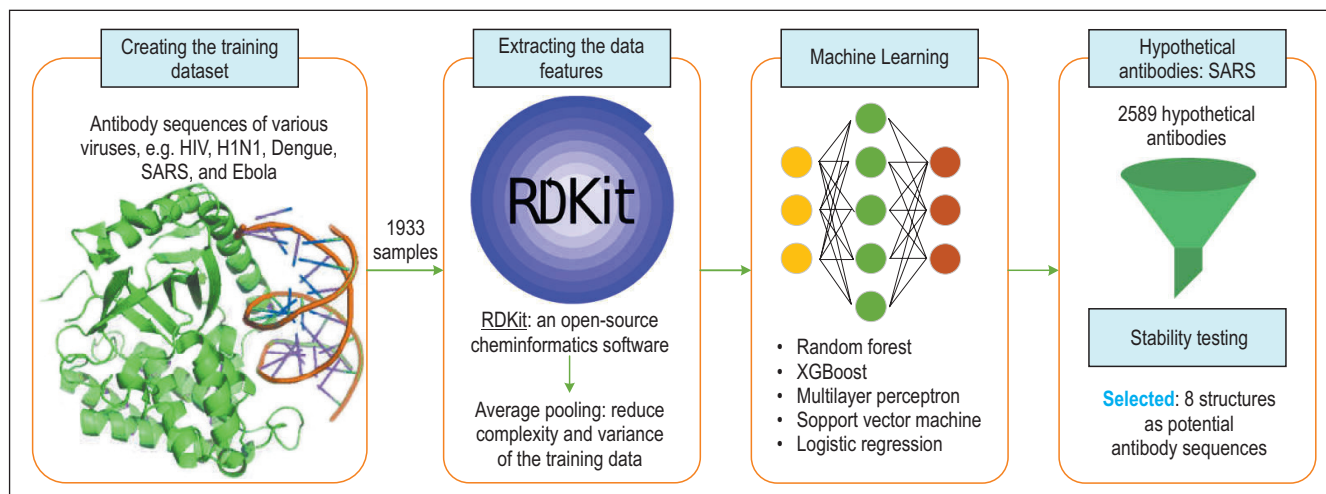
Credit/Source: Kolozsvári and colleagues [114].

**Figure 10.** Observation and predictions for the United States of America (USA).



Credit/Source: Kolozsvári and colleagues [114].

**Figure 11.** Illustration of a data-driven framework for discovering antibody sequences to treat the COVID-19 disease [115].



Credit/Source: Pham and colleagues [49].

**Table 6.** Summary of the state-of-the-art studies on big data applications for COVID-19.

Subjects	Contributions	References
Outbreak prediction	A big data platform is proposed to estimate the outbreak possibility using the huge data sets from Italian Civil Protection sources. The first trial is implemented in Wuhan to predict the population infected with COVID-19 for quarantine	[102]
	A big data-based solution is proposed to implement pandemic modeling to interpret the cumulative numbers of infected people, recovered cases in different regions, i.e., Wuhan, Beijing, and Shanghai. This scheme is able to predict the tendency of the COVID-19 outbreak in the areas at high risks of pandemic.	[103]
	A framework is introduced using a large dataset from various regions and countries such as Korea, China, to estimate the pandemic based on a logistic model that can adjudge the reliability of the predictions.	[104]
	A big data analytic method is investigated in the US with the large-scale datasets collected from American cities. The approach enables to calculate prediction errors to optimize the data modeling model for improving stimation accuracy	[105]
Virus spread tracking	A big data-based analytic methodology for tracking the COVID-19 spread is considered using a large dataset collected from China National Health Commission with 854,424 people. The analytic results show a high correlation between the positive infection cases and the population size.	[106]
	A big data-based analytic model is built using datasets collected from China, Singapore, South Korea, and Italy for virus spread tracking. This model can estimate the maximum number of infected patients in a certain área.	[99]
	A temperature-based model is proposed to evaluate the relationship between the number of infected cases and the average temperature in different countries necessary for coronavirus tracking.	[107]
	A big data-based unsupervised model is designed for COVID-19 spread tracking from online data by incorporating a basic news media coverage metric associated with confirmed COVID-19 cases. The work is in progress for coronavirus tracking tasks.	[108]
Coronavirus diagnosis/treatment	A robust, sensitive, specific and highly quantitative solution based on multiplex polymerase chain reactions is proposed to diagnose the SARS-CoV-2. The proposed scheme has been shown to be an efficient and low-cost method to diagnose Plasmodium falciparum infections.	[109]
	A method is proposed using 6381 proteins in human cells that get infected with COVID-19 virus. This aims to analyze the data gathered from the Kyoto Genes storage to serve COVID-19 diagnosis.	[100]
	An array of clinical tests have been implemented from the big dataset, from Typical and Atypical CT/X-Ray imaging manifestation to hematology examination and detection of pathogens in the respiratory tract. These tests provide a comprehensive guideline with useful tools to serve the diagnosis and treatment of COVID-19.	[110]
Vaccine/drug discovery	A method is proposed to investigate the spike proteins of SARS-CoV, MERS-CoV and SARS-CoV-2 and four other earlier out-breaking human coronavirus strains. It enables critical screening of the spike sequence and structure from SARS-CoV-2 for vaccine development.	[111]
	A project is built using a huge dataset collected from the National Center of Biotechnology Information for facilitating vaccine production. Different peptides were proposed for developing a new vaccine against COVID-19.	[112]
	A solution is proposed based on molecular docking for drug investigations with over 2500 small molecules, which aims prompting drug repositioning against COVID-19.	[113]

Credit/Source: Pham and colleagues [49].

## High-Performance Computing

Directing the issues that originate from COVID-19 demanded research contributions in areas such as bioinformatics, epidemiology, and molecular modeling, and these fields need platforms with the large computational capacity to address complex scientific obstacles and process big datasets in short timeframes. To promote the developments, the White House Office of Science and Technology Policy, the U.S. Department of Energy, and IBM developed the COVID-19 HPC Consortium consisting of the federal government, academia, and industry leaders who are offering free compute time and resources on their world-class machines [118]. Some of the consortium partners include IBM, Hewlett Packard Enterprise, Microsoft, Amazon Web Services, AMD, Google Cloud, NVIDIA, Massachusetts Institute of Technology, Rensselaer Polytechnic Institute, University of Illinois, the University of Texas at Austin, Argonne National Laboratory, Lawrence Livermore National Laboratory, San Diego Supercomputer Center and NASA. “Researchers can submit their proposals to the consortium to access small clusters and some of the largest supercomputers in the world. HPC can be utilized in genome sequencing, understanding the accurate biological structure of the virus, and modeling various treatments” (Figures 12-14). AI-driven HPC platforms can be used to discover appropriate anti-viral drugs and vaccines for COVID-19. The papers from Smith and colleagues and UCL 2020 [119, 120] have discussed the use of HPC infrastructures with supercomputers to tackle COVID-19.

## Blockchain

Blockchain applications own the potential to control disease outbreaks over time by producing ‘ledgers’ that are both secure and updated hundreds of times per day. Also, using blockchain can promote diagnostic accuracy and treatment effectiveness, streamline the fast

isolation of groups of cases, follow drug supply chains and medical supplies, control medical data, and recognize disease symptom patterns. In cases such as a virus outbreak, “blockchain can reduce uncertainty and offer computational trust, and an automated platform for recording and exchanging consistent factual information between multiple parties”, as recently published by the Scientific Foresight Unit (STOA) of the European Parliamentary Research Service [16].

## Lab-on-a-Chip

Microfluidic chips, also known as “Lab on a chip”, are versatile and promising technology [121-125] that can integrate sample preparation, reactions, and detection on a micron-scale chip [126-129]. This advanced technology has both integrated and miniaturized characteristics, which can integrate a traditional laboratory into a small chip. The microfluidic technology detects viruses efficiently in real-time (reportedly 5 min) and accurately (as low as 1 copy), with few steps and no need for professional skills (Figure 15). This technology is also well-suited in Point of Care Testing (POCT) for viral detection [130]. Zhuang and colleagues [27] summarized the current shortcomings of microfluidics (“Lab on a Chip”) in viral detection and proposes ideas for future developments. They presented the performance of microfluidics in virus detection over recent years (Figures 16 and 17).

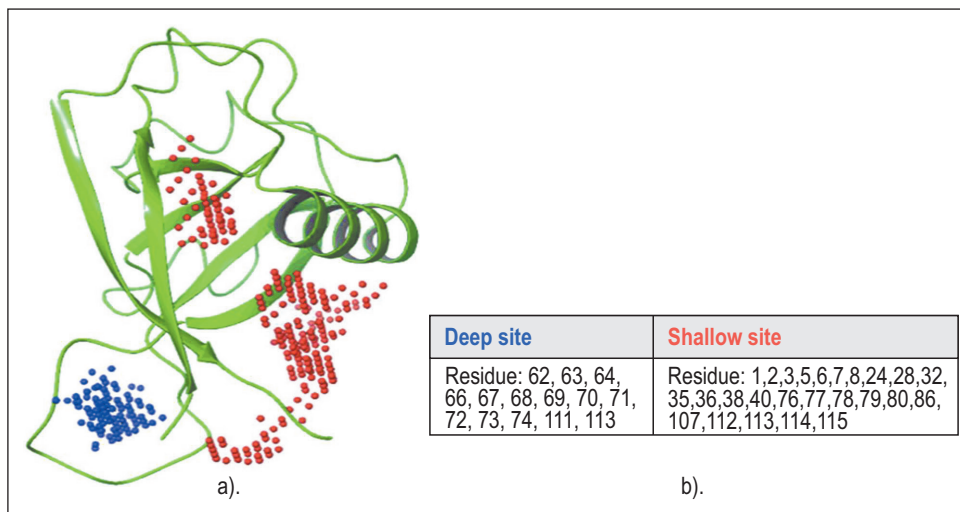
According to Zhuang and colleagues [27] and Knop and colleagues [131], for Covid-2019 detection, the RT-PCR is the gold-standard method. However, the rapid development of the epidemic requires faster and more efficient tests. So, POC instruments such as microfluidic technology play an important role in diagnosing the virus during this epidemic. In their review [27], they found (among others) the ID NOW® instrument (Abbott™) that can detect positive samples in 5 min and negative results in 13 min, and had its emergency use authorized in the US by U.S. Food and Drug Administration (FDA).

**Figure 12.** Sequence analysis COVID-19 (Wuhan-Hu-1) Nsp1.

Wuhan-Hu-1	MESLVPGFNEKTHVQLSLPVLQVRDVLVRGFGDSVEVLSEARQHLKDGTCGLVEVEKGV	60
SARS	MESLVLGVNEKTHVQLSLPVLQVRDVLVRGFGDSVEEALSEAREHLKNGTCGLVELEKGV	60
Wuhan-Hu-1	LPQLEQPYVFIKRS DARTAPHGHV MVELVAELEGIQYGRSGETLGVLPVPHVGEIPVAYRK	120
SARS	LPQLEQPYVFIKRS DALSTNHGHKVV ELVAEMDGIQYGRSGITLGVLPVPHVGETPIAYRN	120
Wuhan-Hu-1	VLLRKNGNKGAGGHSYGADLKSFDLGDDELGTDPEYDFQENWNTKHSSGVTRELMRELNGG	180
SARS	VLLRKNGNKGAGGHSYGIDLKSYDLGDDELGTDPIEDYEQNWNTKHSGSALRELRELNGG	180

The Figure represents alignment between Wuhan-Hu-1 Nsp1 and SARS Nsp1 protein sequence. Red highlights consensus sequences whereas Blue highlights differences in amino-acid sequence. Important residues shown to play a role in affecting host gene expression and anti-viral signaling are highlighted in green and pink color. Green highlighting similar residues whereas Pink highlighting residues that are different in COVID-19. Credit/Source: Sharma and colleagues [28].

**Figure 13.** Model of COVID-19 (Wuhan-Hu-1) Nsp1 with Deep and shallow binding site predicted by SiteMap.

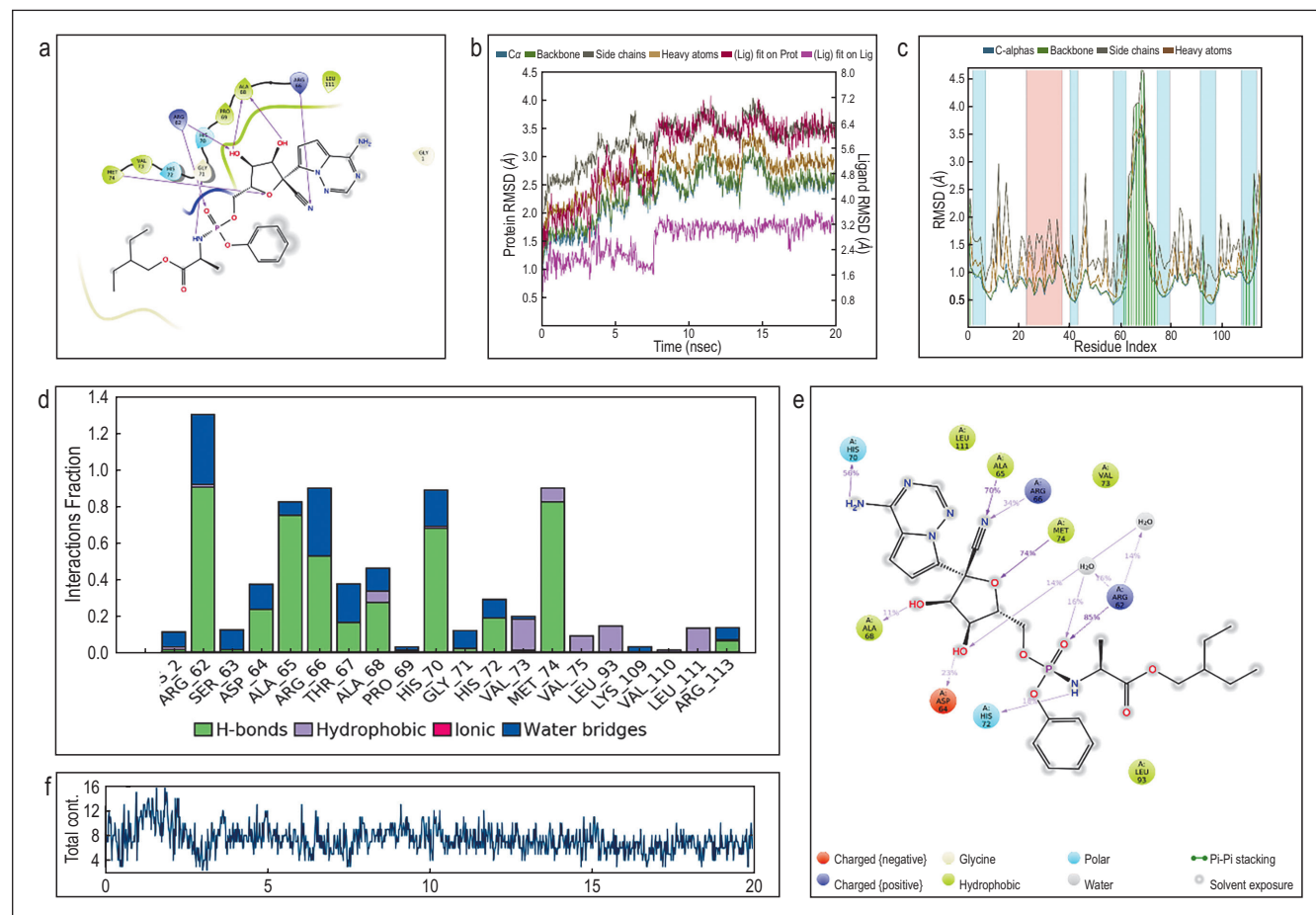


a. Represent COVID-19 Nsp1 model derived using Modeller 9.22, using 2hsx as a template. Red dot represents Shallow binding site consisting region of alpha-helix and beta-sheets. Blue dots represent deep binding site present in mostly loop region. b. Represents residues present in deep and shallow binding site respectively. Residue numbers are as per the structural model (Residue 1 of structure is residue 12 in the sequence) Credit/Source: Sharma and colleagues [28].

Also Filmarray® (BioFire™), which integrates nucleic acid extraction, purification, and PCR amplification into a single chip, resulting in sequential and accurate detection; GeneXpert® (by Cepheid™; approved by the FDA in the US for COVID-19), which works integrating sample preparation, nucleic acid amplification, and detection into a small detection kit; RTisochip® (CapitalBio™) in China, which can detect 6 common respiratory viruses (influenza) including COVID-19 in a single chip within 1.5 h; And

Cannon™, developed in Japan, which that can detect the SARS-CoV-2 in 35 min.

Such advanced technology in POC is bound to change current medical methods. Countries like the USA, China, and Japan, have approved their use, fully demonstrating the application value of the lab on a chip in POC. The authors also point out the challenges that microfluidic chips have yet to overcome when it comes to virus detection, “such as sample preparation integration, quantitative methods, the ability to perform throughput and

**Figure 14.** Docking and MD simulation results for Nsp1-deep-Remdesivir.

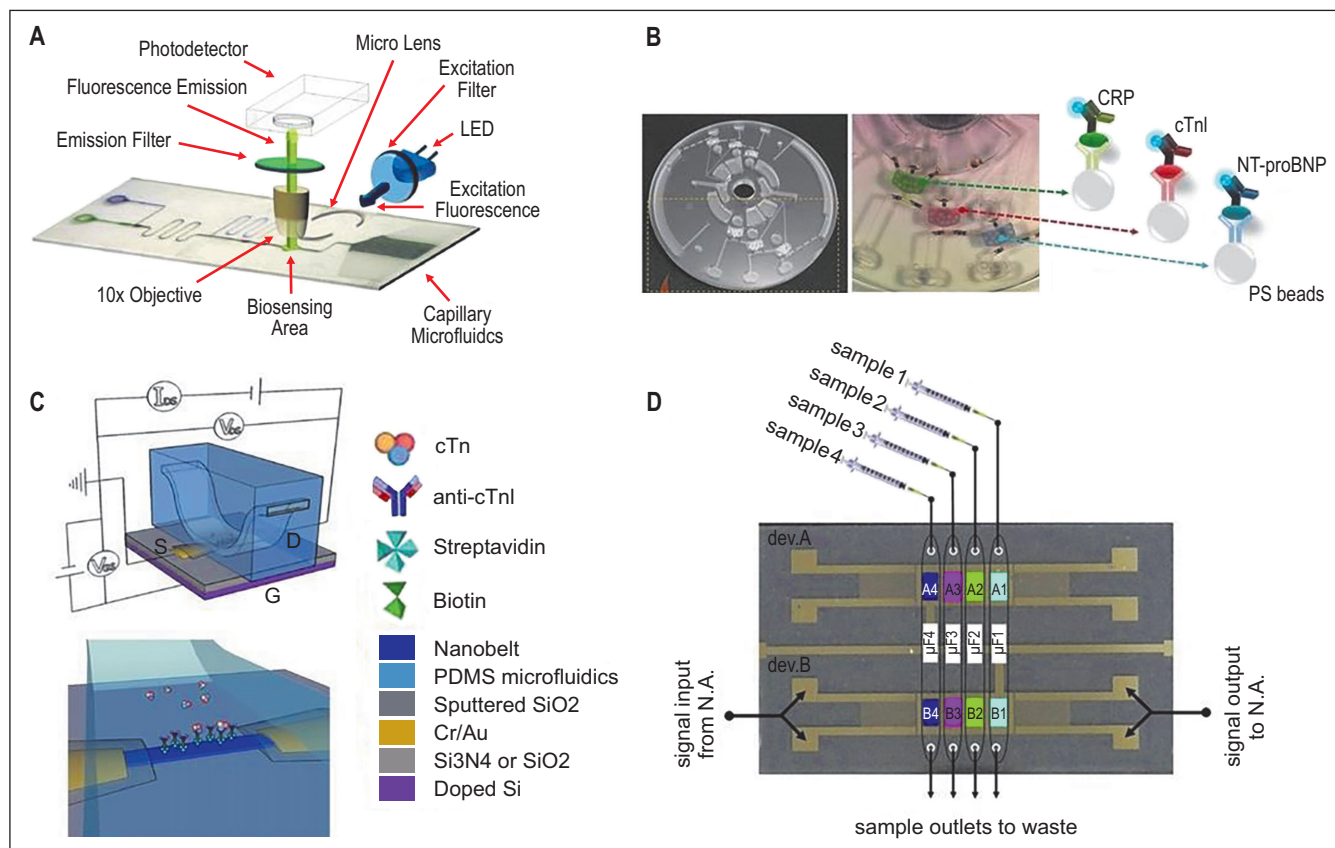
a. Remdesivir -Nsp1 interactions after XP docking b. Interaction types and Interacting residues of Nsp1 with Remdesivir over simulation time. Normalized stacked bars indicate the fraction of simulation time for which a particular type of interaction was maintained. Values more than 1.0 suggest that the residue forms multiple interactions of same subtype with ligand (Remdesivir) c. RMSD plot of Nsp1 and Remdesivir. d. Nsp1-RMSF plot e. Interaction of Remdesivir atoms with Nsp1 residues along with types and duration of interactions. Interactions that persist for more than 10% of simulation time have been shown. If a residue forms multiple interaction of same type with the same atom of ligand then that residue can have more than 100% interaction. Total number of contacts (H-bonds, Water bridges, Hydrophobic, Ionic) between Nsp1 and Remdesivir over the course of MD simulation. Credit/Source: Sharma and colleagues [28].

multiplex during a virus outbreak. The material and design of microfluidic chips, the innovation of detection methods, and the miniaturization of instruments” [27] also need to be improved. If used in association with the Biological mobile phone, Mobile detection station, or Artificial Intelligence, the potential for virus detection is greatly enhanced. In the future, microfluidic products that meet the criteria for POC proposed by WHO (which are: being affordable to those at risk of infection, containing high sensitivity, high

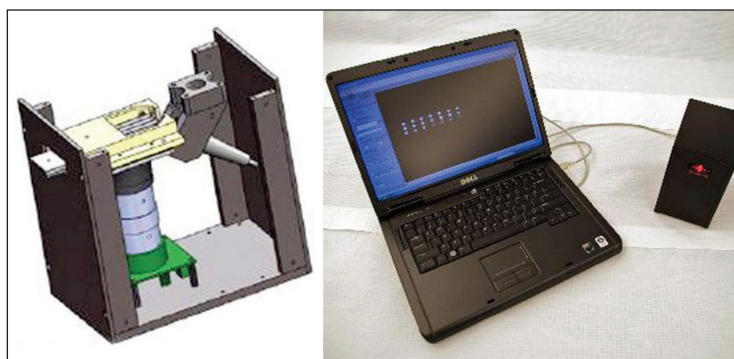
specificity, user- friendly capabilities, being rapid and robust, equipment-free, and delivered to those who need it) will be widely available.

### 3D Printing Technology

According to Brohi and colleagues [34], the rapidly expanding daily curve of COVID-19 cases has made it a challenge for countries to meet equipment demand. There is a worrying shortage of medical devices and Personal Protective Equipment (PPE)

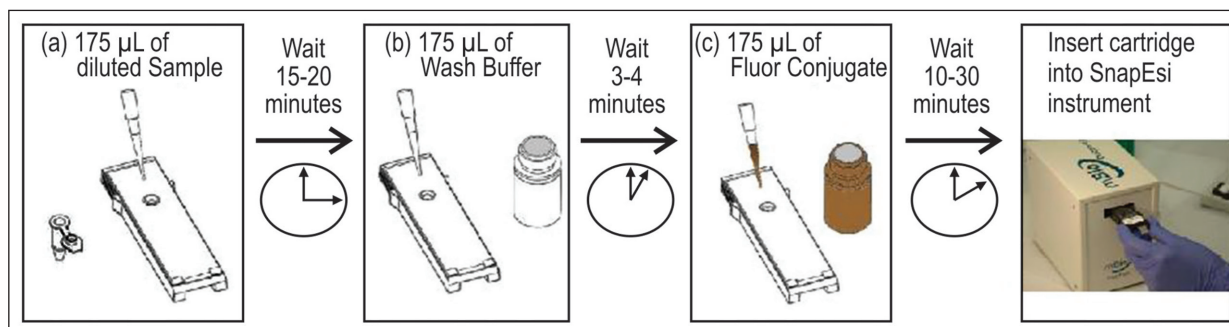
**Figure 15.** Examples of LoC-based platforms for CVD biomarker detection.

(A) An autonomous capillary microfluidic platform with embedded optics for troponin I detection [133]; (B) a lab-on-a-disc platform for fully integrated multiplex cardiac marker immunoassays [134]; (C) functionalized SnO<sub>2</sub> nanobelt field-effect transistor sensors for label-free detection of cardiac troponin [135]; (D) detection of multiple cardiac markers with an integrated acoustic platform for cardiovascular risk assessment [136]. Figure A is reprinted from Mohammed et al., Autonomous capillary microfluidic system with embedded optics for improved troponin I cardiac biomarker detection, *Biosens. Bioelectron.*, 61, 478–484, Copyright (2014), with permission from Elsevier; Figure B is reprinted with permission from Park et al., Lab-on-a-Disc for Fully Integrated Multiplex Immunoassays. *Anal. Chem.* 2012, 84, (5), 2133–2140. Copyright (2012) American Chemical Society; Figure C is reprinted from Cheng et al., Functionalized SnO<sub>2</sub> nanobelt field-effect transistor sensors for label-free detection of cardiac troponin, *Biosens. Bioelectron.*, 26, 4538–4544, Copyright (2011), with permission from Elsevier; Figure D is reprinted from Mitsakakis et al., Detection of multiple cardiac markers with an integrated acoustic platform for cardiovascular risk assessment, *Anal. Chim. Acta*, 699, 1–5, Copyright (2011), with permission from Elsevier. Credit/Source: Wu and colleagues [132].

**Figure 16.** Biochip and biochip reader model for PPC/mBio Inc. (USA)

Credit/Source: Knop and colleagues [131].



**Figure 17.** Biochip protocol (steps).

Credit/Source: Knop and colleagues [131].

for frontline healthcare professionals. During this pandemic, 3DPT has the potential to save lives. The companies of 3DPT can design items such as face shields, face masks, test kit swabs, reusable filter masks, ventilators, oxygen masks, and other medical devices quickly. Further, the simple productions of 3DPT, such as Hands-Free Door Openers and Press Knobs, could inhibit the spread of infectious diseases such as COVID-19. For medical equipment, the FDA has released FAQs on the use of 3D printed PPE to counter COVID-19 in the country. Companies have since then massively used 3DPT to create and provide equipment to hospitals. However, the FDA has indicated technical challenges that need to be addressed for 3DPT invented PPE to be valid. For example, 3D-printed PPE may provide a physical barrier, but 3D-printed PPE is improbable to provide the same fluid barrier and air filtration protection as FDA-cleared surgical masks and N95 respirators [137]. According to Kritikos' research (representing STOA) [11], the significant benefit of this technique is that components that are needed in small quantities "can be produced at a low cost, as only one type of manufacturing machine is needed and the blueprints for designs, computer-aided design (CAD) files, can be distributed or replicated at the cost of locally-sourced materials". Due to its accessibility, tangible design, and product testing and flexibility, 3D printing becomes relevant when the supply chains of critical products are strained, such as in this pandemic where hospitals and healthcare systems around the

world are facing serious deficiencies of protective equipment medical supplies. 3D printing can represent an important role in providing vital equipment when it is hard to source [11, 16]. For example, a group of Italian volunteers utilized their 3D printer to make unofficial copies of a patented valve, because it was missing at Italian hospitals, and they distributed them to a hospital in Brescia where 250 coronavirus patients required breathing machines. In addition, many companies in the US turned their 3D-printer business into a manufacturing place for face shields to be used by health workers that were performing the tests for COVID-19. Meantime, 3D manufacturers around the world are developing 3D-printed face shields, inspired by the 3Dprinted N95 mask to filter out airborne particles that could carry the virus. And, more than 5,000 pairs of 3D printed safety goggles for medical professionals were created, fabricated, and donated in China to Chinese hospitals in just two weeks [11, 16].

### Telecommunication Technology

Lockdown policies were the go-to procedure in several countries in attempts to flatten the curve and contain COVID-19. Although lockdowns have severe impacts on the economy and business, it seems to be an effective process to reduce the casualties caused by the disease. Brohi and colleagues' research [34] considers Telecommunication Technologies a tool to track individuals and assist authorities to ensure

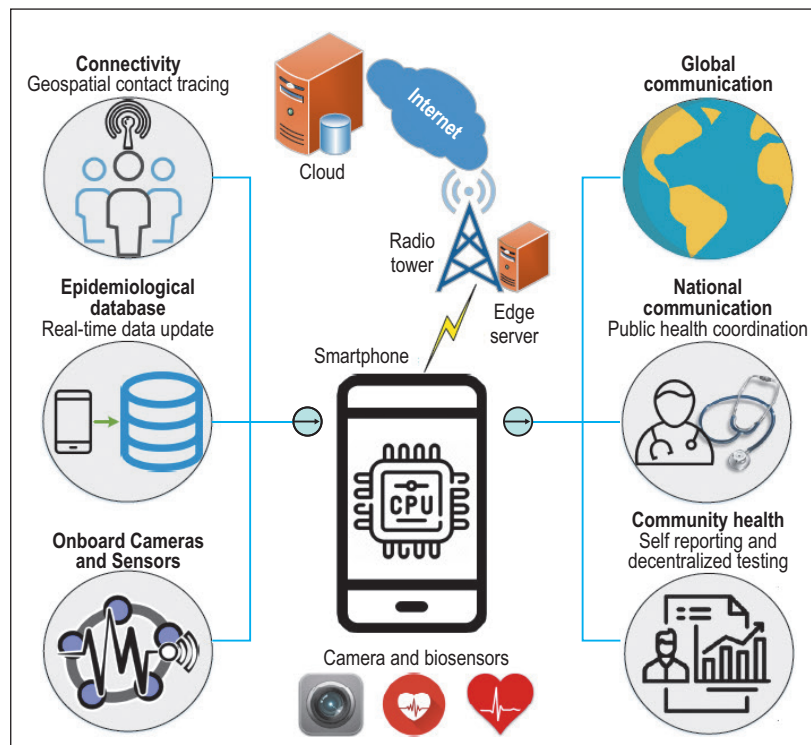
compliance with strict movement orders. It is possible to warn people from visiting COVID-19 hotspots with location-tracking applications, AI, and BDA. Healthcare providers can adopt mobile technology to assess patients with mild symptoms remotely and give them guidelines during the period of self-isolation to reduce the crowd on hospitals [11, 34]. With the union of AI and 5G technology, medical robots can monitor patients' temperature, diagnose and give them recommendations with minimal intervention of healthcare workers. TT played an important role in business continuity during this pandemic. TT has also made a pivotal role in commercial business in ordering necessary items while maintaining social distance and complying with movement control orders to stay indoors. During this pandemic, many telecommunication companies have decided to implement free services to their consumers (Figure 18) [138, 139]. Companies are complying with the Work from Home (WFH) model and managing their business, interacting with their employees

using services such as Microsoft Teams, Zoom, and Skype.

### Issues with the Use of AI and Big Data against COVID-19

According to Naudé [140] and Pham and colleagues [49], there is a critical difficulty to make AI and big data platforms and their applicability a trustful solution in the fight against COVID-19: a lack of standard datasets. Several AI algorithms and big data platforms have been suggested, but they are not experimented with using the same dataset. Moreover, most datasets found in the literature have been created thanks to individual efforts, e.g., the authors obtain some datasets accessible on the Internet, then consolidate them to produce their dataset and evaluate their proposed algorithms. To win this challenge, the government, health organizations (e.g., WHO and CDC), and giant firms represent a pivotal role as they can collaboratively work

**Figure 18.** An AI-based framework using mobile phones for COVID-19 diagnosis and surveillance.



Credit/Source: Pham and colleagues [49].

for high-quality and big datasets. Diversity of data sources can be implemented by these entities, e.g., x-Ray, CT scans from the hospitals, personal information, satellite data, and statements from self-diagnosis apps. Adopting these datasets originated from healthcare organizations, governments, clinical labs, and patients, AI leverages intelligent analytic tools for predicting efficient and safe vaccine/drug against COVID-19, mitigating the diseases, as well as presenting a better way to socially and economical lead with the pandemic. Big data has proved its capability to tackle the COVID-19 pandemic, providing various promising solutions to help fight the COVID-19 pandemic. By combining with AI analytics, big data helps us to understand COVID-19 in terms of virus structure and disease development. It can help healthcare providers in various medical operations from early diagnosis, disease analysis to prediction of treatment outcomes. With its great potentials, the integration of AI and big data can be the key enabler for governments in fighting the potential COVID-19 outbreak in the future, according to Pham and colleagues [49]. Some recommendations that can be considered to promote COVID-19 fighting: AI and big data-based algorithms should be further optimized to enhance the accuracy and reliability of the data analytics for better COVID-19 diagnosis and treatment, and AI and big data can be used in association with other emerging technologies to offer newly effective solutions for fighting COVID-19.

## Conclusion

COVID-19 crisis is promoting the implementation of digital solutions quickly and with an impression never seen before. The list of innovative digital solutions against COVID-19 is fast-growing, especially in health devices. These new innovations include video-visits, mobile-phone applications, and “chatbots”, artificial-intelligence (AI) powered diagnostic tools, voice systems, or mobile sensors such as oxygen

monitors, smartwatches, or thermometers. A new category of digital service is inspecting people under investigation at home in quarantine and/or large-scale population monitoring. Telemedicine and remote consultation such as Zoom, Google, Microsoft Teams, and Skype, among others, have already proven to be useful at a time when access to health services for non-COVID-19 or non-acute patients is limited, not recommended, or postponed. So, it is important to maintain the new innovations and solutions offered today to implement tomorrow’s best practices and models of care and to be prepared for future pandemics.

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