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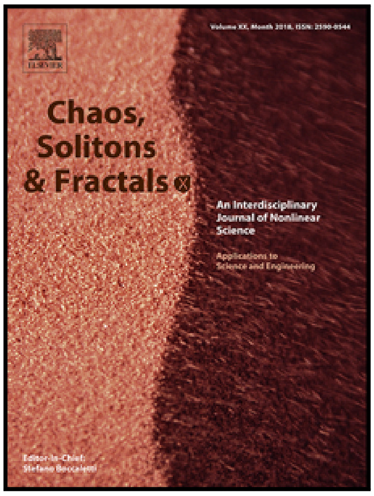

Applications of Artificial Intelligence in Battling Against Covid-19: A Literature Review

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Highlights

- A review on the applications of artificial intelligence on battling against covid-19 is performed

Applications of Artificial Intelligence in Battling Against Covid-19: A Literature Review⋆,⋆⋆

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Abstract

Colloquially known as coronavirus, the Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2), that causes CoronaVirus Disease 2019 (COVID-19), has become a matter of grave concern for every country around the world. The rapid growth of the pandemic has wreaked havoc and prompted the need for immediate reactions to curb the effects. To manage the problems, many research in a variety of area of science have started studying the issue. Artificial Intelligence is among the area of science that has found great applications in tackling the problem in many aspects. Here, we perform an overview on the applications of AI in a variety of fields including diagnosis of the disease via different types of tests and symptoms, monitoring patients, identifying severity of a patient, processing covid-19 related imaging tests, epidemiology, pharmaceutical studies, etc. The aim of this paper is to perform a comprehensive survey on the applications of AI in battling against the difficulties the outbreak has caused. Thus we cover every way that AI approaches have been employed and to cover all the research until the writing of this paper. We try organize the works in a way that overall picture is comprehensible. Such a picture, although full of details, is very helpful in understand where AI sits in current pandemonium. We also tried to conclude the paper with ideas on how the problems can be tackled in a better way and provide some suggestions for future works.

1. Introduction

Colloquially known as coronavirus, the SARS-CoV-2 that causes the COVID-19 is a contagious virus that belongs to the family of coronaviridae. The disease causes flue like symptoms including cough, fever, fatigue and shortness of breath. The main source of the virus is still under debate, but the studies on the genome sequence of the virus has determined it to belong to the group of β-CoV genera of coronavirus family which takes as host bats and rodents [1]. The virus transmits through air and physical contact, and penetrates raspitory cells by bonding to Angiotensin-converting enzyme 2 (ACE2). The most common symptoms of the virus include shortness of breath, fever, cough, loss of smell and taste, headache and muscle ache [2].

SARS-CoV-2 was first reported to be observed in Wuhan City, in China in December 2019. Since then it has continuously spread around the world. As the virus progresses, it creates a great deal of difficulties in any aspect of human life and new problems emerge as time goes by. To solve these rapidly emerging problems, new techniques are being developed every day.

Artificial Intelligence is the study and development of approaches that imitate human intelligence. The technique has been successful in a variety of fields including fraud detection, computer vision, online advertising, robotics, automatic drivers, etc. With its success in areas like disease diagnosis, treatment, patient monitoring, drug discovery, epidemiology, etc, there is a great hope that Artificial Intelligence can be a vibrant area of research to tackle the challenges [3] human faces currently. It is argued that AI will be key to supporting clinical and academic studies of covid-19 and future crises [4]. For example, at the beginning of the outbreak, China initiated a set of actions against the spread of the virus, by adopting a set of AI-based technologies. In this effort, they explored implementation of ideas like the use of facial recognition cameras to track infected people, drones to disinfect places [5], robots to deliver food and medications, etc.

There are different fields of applications for which

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AI approaches are adopted to manage the effects of the disease. We try to organize the research based on the applications. The applications include clinical applications, processing covid-19 related images, pharmaceutical studies and epidemiology. We also organize the research based on the AI approaches they have adopted. The main categorization is based on applications; however, for the same application, the research are subdivided based on the AI approaches they have employed. Examples of AI approaches include Deep learning, machine learning, Artificial Neural Networks and evolutionary algorithms.

Currently, testing to find covid-19 positive cases relies heavily on Reverse Transcription-Polymerase Chain Reaction (RT-PCR), which is time consuming and has false-negative error. Thus, developing new approaches for detecting patients at a faster rate with higher accuracy is a matter of importance. One way of detecting the patients is via CT or X-Ray images which require more easily accessible equipment. By processing these images, one can detect the patients even before they have developed symptoms like fever or coughing [6]. The image based diagnosis of covid-19 consists of three stages, i.e. 1) pre-scan preparation, 2) image acquisition and 3) disease diagnosis. Image processing and AI approaches can come to help when analyzing these images.

For several years, mathematical modelings has been used to predict the behavior of epidemics. This assists the policy makers to adopt adequate measures to curb the pandemic. AI approaches have shown to be very efficient in modeling complex systems. Since the start of the pandemic, many research have targeted the task of modeling the behavior of the pandemic. Not only modeling the epidemic, but also devising policies to curb is has also been a successful field of research in the area. In countries like Taiwan, for example, the national medical database has been infused with database from immigration and customs to build policies based on people symptoms and travel history [7].

Employing AI based approached for drug development has attracted attention since the beginning of the outbreak. The capabilities of AI in discovering new molecules has been extensively used in research.

AI approaches have long been employed for the development of diagnosis and treatment system. Now this pandemic has created a new challenge for this field of science. Developing intelligent systems that can help practitioners in terms of diagnosis, monitoring, prediction of patients conditions and offering treatment measures can be very helpful to help the already under pressure health systems.

The aim of this paper is to perform a comprehensive survey on the applications of AI in battling against the difficulties the outbreak has caused. In this sense, we tried to cover every way that AI approaches have been employed and to cover all the research until the writing of this paper. Surely this would result in covering a large number of research that are hard to put in the same canvas; nevertheless, we tried to organize the works in a way that overall picture is comprehensible. Such a picture, although full of details, is very helpful in understand where AI sits in current pandemonium. Since the pandemic is new and developing problem, many of the research have not yet been peer-reviewed. Therefore, this paper also covers pre-print works. We also tried to conclude the paper with ideas on how the problems can be tackled in a better way and provide some suggestions for future works.

1.1. Related Works

To the date of writing this paper, a number of research have tried to perform a review modern approaches in tacking the pandemic. In this section, we perform an overview on the existing works in the area. In [8], a review on the role of IoT, Drones, AI, Block-chain, and 5G in managing the pandemic is performed. In [9], a review on the current automatic CT scan image processing approaches is performed. A review on the modeling techniques for predicting the pandemic including mathematical and AI approaches is performed in [10]. In another work [11], a review of modern approaches in tackling covid-19 is presented. Another review is performed in [12], where different areas in which AI has been used are discussed. A review on Deep Transfer Learning techniques in managing the pandemic is proposed in [13]. In [14], an overview of audio, signal and speech and language processing has been performed. A review of machine learning and AI algorithms for managing the pandemic is performed in [15]. In [16] the limitations, constraints and pitfalls for application of AI in battling the disease has been over-viewed. A survey on the state-of-the-arts of application of AI and big data for the pandemic is offered in [17]. In [18, 19], an early review on the application of AI in processing chest X-Ray images is presented.

A short review of AI application for covid-19 is presented in [20, 21]. In [22, 23], a review on the potential of using AI in developing countries is performed. A review on automatic detection and forecasting of covid-19 using DNN algorithms is performed in [24]. In [25], re survey on AI-based algorithms for combating the pandemic is performed. A review on machine learning algorithms in processing medical images regarding the disease can be found in [26]. A review on AI approaches on management of covid-19 can be found in [27]. In [28], a review on data-driven methods for monitoring, modeling and forecasting the pandemic is presented. In [29], a survey on epidemic models for the disease is presented. A discussion on how big data can help better manage the pandemic is presented in [30]. In [31], a review on the data science approaches to combat the disease is presented. An overview of recent studies using machine learning in tackling the disease is presented in [32]. A review on the research on using machine learning algorithms in predicting the number of cases is presented in [33]. A review on the application of AI in discovering drugs can be found in [34]. I review is performed in [35] that covers the research on application of AI is managing critical covid-19 patients.

A review on the application of imaging characteristics and computing models applied to covid-19 related images is presented in [36]. In this work, CT positron emission tomography (PET/CT), lung ultrasound and magnetic resonance imaging (MRI) applied for detection, treatment and follow-up are studied.

In [37] some of many considerations for managing the development of AI applications including planning, unpredictable, unexpected or biased results, re-purposing, the importance of data and diversity in AI team membership is addressed. The author provide implications for research and for practice according to each of the considerations. In [38], the role of AI for detection of the patients, finding the current pandemic pattern and possibility of future relapses are discussed. In [39], it is argued that there has been a great enthusiasm in diagnosing covid-19 AI approaches. So the authors examine 14 of the studies to discover the weakness of the solutions. The authors argue that "scientific community should be careful in interpreting statements, results and conclusions regarding AI use in imaging". In [40], five of the most important challenges in responding to covid-19 are presented and it is discussed how each of them can be managed via machine learning and artificial intelligence. In [41], overviews the challenges in fighting covid-19 and presents an overview of ways in which machine learning can help in managing the disease. A review on potential technological strategical to control the pandemic is presented in [42]. In [43], a review on AI techniques in data acquisition, segmentation and diagnosis is presented. In another work [44], a review on machine and deep learning models for detecting and predicting the disease is presented. A review of Biological data mining and machine learning techniques in detecting and diagnosing the virus is presented in [45]. In [46], a review on AI approaches for covid-19 prognosis is presented.

When developing algorithms, it is important to have transparency in the model performance. In [47], a set of experiments are performed to provide a baseline performance metrics and variability for covid-19 detection via X-Ray images. The authors propose an experimental paradigm controlling for train-validation-test split and model architecture. Despite all these efforts, if AI is to be successful in managing the pandemic, a cooperation should exist among the scientists in terms of sharing knowledge, data, tools codes, etc. [48, 49].

The rest of this paper is organized as follows. In section 2 we review the clinical applications of AI algorithms. A review on the AI approaches for processing chest images of covid-19 patients is presented in section 3. In section 5 a survey on the ways in which AI has been employed to develop and study new drugs is performed. In section 7 the application of AI in studying the virus and its properties is discussed. Section 8 provides an overview on publicly available datasets. Finally, section 9 concludes the paper and suggests future directions for future works.

2. Clinical Applications

In this section we review the clinical applications of AI approaches in treating the covid-19 patients.

2.1. Treatment

One important area of application of AI in dealing with the outbreak problem are the approaches proposed for treatment of the disease. In [50] a method is proposed which analyzes the similarities and differences between treatment plans. It is very useful to predict a patient's recovery as it can assist decision makers to prioritize resources. Three machine learning techniques are used in [51] to monitor and predict the patient's recovery. The authors use SVM, regression model and ANN to build the intelligent system. In [52], the potential of AI in predicting disease progression is investigated. The authors use three machine learning algorithms and a deep learning model to build an algorithm to predict if a patient would develop severe symptoms of the disease requiring oxygen.

One problem for treating patients is the limitation in equipments like ventilator systems. In such conditions, sometimes hospitals face with the hard decision making process of choosing which patient to get access to such care. In [53], an AI based multi-criteria decision-analysis algorithm is proposed the prioritize patients based on their health conditions. The approach uses a set of information including laboratory tests.

People who have recently contracted the virus and recovered from the disease have antibodies against the corona-virus circulating in their blood. One way of treating people is the transfusion of these antibodies to patients with severe symptoms. There are two challenges in this regard. First, subjects must meed donor selection criteria and comply standard routines. Second, a multi-criteria decision making process is involved in the selection of the most suitable plasma and prioritization of patients. In [54], a machine learning algorithm is used in the decision making process.

2.2. Diagnosis

It is very important to diagnose the disease as many policy makers, including WHO suggest that testing is key to success in controlling the pandemic as it provides valuable information about small outbreaks that can be capped before they expand. The current method of testing is the RT-PCR with DNA sequencing and identification, but the method is expensive and take long to be available. Tests based on IgM/IgG antibodies have also been presented, but their sensitivity and specificity is low.

Efficiently diagnosing clinical type of covid-19 patients is essential to achieve optimal outcomes. Currently, severe and non-severe patients are differentiated by a few clinical features which do not comprehensively characterize the complicated pathological, physiological and immunological response to the disease. In some research, Artificial Intelligence techniques have been used to diagnose the disease without using RT-PCR or CT scan images.

Generic Machine Learning: In order to build a more accurate diagnosis model for covid-19 based on patient symptoms and routine test results, machine learning algorithms are used with data from 151 published studies [55]. The work reports correlation between being male and having higher levels of serum lymphocytes and neutrophils. According to this study, covid-19 patients can be clustered into subtypes based on serum levels of immune cells, gender and symptoms. The XGBoost model is used in this work which achieves sensitivity of 92.5% and specificity of 97.9%. In [56], machine learning algorithms are used to process clinical data about the patients to perform diagnosis. In order to improve the diagnosis accuracy for clinical purpose, an AI-based general diagnosis index is proposed in [57]. In [58], a machine learning algorithm is proposed that collects data from hemodialysis patients, due to kidney failure, and predict the chance of the patient having undetected covid-19 infection.

An AI algorithm is proposed in [59], that uses CT images, clinical symptoms, exposure history and laboratory testing to diagnose covid-19 cases. The authors collect data from 905 patients, of which 419 are laboratory-confirmed covid-19 positive cases. In [60], assay designs and experimental resources are proposed to be used with CRISPER-based nucleic acid detection that can be used for ongoing surveillance. The authors use machine learning algorithms to provide assay design for detection of 67 viral species and subspecies of SARS-CoV-2. In [61], random forest models are used to classify the covid-19 patients.

In [62], machine learning algorithms are used to process symptoms of patients to diagnose covid-19 patients. The symptoms are assessed by asking basic questions from the patients. Using the data from emergency care admission exams, in [63] a machine learning algorithm is used to diagnose covid-19. A research [64], analyses the underdiagnosis of covid-19 via nowcasting with machine learning in Brazil. The machine learning algorithm is used to classify cases which had no diagnosis yet, producing nowcast. In [65], an ANN is used to classify the data about the respiratory pattern of patients to identify covid-19 cases.

Ensemble Machine Learning: Ensemble of machine learning algorithms has been used in a number of works to diagnose the disease. In [66], four machine learning approaches including logistic regression, Support Vector Machine, Decision Tree and Random Forest are used to process patients data and diagnose the covid-19 cases. A number of machine learning approaches including KNN, ANN and Naive Bayes algorithms have been used in [67] to diagnose the disease. It is shown that respiratory pattern of covid-19 is different from that of common cold and flu.

Benefiting from mobile applications: Mobile phones can provide good platform for developing AI methods for diagnosis. They are widely available, they can collect a great deal of data from people from symptoms to behavior and traveling and they can inform people from any risk they may face. An AI-based algorithm which runs on the could is implemented as a mobile phone app is proposed in [68] that monitors people's cough in order to identify covid-19 cases.

Telehealth algorithms: Artificial telehealth systems are very useful during the pandemic as they can people receive the services they require from home which in turn helps curb the spread of the virus. In some work AI approaches have been used to develop artificial telehealth algorithms. In [69], a novel AI-based approach is proposed for covid-19 infection risk assessment in virtual visits. The algorithm uses a natural language processing algorithm that performs on data collected through telehealth visits. In [70], a natural language processing algorithm is proposed to provide free preliminary healthcare education, information and advise to covid-19 patients. The system provides preventive measures, homeremedies, interactive counseling sessions and healthcare tips for clients.

Deep learning algorithms: In order to accelerate the process of diagnosis and treatment of the covid-19 disease, some deep learning algorithms including Generative Adversarial Networks (GANs), Extreme Learning Machine (ELM), and Long /Short Term Memory (LSTM) are adopted in [71]. The authors argue that these approaches can put together a continuum of structured and unstructured data sources. A DNN algorithm with some machine learning algorithms are used in [72] to monitor patients and offer augmented curation. A framework called CovidDeep is proposed in [73] that combines a DNN with wearable medical sensors for pervasive testing of the virus and the disease. The algorithm does not depend on manual feature extraction and operates on the data collected from wearable device and some easy-to-answer questions in a questionnaire.

Diagnosis via blood tests: A machine learning algorithm is used in [74] to diagnose the disease using blood tests. The algorithm uses five blood parameters as features, which are MCHC, eosinophil count, albummin, INR and prothrombin activity percentage. In [75], a machine learning based method is proposed to analyze blood exams as input and find the suspect cases of covid-19. Using hematochemical values from routine blood exams, namely white blood cells counts, and the platelets, CRP, AST, ALT, GGT, ALP, LDH plasma levels as features, a machine learning algorithm is proposed in [76] to diagnose the disease. Experimental analysis suggest that the method can offer good accuracy. A random forest algorithm is used in [77] to build a classifier to diagnose the disease via 11 key blood indices. A machine learning and an ANN with a simple statistical test is used in [78], to identify covid-19 patients based on full blood counts without data from symptoms or history of the individuals.

In [79], a machine learning algorithm to perform test based on blood tests is proposed. A Naive-Bayes model is used in [80] to build a model of hemogram data taken from symptomatic patients in order to predict qRT-PCR test resutls.

In order to prescribe adequate medicine, it is important to have temporal inference from laboratory testing and their triangulation with clinical outcomes. In [81], the data of 181 covid-19 positive and 7,775 negative cases related to 1.3 million tests are studied and it is found that covid-19 patients tend to have higher plasma fibrinogen levels, low platelet counts and around 25% of patients showing outright thrombocytopenia. The data were fed to a neural network-powered extraction system for the analysis.

Diagnosis via cough: Coughing is a symptom of covid-19, the type of which can distinguish the disease from other types of diseases. Processing the cough voice signal has been studied in some research. An end-to-end portable system based on machine learning is proposed in [82] that records data from patients including coughs and use them to train a classifier for diagnosing the disease. In order to diagnose the disease via coughs and breathing, a binary machine learning classifier is used in [83].

Text Processing: A lot of data around the disease are stored in the form of text and to exploit them text processing algorithms should be adopted. In [84], an online questionnaire is developed to collect data about covid-19 patients. The data were then fed to some machine learning prediction algorithms including SVM, Logistic Regression, and MLP to predict potential covid-19 patients based on their signs and symptoms. In [85], textual clinical reports are collected and feature extraction tools like Term frequency/inverse document frequency (TF/IDF), Bag of words (BOW) and report length are used to collect data. Then Logistic Regression, Multinomial Naive Bayes are used to classify the data.

Combination of different types of data: A large variety of data can be collected from patients that all can be representative of the disease. In some work the goal has been to collect a variety of data types and process them. A diagnosis algorithm is presented in [86] which uses chest CT images. In this method, radiomics features are extracted from the region of interest and are fed to an AI segmentation algorithm. For classification, the algorithm also takes clinical symptoms, epidemiology history and biomedical results as input.

Improving DNA tests: The mainstream in diagnosing the disease is DNA identification of the virus. In order to improve the process of DNA identification, a pseudo-convolutional machine learning is proposed in [87], which divides the DNA sequence into smaller sequences with overlap. The method uses co-occurrence matrices and analyses DNA sequences obtained by the benchmark RT-PCR method which eliminates sequence alignment.

Other examples of using machine learning for diagnosis can be found in [88, 89].

2.3. Monitoring Patients

One problem in hospitals is to monitor the condition of covid-19 patients. In this section we review the works that monitor patients in order to predict their conditions.

2.3.1. Predicting Recovery and Mortality

Because of the limitations on resources, hospitals may not be able to provide monitoring, assessment and treatment services required for all patients with severe symptoms. In this respect, predicting recovery or mortality rate of a patient it very important, as this information can help hospitals to distribute the medical facilities more efficiently.

Generic machine learning algorithms: In [90], a neural network method is used to classify data collected about the patients in South Korea. The algorithm predicts the recovered and death cases in hospitals. Random forest classification algorithm is used in [91] to identify important predictors and their effect on mortality in hospitals. In [92], a fuzzy classifier is proposed for disease assessment and predicting the mortality of covid-19 patients from their biomarkers. In another work [93], a machine learning tool is developed that monitors three biomarkers that predict the mortality of individual patients more than 10 days in advance with more than 90% accuracy. A machine learning-based risk prioritization tool is used in [94] to predict the ICU transfer within 24 hour and facilitate efficient use of the resources. In order to train the machine learning algorithm, data including vital signs, nursing assessments, laboratory data and electrocardiograms were used. In [95], data of 117,000 patients world-wide are used to develop an AI method to predict the mortality risk of patients with covid-19.

Ensemble methods: In [96], five machine learning algorithms including logistic regression, support vector machine, KNN, random forest and gradient boosting algorithms are used to predict the mortality of confirmed covid-19 patients in South Korea. In [97], a machine learning approach is presented to predict the patient's recovery. The authors use support vector machine algorithm, ANN and regression model to build the model. A fine-tuned Random Forest model boosted by the AdaBoost algorithm is presented in [98] which uses patient's geographical, travel, health and demographic data to predict the severity of the cases and the possible outcome, recovery or death. In [99], five machine learning algorithms, namely logistic regression, partial least square regression, elastic net, random forest and bagged flexible discriminant analysis are used to process patients' data records and predict the mortality risk of patients. In [100, 101], a number of machine leaning approaches including KNN, random forest and SVM is used to build a model that predict the mortality of patients. In another similar attempt [102], a machine learning algorithm is used to predict mortality and critical events in New York.

Comparing the algorithms: Different algorithms perform differently on different problems. In some works, the performance of the AI algorithms are compared. In order to predict the discharge time likelihood based on the clinical data, several computational intelligence approaches are implemented and used in [103], that is performed on data records of 1182 patients. The authors argue that the Gradient Boosting survival analysis model outperforms other algorithms.

Deep learning algorithms: In order to predict the mortality of the patients, a DNN algorithm is used in [104], which gets as input a large number of clinical variables associated with the disease. The proposed system identifies top clinical variable predictors and derives a risk stratification score system to help clinicians triage COVID-19 patients.

2.3.2. Predicting Severity of a Patient

The covid-19 patients may show severe symptoms and some of the patients with severe condition may die or suffer from major organ failure. In some work, the aim has been to predict the severity of symptoms.

Using generic machine learning: In [105], multivariate logistic regression combined with a feature selection algorithm is used to identify patients who may develop severe covid-19. In [106], a framework is presented for new edge features in Graph Neural Networks via a combination of self-supervised and unsupervised learning which is then used for node classification tasks. The system is used to predict the infection and severity of the disease in patients. In [107], multivariate logistic regression and a deep learning algorithm is used to predict the probability of a patient with mild symptoms developing malignant infection. A data set of 13,690 patients in Brazil is used in [108] to build a model that predicts the poor prognosis in covid-19 patients. The authors use machine learning to build the model.

Blood test data: In [109], blood samples from 404 infected patients have been collected and machine learning techniques have been used to identify crucial predictive biomarkers of the disease severity and predict the survival of patients. The blood and urine tests of covid-19 patients are analyzed to predict the severity of disease in [110]. The authors use SVM to build a model and report that blood tests are more representative of the disease. In [111], a machine learning algorithm is used to find the risk factors for the disease. The authors report factors like blood type, vitamin D intake, smoking and obesity as major risk factors.

Voice Signal: A speech processing algorithm is proposed in [112] which analyses the speech signals of people diagnosed with covid-19 to automatically categorize the health state of patients from four aspects, including severity of illness, sleep quality, fatigue and anxiety. The work uses acoustic feature sets and support vector machines.

Clinical and laboratory data: Covid-19 patients can be detected via data from their clinical and laboratory tests. Some research have tried to study the use of AI approaches in identifying covid-19 cases via these data. Using the clinical and laboratory features obtained at admission, a machine learning algorithm is proposed in [113] which predicts if patients require mechanical ventilation or will die or survive when hospitalized. In order to evaluate the early risk assessment for patients, in [114] demographic data, physiological clinical variables and laboratory results from electronic healthcare records are extracted and used with applied multivariate logistic regression, random forest and extreme gradient boosted trees. In order to predict survival analysis and discharge time based on clinical data, some machine learning algorithms are used in [115]. The data include various features including gender, symptoms, chronic disease history and travel history. The authors use Stagewise Gradient Boosting, Componentwise Gradient Boosting, and Support Vector Machines. In [116], a XGBoost machine learning algorithm is used to predict the criticality of patients. The model uses three key clinical features, namely lactic dehydrogenase dyspnea, lymphocyte and High-sensitivity C-reactive protein from a pool of more than 300 features. In [117], 21 clinical features with significant difference between severe and nonsevere cases were analyzed and used to build a predictive model via machine learning. The data were collected from 455 patients, and 11 discriminative features were selected in training and validation set for modeling. In order to provide decision-making support for clinicians, artificial intelligence algorithms are developed in [118] to automatically identify the clinical characteristics of patients to predict which patients develop severe symptoms.

Deep learning: In [119], data from a cohort of 1590 patients from 575 medical centers are used to train a deep learning model that predicts the risk of covid-19 patients developing critical illness based on clinical characteristics.

2.3.3. Monitoring Symptoms

An AI-based smartphone application is proposed in [120], which uses different sensors including temperature, microphone, camera and color sensor to monitor people and patients. A combination of classic epidemiological methods, natural language processing and machine learning techniques is proposed in [121] to process the electronic health records of covid-19 patients. This system is then used to predict which patients require ICU admission. In [122] a machine learning algorithm is presented to assist clinical decision making during the pandemic. In [123], different machine learning models including SVM, KNN, Decision Tree, Gaussian Naive Bayesian, etc. are used to predict which age groups are mode affected by the disease.

3. Chest Computed Tomography and X-Ray Image Processing

Since early identification of patients is crucial in treating the patients and to isolate the infected patients to prevent the spread of the virus, many research put effort in developing methods that can identify patients more quickly and less costly. The standard testing system, the Reverse transcription polymerase chain reaction method is time-consuming and in short supply. This has encouraged researchers for developing alternative screening methods. The chest Computed Tomography (CT) scan and X-Ray images of the covid-19 patients provide important information about the patients. Viral pneumonia often exhibit different visual appearances on these images. In this regard, AI can come to help in processing these images [124, 125, 126].

Diagnosing covid-19 patients based in CT or X-Ray images is a classification problem which consists of several steps. First, the images of lungs are preprocessed. Then, using Convolutional Neural Networks, or other methods, the features are extracted. Finally the features are used in a classifier system to perform diagnosis. In this section we review these research.

3.1. CT Scan and Deep Neural Networks

Deep learning has recently been a vibrant area in AI. These methods have been considered as a powerful tool in automatically detecting the disease via CT scan and X-Ray images. Many of these works first employ Convolutional Neural Networks (CNN) on an already existing large-scale chest X-Ray image dataset which is then fine tuned with covid-19 datasets at a smaller scale. In many works traditional machine learning methods are employed. In this section we provide an overview on these approaches.

3.1.1. CT Scan and Deep Neural Networks Application

Cluster of viral pneumonia occurrences in a short period of time can be an indicator of an outbreak. Rapid and accurate detection of viral pneumonia can be helpful for epidemic prevention. The evolution of viruses and emergence of new mutations, results in dataset shift, which limits the performance of classifications. In order to manage this, the task of differentiating viral pneumonia from non-viral ones is formulated in [127], into a one-class anomaly detection problem. This work proposes confidence-aware anomaly detection model which consists of a feature extractor, an anomaly detection module and confidence prediction module. The authors use deep learning for the classification task.

Generic deep learning: In some works the generic version of deep neural networks without any innovation has been used to process images. In order to screen covid-19 patients, a large number of CT images (1065 cases) are used in [128] to train deep learning algorithms. In [129] a self-supervised learning mechanism guided by a super sample decomposition is proposed for deep convolutional neural networks in processing CT scan images for covid-19 detection. In [130], the CT scan images of 14,435 are used to train a deep neural network. In another work [131], 5372 patients from 7 cities in China have been studied and their CT images have been used to train a DNN. In order to establish an early screening model to identify covid-19 via CT images, a DNN algorithm is performed in [132] on 618 CT images from 110 patients. In [133], a multi-task DNN is proposed for lung infection segmentation. The algorithm starts segmenting the lung regions than can be infected and then segments the infections in these regions. Also, in order to perform a multi-class segmentation, the algorithm is trained via two-stream inputs that allows overcome shortage of labeled data.

In [134], DNN is used for detection, localization and quantification of covid-19 pneumonia. In [135], a DarkNet model is presented to identify covid-19 patients via chest X-Ray images. In [136], the YOLO predictor is used to develop a deep learning computer-aided diagnosis system that simultaneously detects and diagnoses covid-19 among eight other lung diseases.

New deep neural networks: In some works, new versions of deep neural networks are developed to classify CT or X-Ray images. In [137], a new deep neural network algorithm called convolutioanal support estimator network is used for detecting covid-19 patients. In [138], an Attention-based Deep 3D Multiple Instance Learning (AD3D-MIL) approach is used for a DNN to process the CTscan images. This method is capable of semantically generating 3D instances of the CT scan images. It learns Bernoulli distribution of the bag-level labels for more accessible learning. In [139], an eXplainable deep learning algorithm is proposed for processing CT images. A U-Net DNN based segmentation network is proposed in [140] which benefits from attention mechanism. In the proposed method, an attention mechanism is adopted to find the features collected from the encoder that contribute more to the classification process. A DNN algorithm called nCOVnet is proposed in [141], to process the CT-Scan images and identify the covid-19 patients.

Transfer learning: Transfer learning is a method in which the knowledge collected while solving a particular problem is used to solve a similar but not identical problem. This approach is particularly attractive when not enough data are available for training algorithms. Dense convolutional neural networks and transfer learning is used in [142] to classify chest X-Ray images. A transfer learning algorithm is proposed in [143] which has three phases. The authors use some wellknown pre-trained architecture including ResNet18, ResNet50, ResNet101, and SqueezeNet. A classification algorithm based on transfer learning is proposed in [144] which uses four state-of-the-art pretrained deep learning mode. The research uses VGG16, ResNet-50, Inception-v3, and Xception as backbone. A DNN is proposed in [145] to identify covid-19 via X-Ray images. The research uses a transfer learning approach on Pruned EfficientNet-based model and is interpolated by post-hoc analysis for the explainability of the predictions. In [146], a generative adversarial network (GAN) with deep transfer learning is proposed. In this method, first all the possible images of covid-19 that exist until the time of writing the research are collected and then GAN is used to generate more images.

In [147], an already existing deep learning algorithm that is used for detection of tuberculosis via CT images is generalized to identify covid-19 cases as well. In order to manage small data set problem, transfer learning techniques are used in [148]. A transfer learning based on the Residual Network (RESNET-50) was proposed in [149] to model the development of CT images.

New frameworks: In some works deep neural networks are used in a new framework. For example, a framework is presented in [150] which collects a good amount of data from different sources and trains a deep learning model over a decentralized network for the newest information about covid-19 patients. The authors propose a way to improve the recognition accuracy.

New way of diagnosis: Most of the works on processing X-Ray images, focus on detection of few pathologies. In some work new features are used to detect the patients. In [151], a hierarchical taxonomy mapped to the Unified Medical Language System terminology is used to identify 189 radiological findings, 22 differential diagnosis and 122 anatomic locations, including ground glass opacities, infiltrates and consolidations. The system is trained with a large database of 92,584 X-Ray images.

Ensemble methods: In machine learning, combining different learning methods usually results in a better algorithm. A holistic approach using different versions of DNN models including sequential, DenseNet121, ResNet152, etc. is proposed in [152] to recognize covid-19 via CT images. Different deep learning approaches including ResNet, Inception-v3, Inception ResNet-v2, DenseNet169, and NASNetLarge are used in [153] to process CT and X-Ray images to identify the patients. In [154], an ensemble of two types of transfer learning algorithms, namely DenseNet121 and SqueezeNet1.0 is proposed. In [155] AlexNet, GoogLeNet, Squeeznet, and Resnet18 are used as deep transfer learning models. The authors argue that these models are selected because of their small number of layers on their architectures which results in reducing the complexity of the models and their consumed time and memory.

New architecture: Architecture of machine learning algorithms is important in their performance. Thus, many research study and develop new architectures for the algorithm. In [156], a multi-task pipeline with specialized streams in DNN is proposed to perform segmentation of CT scans. In order to classify covid-19 patients against pneumonia, in [157] a method is proposed that first segments lung images and then feeds abnormal CT slices images into the EfficientNet B4 DNN. The output of this algorithm is then fed into a two-layer ANN so the slices are pooled together. A deep learning algorithm is proposed in [158], that consists of a pipeline of image processing algorithms which includes lung segmentation, 2D slice classification and fine grain localization. A semi-supervised learning approach is proposed in [159] that is based on AutoEncoders. The algorithm first extracts the infected legions in chest X-ray image. Then a highly tailored deep architecture is used to extract the relevant features specific to each class.

Improving the computational cost: Deep neural network algorithms are computationally expensive. The focus of some works has been to develop methods that are less computationally costly. Despite their success, the standard deep-learning algorithms are computationally costly. In order to build a more efficient system, EfficientNet family of DNN, which are well-known for their high accuracy are used in [160]. The work also uses a hierarchical classifier which exploits the underlying taxonomy of the problem. A lightweight deep learning algorithm is proposed in [161] . The algorithm is used to perform segmentation on covid-19 CT images. A novel semi-supervised shallow learning network model comprising parallel quantum-inspired self supervised network with fully connected layers is proposed for segmentation of CT images. The model is incorporated with a CNN model for feature learning [162].

Improving the performance of DNNs: Improving the performance of DNNs with new approaches has been applied in some works. It was observed that the boundary of the infected lung can be enhanced by adjusting the global intensity in DNNs. Therefore, in [163], a feature variation block which adaptively adjusts the global properties of the features for segmenting covid-19 infection is proposed. This method can enhance the capability of feature representation effectively. In [164], a multitask deep learning model is proposed which leverages useful information contained in multiple related tasks that improves segmentation and classification performance. The algorithm consists of an encoder and two decoders for reconstruction and segmentation and a multi-layer perceptron for classification.

Comparing the performance of different deep learning: Different algorithms perform differently on different problems. Finding the best algorithm for a particular problem is a question that is targeted by many works. In [165], ten different DNN algorithms have been used to identify covid-19 via CT scan images and it was shown that ResNet-101 offers the best performance. In [166], a comparison between MobileNet, DenseNet, Xception, ResNet, InceptionV3, InceptionRes-NetV2, VGGNet, NASNet deep learning algorithms has been performed.

Pre-trained Deep Neural Networks: One issue in developing algorithms for processing covid-19 images is the lack of large datasets. In [167, 168], it is argued that pre-trained networks can be of help for such data. Because the data for training DNNs is usually inadequate, a new concept called domain extension transfer learning is proposed in [169]. In this method a pre-trained DNN is employed on a related large chest X-Ray dataset. To get an idea about the covid-19 detection transparency, the concept of Gradient Class Attention Map is used to detect the regions where the model paid more attention during the classification. A pre-trained transfer learning technique is used in [170] and compared with different CNN architectures.

Managing small datasets: One practical difficulty is the limited data. In order to manage this, it is suggested in [171], to conduct domain knowledge adaptation from typical pneumonia to covid-19. However, there are two challenges in this matter. First is the discrepancy of data distribution among domains, second is the task difference between the diagnosis of typical pneumonia and covid-19. Therefore, the authors propose a new deep domain adaptation method. In [172], a contrastive learning algorithm is proposed to manage small dataset problem. The contrasive learning algorithm is used to train an encoder which can capture expressive feature representations on large datasets and employ the prototypical network for classification.

Smart phone applications: Mobile phones provide very interesting frameworks for developing covid-19 detection software. They are widely used and can collect data easily. In some work mobile devices are used to develop algorithms. In [173], a light-weight DNN based mobile app is proposed, which is a novel three-player knowledge transfer and distillation framework including a pre-trained attending physical network that extracts CXR imaging features from large scale of CT images. Recently, in some research, the use of Deep Learning in smartphones is suggested to process X-Ray images and detect covid-19 cases. In [174], however, some experiments are performed and it is argued that the quality of the images takes this way is not adequate to manage this application.

Noise reduction: The CT and X-Ray images are usually affected by noise. Thus, performing a noise reduction algorithm on the data can be helpful. In order to reduce noise from X-Ray images so that deep learning algorithms perform better, a semi-automated image pre-processing model is proposed in [175] to create an image dataset for developing and testing methods. The authors then use build a deep learning algorithm consisting of VGG, Inception, Xception and Resnet. In [176], a top-2 smooth loss function with cost-sensitive attributes is utilized in training DNNs to handle noisy and imbalanced datasets.

Long Short-Term Memory networks: Long Short-Term Memory (LSTM) are a type of recurrent neural networks that unlike feedforward networks, contain feedback connection. This makes the networks capable of processing sequences of data and application with unsegmented and connected data, like handwriting. In [177], a deep learning nested sequence prediction model with Long Short-Term Memory architecture is proposed for continuous monitoring of the infection and the recovery process. The model in this research is built based on epidemic data from 79 countries.

Pre-processing Images: Performing a pre-processing on the images can improve the performance of classification significantly. In [178], X-Ray images are reconstructed, where fuzzy color technique were used as preprocessing step and the images structured with the original images were stacked. Then deep learning methods were trained via the stacked data set and the feature sets were processed. In order to estimate the severity of cases of the patients, a DNN is proposed in [179] which first segments the intact part of the lung. Then the infected regions are segmented. The proportion of the infected volume of the lung is then used as an estimate for the severity of the disease.

Segmenting infected regions from CT images creates a number of challenges including high variation in infection characteristics and low intensity contrast between infections and normal tissues. Also providing large enough set of data is an issue. To tackle these problems, a novel Lung Infection Segmentation Deep Network (Inf-Net) is proposed in [180]. In the proposed method, a parallel partial decoder is adopted that aggregates the high-level features and builds a global map. The authors then employ implicit reverse attention and explicit edgeattention to model the boundaries and enhance the representations. Also, to manage the shortage of data, a semi-supervised segmentation framework is used which is based on a randomly selected propagation strategy.

Open source DNNs: Sharing data and codes is very important to enable other researchers to progress faster. To satisfy this, some works develop open source DNNs. In [181], an open source DNN for processing CT images is proposed.

EfficientNet: EfficientNet is an open source DNN designed by Google. This algorithm is known for its accuracy and efficiency. In [182], EfficientNet DNN is used with three different learning rate strategies for processing X-Ray and CT scan images. It is proposed in the paper to use a reducing learning rate when model performance stops increasing, cyclic learning rate and constant learning rate. Several DNN models are proposed in [183] for processing the CT scan images. A slice voting-based deep learning algorithm is proposed in [184] which is an extension of the EfficientNet family. The algorithm is applied to detection the patients via CT images.

Weakly supervised deep learning: Weakly supervised learning is when noisy, limited or imprecise data labeling is provided. This usually happens when there is a large amount of data and labeling the data is time consuming. A weakly supervised deep learning framework is presented in [185], which uses 3D CT volumes for covid-19 classification and lesion localization. In this method, a UNet is used to segment the lung regions. Then the segmented 3D lung region is fed to a 3D DNN to predict the probability of covid-19 infection. A weakly supervised learning strategy is proposed in [186] to process X-Ray images.

Combination of deep learning with traditional machine learning: In [187], a deep learning based decision tree classifier is proposed for processing CXR images. The algorithm consists of three binary decision trees, each trained by a deep learning model with CNN. In this model, the first tree classifies the normal images from abnormal. The second tree identifies the abnormal images that contain tuberculosis and the third tree diagnoses covid-19 cases. In [188], it is argued that Bayesian CNN can estimate uncertainty in deep learning solutions which can be used to improve the performance of diagnosis.

Processing new features: Feature selection plays a crucial role in classification. In some works new features are analyzed to detect the disease. In [189], a DNN is used to classify patients via CT scan images. The authors use extreme gradient boosting (XGBoost) algorithm that is trained with some features including lactic dehydrogenase (LDH), comorbidities, CT lesion ratio (lesion%), and hypersensitive cardiac troponin I (hs-cTnI). In processing CT images of patients, there are two type of important information, one is identifying the covid-19 patients, and the other is the description of five lesions on the CT images associated with positive cases. In [190], a Lesion-Attention DNN is proposed to classify the images into covid-19 and non-covid-19 patients, and an auxiliary multi-label learning task is implemented to build a model to distinguish the five lesions associated with the disease.

An adaptive feature selection guided Deep Forest is proposed in [191] for the classification of chest CT scan images. The work first extracts local specific features and then captures the high-level representation of these features with relatively small-scale data, and then a deep forest model is used to learn high-level representation of the features. A feature selection method is also applied on the trained deep forest model to reduce redundancy in the features.

New training methods: Some research have developed new training methods for DNNs in processing CT images. In [192], a grid search algorithm is used for training a DNN to identify covid-19 patients. In [193, 194], new training techniques are used to manage the unbalanced data set of covid-19 data sets, where Xception and ResNet50v2 networks are used. In [195], CNN is used to classify the images of covid-19 patients. The authors then use a multi-objective differential evolution is used to optimize the initial parameters of the CNN. In [196], the Gravitational Optimization Algorithm is used to determine the hyperparameters of a DenseNet121 architecture when processing X-Ray images.

The aggregated residual transformations is proposed in [197] to build a robust and expressive feature representation and to apply the soft attention mechanism to improve the performance of the system in distinguishing a variety of symptoms. In order to reduce the risk of overfitting, a self-trans approach is proposed in [198]. The proposed method synergistically integrates contrastive self-supervised learning with transfer learning which makes the algorithm able to learn powerful and unbiased representations.

Many work study the applications and advantages of DNN in processing covid-19 images, but not many address the weakness these networks may show. In order to target the vulnerability of these networks, the universal adversarial perturbation (UAP) problem is discussed in [199]. UAP happens when a very small perturbation vectors results in a high probability misclassification. The research consider nontargeted UAP which results in an input being misclassified, and targeted UAP which cause DNN to label an image to a specific class. The authors argue that DNN suffer from UAP when classifying covid-19 images.

Other examples of deep neural networks in processing CT scan images of chest include [200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235].

3.1.2. CT Scan and Combination of Deep Neural Networks

Some works try to build a combination of DNNs to improve the performance of the algorithm in detecting covid-19 patients. In [236], a combination of Nu-SVM, DenseNet and ResNet DNNs are used to process CT scan images. A CNN-based feature extractor algorithm conjoined with an average pooling and a classifier is used in [237] to process CT scan images. A combination of white balance followed by Contrast Limited Adaptive histogram Equalization and depth-wise separable CNN is proposed in [238]. This strategy is adopted in this research for enhancing the visibility of CXR images and for image classification with lesser parameters. In [239], seven different architectures of deep CNN including modified Visual Geometry Group Network (VGG19) and the second version of Google MobileNet are used to build a model. In [240], five different deep learning models namely ResNet18, ResNet34, InceptionV3, InceptionResNetV2, and DenseNet161 and their ensemble are used to classify X-Ray images. The authors use multi-label classification to predict pathalogies for patients. Also, the authors use techniques like occlusion, saliency, input X gradient, guided backpropagation, integrated gradients, and DeepLIFT to study the interpretability of each network.

Different machine learning algorithms including segmentation, data augmentation and the generative adversarial network (GAN) are used in [241] to classify CT images.

3.1.3. CT Scan and Convolutional Neural Networks

Convolutional Neural Networks (CNN) are a group of deep neural networks that have recently been studied by many researchers. Many researchers use CNNs in identifying covid-19 CT images [242, 243].

Weakly-Labeled Data: One problem in training DNNs for classification of covid-19 related images is the few number of training images. In order to manage this, weakly-labeled images pooled from publicly available collections with pneumonia-related opacities are used in [244, 245]. The images are used in a stage-wise strategic approach to train a CNN. A convolutional Siamese neural network algorithm is used in [246], to measure the disease severity on anterior-posterior CXRs that uses weakly-supervised pertaining on 160000 images. In [247], a weakly supervised deep learning is proposed which can minimize the requirements of manual labeling but still obtains accurate precision.

Pre-trained Networks: In many works, the CNN is first trained on an existing large-scale dataset and then is fine-tuned with covid-19 samples. The problem this causes is that the transfer across datasets from different domains can lead to poor performance due to the shift in the domain. This is particularly true for biomedical images as they are collected in different ways in different environments. Also the small covid-19 datasets results in the over-fitting problem. In order to manage this, in [248], the problem is formulated in a semi-supervised open set domain adaptation setting which overcomes the domain shift and over-fitting problems. In [249], a new stacked CNN model is proposed which obtains different sub-models from VGG19 and develops a 30-layered CNN model, and the sub-models are stacked via logistic regression. A CNN model called CoroNet is proposed in [250], to classify X-Ray images. The algorithm is based on Xception architecture that is pre-trained on ImageNet dataset and is traned end-to-end on a dataset. In [251], several pre-trained CNN were compared to find the best model.

A CNN based multi-image augmentation technique for detecting covid-19 via X-Ray and CT scan images is presented in [252]. The multi-image augmentation makes use of discontinuity information generated in the filtered images to increase the number of examples for training CNN model.

Ensemble Methods: In machine learning, sometimes it is better to combine the advantages of different learning techniques. This way, the ensemble of the learning algorithms obtain better performance than any of the individual algorithms. In [253], an ensemble of ten CNN algorithms has been used to diagnose covid-19 using chest X-Ray. In [254], three CNN algorithms (ResNet50, InceptionV3 and Inception-ResNetV2) are proposed to process X-Ray radiographs. In [255], a CT dataset is introduced and a series of convolutional neural networks are used on the data. In [256], a CNN combined with KNN is used to classify CT images. The algorithm consists of two phases. In the first phase, the volume and density of lesions and opacities of the CT images is calculated. In the second phase, the machine learning algorithms are used to classify the images.

In [257] two complementary deep learning approaches based on densely convolutional network architecture are proposed. The joint response of the two approaches enhances the performance of the individual methods. In [258], CNNs are used as feature extraction and SVM is used as classification. In [259], an ensemble of pretrained CNN with Resnet50 and VGG16 is proposed to process X-Ray images.

Light Convolutional Neural Networks: Deep leaning algorithms are usually computationally expensive systems to develop and train and they have a huge number of parameters to set. In some works, the aim has been to use lighter netwroks. In [260], a light CNN design based on SqueezeNet is proposed. In [261], the SqueezeNet is used with a light network design. The authors use Bayesian optimization to optimize the network.

To overcome the large number of parameters in DNNs, shallow CNN are proposed. In [262] a shallow CNN-tailored architecture is used to identify covid-19 cases via X-Ray images.

Transfer Learning: Transfer learning in machine learning refers to storing knowledge gained while solving one problem and applying the achieved knowledge on a another related problem. Since there is not many datasets, transfer learning has been attractive in dealing with covid-19 images. A type of CNN called Decompose, Transfer and Compose (DeTraC) can deal with irregularities in image dataset by investigating its class boundaries using a class decomposition mechanism. To benefit from this characteristic, DeTraC is used in [263] to process covid-19 X-Ray images. In [264], an Inception Residual Recurrent Convolutional Neural Network with Transfer Learning is proposed. In this method, a NABLA-N network model for segmenting the regions infected by covid-19 is proposed. A transfer learning pipeline for classifying covid-19 X-Ray is presented in [265], where multiple pre-trained convolutional backbones are used as feature extractors.

In [266], a deep transfer learning method that uses CNN based models InceptionV3 and ResNet50 with Apache Spark framework for classification of X-Ray images is proposed. Transfer learning was used in [267] to train four CNN algorithms including ResNet18, ResNet50, SqueezeNet, and DenseNet-121, to identify COVID-19 disease. A new computer-aided diagnosis scheme is presented in [268] which includes some image pre-processing algorithms to remove diaphragms, normalize image contrast to noise ration and generate three input images. The method then uses a transfer learning CNN to classify chest X-Ray images.

Generic Convolutional Neural Networks: Some works have simply used CNN for solving the problem with no specific modification. A 23-layer CNN was proposed in [269] to process CT scan images. A three-dimensional CNN is proposed in [270] and is applied to 498 CT images of 151 patients. An early screening model, based on an improvement on a classical visual geometry group network with a CNN is proposed in [271] to identify covid-19 via X-Ray radiographs. A deep neural network algorithm called Convolutional Support Estimation Network is proposed in [272] to identify X-ray images of covid-19 patients. It is argued in [273] that no research has considered study triage as a computer science problem. So the authors describe two setups, identification of covid-19 to prioritize studies of potentially infected patients to isolate them, and severity quantification to highlight studies of severe patients and direct them for emergency medical care. The task is formalized as a binary classification task and estimation of affected lung percentage.

In order to identify five conditions including covid-19, pneumonia, non-covid-19 viral pneumonia, bacterial pneumonia, pulmonary tuberculosis and normal lung, a CNN is proposed in [274]. The model is trained with the data collected from Wuhan Jin Yin-Tan hospital. In processing CT images, many of research ignore the cardiovascular metrics that can be representative of covid-19 patients. In [275], it is argued that these features can be used to identify the disease. The authors use a CNN algorithm to extract cardiovascular features from chest CT images, including total pericardial volume, total volume of coronary calcification, diameter of ascending aorta at the level of the right pulmonary artery, diameter of aorta, diameter of descending aorta. Then binary logistic regression analysis is used to classify the patients.

Comparing different networks: A number of works have performed comparison between existing methods. For example, a comparison over a number of CNN architectures is performed in [276] to find the best one in processing X-Ray and CT images. Different CNN architectures are trained and tested to process X-ray images in [277]. The authors suggest that VGG16 offers the best performance. In [278], the U-Nets and Fully Convolutional Neural Networks are compared for the CT scan image processing and it is suggested that Fully Convolutional Neural Networks achieve better performance.

Improving the performance of CNNs: There are many approaches in machine learning that can be used improve the performance of CNNs when identifying covid-19 cases. In [279], a twofold algorithm is proposed to process X-Ray images. First, 12 CNNs are used to analyze covid-19 images. Then a technique called class activation map is used to perform a qualitative investigation to inspect the decisions made by CNNs. The class activation map can be used to map the activation contributed most to the decision of CNNs back to the original image to visualize the most discriminating regions on the input image. A CNN is proposed in [280] that utilizes depthwise convolution with varying dialation rates for efficiently extracting diversified features. The algorithm first is trained with normal and pneumonia patients. Then an additional fine-tuning layers applied that are further trained with another set of covid-19 patients.

In [281], a pseudo-coloring methods and a platform for annotating X-Ray and CT images is used to train and evaluate a CNN. The CNN regression provides strong correlation between the lesion areas in the images and five clinical indicators that improves the interpretation accuracy of the classification. An iteratively pruned deep learning model ensemble for detecting covid-19 via X-Ray images is proposed in [282]. A CNN and a set of ImageNet pretrained models are used in this work. The proposed algorithm reduces complexity and improves memory efficiency.

3-Dimensional Convolutional Neural Networks: In a 3D CNN, the kernels move through three dimensions of data (height, lenght, and depth) which results in a 3D activation map. In some works, 3D CNNs have been used. A dual-sampling attention network and a novel online attention module with a 3D CNN to focus on the infection regions in lungs is proposed in [283]. The dual-sampling strategy is adopted to mitigate the imbalanced learning. In [284], a 3D CNN is proposed that uses patients CT volume to detect covid-19.

Managing small datasets: Some works have tried to manage the problem of small datasets with different approaches. For example, to overcome this, a type of CNN, called Capsule Networks are used in [285] which manages this problem. A new convolutional CapsNet is proposed in [286] for the detection of covid-19 cases by using X-Ray images with capsule network. In another work [287], the same problem is targeted. In [288], in order to manage the problem Convolutional LSTM-based deep learning is proposed. In [289], that generates synthetic chest X-Ray images based on Auxiliary Classifier Generative Adversarial Network (ACGAN). The synthetic dataset can be used to enhance the performance of CNN in detecting covid-19.

Open source algorithms: During the pandemic, it is very useful to share the finding with other researchers so the discoveries can progress faster. One way is to share the codes of algorithms with other researchers. In [290], an open source CNN algorithm is proposed for analysing CT images. In [291], an open source CNN is presented which uses state-of-the-art training techniques including progressive resizing, cyclical learning rate finding and discriminative learning rates for fast training and accurate residual NN.

New structures for CNNs: The neural network architecture is very important in its performance. Some research have tried to develop new architectures for covid-19 detection. A parallel-detailed CNN is proposed in [292], for processing X-Ray Images. The algorithm first preloads and enhances the images and then classifies them. The method is assisted with two visualization methods which are designed to provide an understanding of the key components associated with the infection. The visualization methods compute gradients for a given image related to feature maps of the last convolutional layer to create a class-discriminative region. A novel CNN architecture, called Residual image-based COVID-19 detection Network (ReCoNet) is proposed in [293]. The architecture consists of a multi-level preprocessing filter block in cascade with a multi-layer feature extractor and a classification block. The pre-processing block is trained via a multi-task learning loss function. To boost the network performance, a data augmentation technique is applied.

New data types: In most of the works CT or X-Ray images have been used to detect the infection. In a new approach, in [294], using ultrasound imaging of lung tissues is proposed for detecting the disease. In this method, a CNN is used to process the images.

Other examples of the research that use CNN for detecting covid-19 via CT images include [295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310].

3.1.4. CT Scan and Combination of Deep Neural Networks with other Algorithms

In [311], a deep learning model called truncated VGG16 is used for the classification of X-Ray images. The algorithm is fine tuned to extract features from CT scan images. In order to find the best features, Principal Component Analysis is proposed. Then CNN, Extreme Learning Machine (ELM), online sequential ELM and bagging ensemble with SVM is used to classify the data.

In [312], classical data augmentation techniques are combined with Conditional Generative Adversarial Network (CGAN) to process CT scan digital images. An pipeline consisting of ResNet-50 for deep feature computation and ensemble of machine learning classifiers is used in [313] to classify CT Scan images of codiv-19 patients. A combination of deep learning with a Q-deformed entropy approach is used in [314] to process CT images. The authors also propose a pre-processing to reduce the effect of intensity variations between CT images. In [315], a hybrid method is proposed to detect covid-19 cases via X-Ray images. The authors use a 2D curvelet transformation, a chaotic salp swarm algorithm and a deep learning technique to find the patients.

In order to identify covid-19 cases a new framework for processing CT images is proposed in [316]. In this method, two 3D-ResNets are combined to build a prior-attention residual learning. Also, a 3D-ResNet is trained as a binary classifier to highlight the lesion areas in the lungs. Then prior-attention maps are generator to guide another branch to learn mode discriminative representation for the classification. In [317], a method is proposed that takes as input a non-contrasted chest CT image and segments the lesions, lungs and lobes into three dimensions. In this method a deep learning algorithm is combined with deep reinforcement learning to measure the severity of lung and lobe involvement which quantifies both the extent of abnormalities and presence of high opacities. In [318], a system is proposed that uses robust 2D and 3D deep learning that modifies and adapts existing machine learning models and combines them with clinical methods.

In [319], a genetic algorithm is used to optimize the Dropout module in deep neural network for identifying covid-19 cases via CT images.

3.2. CT Scan Using Machine Learning Techniques

Although DNNs have been very successful in processing images, classic machine learning algorithms have also attracted the attention of some researchers.

Evolutionary algorithms: Evolutionary algorithms, as successful optimization algorithms have been used to solve many problems in image processing. In [320], genetic algorithms are used as wrapper methods for feature selection for an enhanced KNN algorithm for classification of CT scan images of covid-19 patients.

Statistical machine learning: The conventional statistical approaches are hybridized in [321] with machine learning tools to extract features from CT scan images and identify patients. In [322], a dataset of 3,777 patients is used in an AI system to diagnose the patients.

Improving classification: The main task in processing covid-19 images is the classification phase. In some work the aim has been to improve the classification process. In order to solve the segmentation problem, in [323], a consistency-based loss function is proposed that encourages the output predictions to be consistent with spatial transformations of the CT images. A hierarchical classification scheme is proposed in [324] to manage the imbalance data sets in the class distributions. The authors report that texture is one main visual attribute of CXR images. In diagnosing the disease via CT images the main challenge is how to distinguish between covid-19 and community acquired pneumonia cases which show very similar clinical features. To tackle this, an Uncertainty Vertex-weighted Hypergraph Learning (UVHL) is proposed in [325]. In this work, multiple types of features are extracted, then the relationship among different cases is formulated by a hypergraph structure, where each case is a node in the hypergraph. Then the uncertainty of the nodes is computed via a measurement and is used as weight in the hypergraph. Finally, a learning process is performed on the hypergraph to predict the new testing cases.

A real-time and explainable joint classification segmentation algorithm is proposed in [326] to diagnose cases via CT scan images. The system is trained via a large dataset of 144,167 images of 400 patients.

Using image processing techniques: Image processing techniques have been used in some research to improve the performance of the recognition. In processing CT scan images, the active learning methods usually process the whole image to find disorders. This is a time consuming process. In order to manage this, an annotator method is presented in [327], where the promising regions in the images are identified so only the regions that promise high information content are processed.

Support Vector Machines (SVM): Support Vector Machines have been successful in many classification tasks. In this regard, many works employ SVM to classify covid-19 related images. In [328], SVM is used to classify X-Ray images. A feature extraction process is used in [329] that is applied to patches to increase the classification performance of a SVM algorithm. In [330], SVM is used to classify X-Ray images based on deep features.

Comparing different machine learning algorithms: The question of how AI can help screening covid-19 pneumonia is targeted in [331] and the potential of different algorithms are discussed.

Artificial Neural Networks: In [332], image data are processed and local patterns are extracted by exploiting the frequency and texture regions to generate a feature pool. This feature pool is provided as an input to an Extreme Learning Machine. A group of backward neural networks is used in [333] to identify the covid-19 patients. In [334] a Generative Adversarial Network algorithm is used to process CT scan images of covid-19 patients. Cascade neural network algorithm is proposed in [335, 336] and to detect the disease in X-Ray images. In order to compare different approaches in classification of X-Ray images, Sixteen versions of neural networks are compared in [337]. A hierarchical attention neural network model is proposed in [338] which captures the dependency of features and improves the model performance. The adopted mechanism is proposed to make the model interpretable and transparent. In [339], a combination of convolutional NN and long short-term memory method is used to diagnose covid-19 via X-ray images.

Ensemble of machine learning algorithms: Ensemble learning has been used in some research. In [340], several classifiers including Naive Bayes, KNN, Decision Tree, Random Forest and SVM are used for the classification of CT scan images. The authors implement the system via a sequence of algorithms including multi-thresholding, image separation using threshold filter, feature-extraction, feature-selection, feature-fusion and classification.

Ensemble methods use a number of machine learning algorithms in the hope of taking advantage of each method, in a way that each learning algorithm covers the weakness of the others. Some work have developed ensemble methods to process CT Scan images. In [341], an ensemble of a number of machine learning algorithms has been used. In [342], an ensemble of different machine learning approaches, including CNN, Softmax, SVM, Random Forest and KNN is used to process X-Ray images to detect covid-19 patients.

Decentralized machine learning: Unlike centralized machine learning in which all the local datasets are uploaded to one server, in decentralized machine learning an algorithm is trained across multiple decentralized edge devices. In [343], federated learning is used to process X-Ray images. Federated learning can address the issue of data silos and get a shared model without obtaining local data.

Random Forests: In [344], an infection size aware random forest method is proposed and trained on 1658 patients with covid-19. An unsupervised hierarchical clustering algorithm is used in [345] to compare the distribution of these features across the collected data and identify the covid-19 patients. The features are then used in a classification algorithm which consists of logistic regression and random forest. A deep learning algorithm is also used to classify patients based on 3D features of CT images. In [346], a random forest algorithm is used to predict the severity of the infection via CT images.

Feature Extraction: Feature extraction is the process of selecting and combining variables into features and thus reducing the amount of data to be processed, while accurately maintaining the information within the data. In order to extract features from the X-Ray images, a new In [347], a machine learning based pipeline is presented which consists of segmentation of covid-19 affected parts, social group optimization and Kapur Entropy thresholding, k-mean clustering and morphology based segmentation and feature extraction. Then a PCA based fusion algorithm is used to fuse the features, the result of which is then fed to train random forest, KNN, SVM, Radial Basis Function and decision tree algorithms. Fractional Multichannel Exponent Moments method is used in [348]. Then a Monta-Ray Optimization, based on differential evolution is used to select the most significant features.

Other machine learning techniques: In [349], a frequency domain algorithm, called FFT-Gabor scheme is used to classify chest CT scan images. Most discriminative features of the disease in CT images are percentage of airspace opacity, ground glass opacities, consolidations, and peripheral and basal opacities. In [350], machine learning algorithms are used to predict the mortality of patients via X-Ray images. In [351], a cost sensitive learning algorithm is proposed to process X-Ray images. In [352], AI is used to analyze CT images of recovered patients to evaluate if the patient is ready for discharge.

Other examples of approaches that use machine learning techniques for processing CT scan and X-Ray images can be found in [353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371].

3.3. CT Scan Using Evolutionary Algorithms

In processing CT images, some works use evolutionary algorithms. The Cuckoo search algorithm is used in [372], to monitor a Kapur/Otsu image thresholding and a segmentation algorithm to extract the pneumonia infection. In [373], an improved marine predator algorithm is proposed for X-Ray image segmentation.

4. Applications of AI in Epidemiology

In this section we review the AI approaches in different aspects of epidemiology.

4.0.1. Epidemic Prediction

One important problem during the current pandemic is to predict the evolution of the disease. Building a forecasting model, allows governments to develop strategic planing in public health system which results in a reduction in the number of deaths. While many classic statistical modeling approaches can provide rather satisfactory prediction for the pandemic, the intricacies contained in the data are usually hard to capture with classic methods. AI methods, including learning approaches are more capable of capturing these complications. Therefore, many research apply AI approaches in understanding the pandemic. In this section, we provide an overview on these approaches.

4.0.2. Epidemiology and Neural Networks

Neural networks are loosely models of human brain that are widely used to recognize patterns.

Recurrent Neural Networks: RNNs are a type of artificial neural networks in which the connections between the nodes form directed graphs along a temporal sequence. This makes the algorithms able to model temporal information. In [374], a recurrent neural network is proposed to predict the epidemic curve. Two prediction models are created in this work, first the data are fed to a dense neural network and then a consequent regression output layer is used to predict the value. In [375], a recurrent NN is proposed to build a model of the pandemic in Italy. In [376], Graph Neural Networks are used for the prediction of the pandemic in the US. The method learns from a single large-scale spatio-temporal graph, where the nodes represent the region-level human mobility, spatial edges represent the human mobility based inter region connectivity and temporal edges represent node features through time.

Autoregressive neural network: In [377], a non-linear autoregressive neural network is deployed to build a model of the epidemic to predict the behavior of the epidemic. In [378], Autoregressive integrated moving average neural network is used to predict the pandemic in Italy, Spain an France. In [379], Artificial Neural Networks (ANN) and Auto-Regressive Integrated Moving Average (ARIMA) are used to predict the number of cases in Iran. In [380], a hybrid approach based on auto-regressive integrated moving average model and wavelet based forecasting model that provides short term prediction. The proposed method also provides a risk assessment algorithm. The algorithm uses optimal regression tree algorithm.

The polynomial regression and neural network algorithms are used in [381] with the data made available by John Hopkins University to build a model of the pandemic. Since the number of cases for each country is limited, the authors use a single layer neural network called the extreme learning machine learning to manage the over-fitting problem. Because the data are not stationary, the algorithm uses a sliding window to provide better prediction. In [382], Holt's second-order exponential smoothing method and autoregressive integrated moving average model is used to predict the pandemic in India. In [383], a number of machine learning algorithms including autoregressive integrated moving average, cubist regression, random forest, ridge regression, SVM and stacking ensemble are evaluated to build a predictive model of the pandemic.

New training algorithms: In [384] a forecasting model for the epidemic is presented that integrates an improved interior search algorithm based on chaotic learning strategy into a feed-forward ANN. The algorithm optimizes the parameters of the ANN via the search algorithm.

Multilayer perceptorns: Multilayer perceptron is a set of feedforward neural networks which consist of at least three layers of nodes, an input layer, hidden layers and the output layer. In [385], a multilayer perceptron and and vector aggression method are used to design a forecasting model for the epidemic in India. In [386], ANN and time series analysis are used to build a predictive model of the pandemic in Taiwan. In order to analyze the spatial evolution of the pandemic, an unsupervised neural network algorithm called self-organizing map is proposed in [387], which spatially groups together the countries that are similar to one another with respect to the pandemic, so can benefit from using similar strategies. In order to predict the incidence rate of the pandemic in United States, a multilayer perceptron neural network is used in [388]. In [389], an ANN-based curve fitting algorithm is presented for forecasting the number of cases in India, US, France and the UK, considering the progressive trends of China and South Korea. In [390], neural networks are used to predict the number of covid-19 cases in Mexico.

A Neural Network approach is presented in [391] which is a modified auto-encoder and is used to predict the epidemic curve of different regions in Italy. In [392], an ANN is used on a publicly available dataset that contain information on infected, recovered and deceased patients. In this work, the data are transformed into a regression dataset and used in a multilayer perceptron to build a model of the number of patients across all locations. An ANN is used in [393], to predict the number of cases in Hubei, China. The model gets as input some factors including maximum, minimum and average temperature, the density of the city, relative humidity and wind speed and generates as output the number of confirmed cases for the next 30 days.

Ensemble learning: In [394], an ensemble empirical mode decomposition and ANN are used to predict the pandemic. In [395], the Auto-Regressive Integrated Moving Average is used along with Multi-Layer-Perceptron (MLP), Extreme Learning Machine (ELM) and Generalized Linear count time series Model (GLM) to model the behavior of the pandemic. The model also includes the meteorological variables like temperature and humidity into consideration. Statistical and AI-based approaches are combined in [396] to model and forecast the prevalence of the pandemic in Egypt. The work integrates ARIMA and Non linear Auto Regressive Artificial Neural Networks (NARANN). An ensemble of neural networks is presented in [397] to build a model of the pandemic in Mexico. The approach then uses a fuzzy logic system to aggregate the response of these neural predictors. In [398], Neural Networks and LSTM are used to build a model to forecast the pandemic.

In order to study the effectiveness of the public health measures on the epidemic, some neural network forecasting methods including Multi-Layer Perceptron, Neural Network Auto-Regressive, and Extreme Learning Machine are used in [399]. The model is used to predict the number of active, confirmed, recovered, death and daily new cases in Jakarta and Java.

Wearable devices: In [400], a framework is proposed that collects data about heart rate and sleep data collected from wearable devices to predict the pandemic trend. In this approach, an online neural network algorithm is proposed to build the required model.

4.0.3. Epidemiology and Deep Neural Networks

Many works have applied deep learning techniques in predicting the trend of the epidemic.

Long Short Term Memory deep neural networks: In [401], LSTM, vanilla, stacked and bidirectional LSTM were used to predict the pandemic. The LSTM networks are used in [402], to build a predicting model for the trend and possible finishing time of the outbreak in Canada. In order to build a predictive model for the pandemic, a new architecture for DNN is proposed in [403], which consists of a LSTM layer, dropout layer and fully connected layers to predict regional and worldwide forecasts. A Long-Short Term Memory Neural Network is proposed in [404] to build a predictive model of the number of covid-19 cases. To predict the epidemic growth rate, a deep learning algorithm is used in [405]. In the proposed method, a Long short term memory method is used and its structure is searched heuristically until the best validation score is achieved. In another work [406], LSTM algorithm and Holt-trend are applied to predict confirmed number of death cases.

In [407], LSTM with dynamic behavioral model is adopted which considers the effect of multiple factors to enhance the accuracy of the prediction across top 10 most affected countries. In [408], LSTM and curve fitting methods are used for the prediction of the number of cases in India. In [409], a long short-term memory algorithm is used to model the data obtained from Google Trends website and estimate the number of positive covid-19 cases. The authors report that the most effective predictive factors are the search frequency of hand-washing, hand sanitizer and antiseptic topics.

Combination of DNNs with classic machine learning: There are works that combine DNNs with some of traditional machine learning algorithms. In [410], a deep learning algorithm and a Bayesian Poisson-Gamma model are used to estimate the evolution of the pandemic in Spain. An algorithm is proposed in [411], which is a combination of the Long Short Term Memory and Gated Recurrent Unit to predict the trajectory of the pandemic. In [412], a DNN is proposed to predict the epidemic in Spain. The method consists of a data generation process based on Monte Carlo simulations of SIR epidemiology models. LSTM algorithm, combined with a recurrent neural network is used in [413] to build two prediction model of the pandemic in India. In [414], recurrent NN based Deep LSTM, convolutional LSTM and bi-directional LSTM are used to predict the pandemic in India.

A shallow long short-term memory based neural network is proposed in [415] to predict the epidemic in different countries. The authors use a Bayesian optimization framework to optimize the network. In order to build the prediction model, the trend data and weather data are used. A combination of Xgboost, K-means and LSTM algorithms is used in [416] to build a model to predict the pandemic in Louisiana, USA. The authors use the weighted k-means which is based on extreme gradient boosting.

Incremental deep learning: In machine learning, incremental learning is an approach where the input data is continuously used to further train the model. This system is useful when training data are increasingly available over time. An incremental deep learning technique is proposed in [417] to build a model of the epidemic. The method is capable of continuously being updated as new data are available.

*Convolutional Neural Networks:*A CNN is proposed in [418] to build a model of the epidemic in Romania. The authors use a grid optimization algorithm for the neural network. Mathematical models of the epidemic consist of a set of differential equations that include some parameters. The process of finding these parameters to fit the data is called the inverse problem. One dimensional CNNs have shown success in performing analysis on time-series and sequence data. In [419], a 1D CNN is applied to the time-series data of confirmed covid-19 cases for all countries and territories. The algorithm is used to track and classify progress of the pandemic in different countries.

*Generic Deep Neural Networks:*In [420], the data on South Korea are collected and a DNN is used to to find the best time-varying parameters for the model.

*Ensemble of deep neural networks:*In [421], an ensemble of DNN, LSTM and CNN is proposed to predict the pandemic which takes advantage of the strength of each algorithm. In [422], various Recurrent Neural Networks, including the LSTM and 10 types of slim LSTM are presented to predict the pandemic in the US.

Comparing different deep learning algorithms: A comparative study over a number of DNN algorithms in predicting the epidemic is presented in [423]. In this work, simple Recurrent Neural Network (RNN), Long short-term memory (LSTM), Bidirectional LSTM (BiLSTM), Gated recurrent units (GRUs) and Variational AutoEncoder (VAE) algorithms have been studied based on daily confirmed and recovered cases collected from six countries namely Italy, Spain, France, China, USA, and Australia. The authors suggest that VAE offers the best performance among the algorithms.

Other example of the research that use DNN in predicting the trend of the pandemic can be found in [424, 425, 426, 427, 428, 429].

4.0.4. Epidemiology and Machine Learning

Understanding the dynamics and behavior of the pandemic can provide invaluable information for decision makers to build more systematic and successful policies to manage the outbreak.

*Combination of machine learning techniques:*In order to understand the behavior of the outbreak in sub-Saharan Africa, supervised machine learning and Empirical Bayesian Kriging algorithms are used in [430]. The authors report that seven variables are associated with the risk of infection, including, HIV infection, pneumococcal conjugate-based vaccine and incidence of malaria and diarrhea treatments. In order to build a model for predicting the instantaneous reproduction number (R_t), two AI methods, namely SHAP and ECPI are used in [431]. The authors apply their method on 18 countries. To study this, various machine learning models are proposed in [432] to extract the relationship between the spread of the disease and factors like weather variables, temperature and humidity. In [433], 24 variables linked to covid-19 are used to build a model with CatBoost regression and random forest algorithms. The work uses SHAP feature importance and Boruta algorithm to find the relative importance of features on covid-19 mortality in the US.

In [434] the impact of weather factors including temperature and pollution on the spread of the virus is studied. The authors also include social and demographic variables including per capita Gross Domestic Product and population density into consideration. The work employs the theories from epidemiology to develop a framework to build analytical models. Then machine learning methods including linear regression, linear kernel SV, radial kernel SVM, polynomial kernel SVM and decision tree are used. In [435], naive method, simple average, moving average, single exponential smoothing, Holt linear trend method, Holt Winter method and ARIMA are used to build a model for the prediction of the pandemic. A hybrid machine learning approach is proposed in [436] to predict the pandemic in Hungry. The algorithm consists of an ANFIS and MLP-Imperialist Competitive Algorithm to predict the mortality rate.

In order to investigate the role of environmental parameters, the climate and urban parameters of four cities in Italy are studied in [437]. The weather parameters studied in this work include daily average temperature, relative humidity, wind speed and as urban parameter, the population density is used. The authors use ANN, PSO and DE optimization algorithms for prioritizing climate and urban parameters.

It is a well-known fact about this disease that many people are infected asymptomatic, and so a large part of the epidemic remains undetected. In order to estimate the unobserved covid-19 infection cases and so to predict potential infections, a machine learning model is presented in [438] to uncover hidden patterns based on reported cases. In this work, first a dimensionality reduction method is applied to find the parameters that are important to uncovering hidden patterns. Then, an unbiased hierarchical Bayesian estimator is used to infer past infections from current fatalities.

Different machine learning algorithms, including Auto-Regressive Integrated Moving Average (ARIMA), Nonlin- ear Autoregression Neural Network (NARNN) and Long-Short Term Memory (LSTM) approaches are used in [439], to predict the number of new cases in Denmark, Belgium, Germany, France, United Kingdom, Finland, Switzerland and Turkey. In [440], four different machine learning algorithms including Decision Tree, Random Forest, Logistic Model Trees and Naive Bayes classifiers are used to predict the development of the disease.

In order to build a predictive model of the disease to help allocate medical resources and determine social distancing measures more efficiently, three machine learning models, namely hidden Markov chain model (HMM), hierarchical Bayes model, and long-short-term-memory model (LSTM) is proposed in [441]. Four type of forecasting machine learning methods are proposed in [442], including Linear Regression, Least Absolute Shrinkage and Selection Operator (LASSO), SVM, and Exponential Smoothing. The models make three types of predictions, including number of newly infected cases, the number of deaths and the number of recoveries within the next 10 days.

Forecasting the occurrence of future pandemic waves is important as it helps governments adopt adequate policy and suppress the pandemic at its early stages. To study the risk of a second wave of infection, an AI framework is presented in [443] which is based on three approaches, Bayesian susceptible-infected-recovered (SIR), Kalman filter, and machine learning. In [444] Bayesian regression neural network, cubist regression, k -nearest neighbors, quantile random forest, and support vector regression, are used to perform time series into several intrinsic mode functions. The model is used to predict the pandemic in Brazil and the US.

Clustering approaches: Clustering algorithms are used when the data are not labeled, and the aim is to explore the existence of patterns in the data. In [445], a clustering algorithm is used to process data from Internet searches and news alerts to perform a real-time forecasting of the outbreak. In order to study the epidemic behavior in different zones in New York city, a clustering algorithm is proposed in [446], that models the outbreak in the city. In order to classify countries according to the number of cases, a k-means clustering algorithm is proposed in [447]. The countries are clustered based on disease prevalence estimates, air pollution, socio-economic status and health system coverage. In [448], a clustering algorithm is applied to the world regions for which epidemic data are available and the pandemic is at an advanced stage. Then a set of features representing the countries response to the early spread of the pandemic are used to train an Auto-Encoder Network to predict the future of the pandemic in Brazil.

New learning approaches: In some works, new machine learning approaches are developed to predict the trend of pandemic. In [449], a new intelligent model called HH-COVID-19 is proposed for modeling the epidemic. In [450], machine learning algorithms are used to quantify the effect of covid-19 lock-down concentrations of four air pollutants. In this method, first the confounding effects of weather conditions on the pollution are eliminated. Then a new Augmented Synthetic Control Method is used to estimate the impact of the lock-down on pollution relative to control group of cities with no lock-down.

A partial derivative regression and nonlinear machine learning method is proposed in [451] to predict the global pandemic. In this algorithm, the non linear machine learning models the behavior and the partial derivative linear regression acts as the search algorithm for the optimization of the model parameters. Alternative to building an epidemiological model, a combination of reinforcement learning and recurrent neural networks is proposed in [452] for predicting the public health intervention strategies effect on the spread of covid-19 cases.

Support vector machine: In [453] support vector regression is applied to predict the number of covid-19 cases in 12 most affected countries. In this work, different structures of nenlinearity using Kernel functions are tested and the sensitivity of the predictive models is analyzed. In order to predict the spread of the virus, analyze the growth rate, predict how the epidemic will end and correlate the pandemic with weather conditions, a novel Support Vector Regression method is proposed in [454]. In [455], an AI algorithm is proposed for real-time forecasting of covid-19 to estimate the size, length and ending time of covid-19 across China. One question in dealing with the problem is that if the weather condition has any impact on the spread.

Generic machine learning algorithms: Some researches have used the classical machine learning algorithms with no modification or improvement. A Markov chain model has been used in [456], to predict the pandemic in India. The Gaussian model functions are used in [457] to predict the pandemic trends. In [458], a Reduced-Space Gaussian Process Regression model is proposed to predict the epidemic in the US. In [459], a non-linear machine learning model was used on data of 95 countries to assess the effect of 31 different containment measure on the infection rate. In [460], a Bayesian Poisson model for covid-19 in West Java Indonesia is proposed. In order to study the relationship between pollution emissions, economic growth and number of deaths in India, a machine learning algorithm is used in [461]. A classification model based on Reduced-

Space Gaussian Process Regression is proposed in [462] that studies the correlation between the number of covid-19 cases and air pollution.

In [463], machine learning techniques are used to analyze the statistics of different countries and find out if the countries are clustered with respect to the covariates. In order to find the best policy, some machine learning tools including Enerpol is used in [464] to find the impact of different scenarios on the epidemic in Switzerland. By tailoring the spatio-temporal characteristics of the spread to match the local facilities capabalities, the approach finds appropriate logistic needs.

In [465], machine learning algorithms have been used to identify the dominant factors of the epidemiological factors apart from management policies. The finding suggest that BCG and smoking are among the most important factors. In [466] a machine learning analysis of the pandemic is presented to extract actionable public health insights. The insights include the infectious force, the rate of a mild infection becoming serious, estimates for asymptomatic infections and predictions of new infections over time. In [467], the exponential growth model is used to derive the epidemic curve, and then a linear regression model is proposed to predict the epidemic curve. The logistic model is used in [468] to fit the cap of the epidemic trend and then feed the cap value in to a FbProphet model, a machine learning modeling algorithm proposed to model the epidemic curves.

A machine learning algorithm is proposed in [469] to analyze the effect of the quarantine on the spread of the virus in different countries.

Comparing different algorithms: A comparative analysis of machine learning and soft computing models in building predictive models is performed in [470], where a wide range of machine learning models are investigated. Among the approaches, MLP and Adaptive Network Fuzzy Inference System have shown better performance. In [471], machine learning algorithms are used to predict the spread of the disease including the number of confirmed and fatality cases at national and state level in the US. A machine learning algorithm is used in [472] to study the impact of nationwide measures on the pandemic. In order to predict number of infected, recovered and deaths due to covid-19 as well as contact, recovery, death rates, basic reproduction number and doubling times a machine learning algorithm is proposed in [473].

Open source algorithms: In [474], XGBoost is used to predict the number of infections in South Korea.

Improved versions of existing learning algorithms: The performance of existing learning algorithms has been improved in some research to build a model of the pandemic. An improved version of ANFIS is used in [475] to predict the spread of the virus in Italy, Iran, Korea and USA. The proposed algorithm uses marine predator algorithm to optimize the parameters of ANFIS. An empirical top-down modeling algorithm is proposed in [476], which uses a combination of epidemiological, statistical and neural network applications. In this approach, a neural network is used to develop leading indicators for different regions. These indicators are used to asses the risk of an outbreak, determine the effectiveness of the measures, predict the outbreak with the associated uncertainty.

New training approaches: The training process in learning algorithms is an optimization problem. This problem has been targeted in some research. In [477], an epidemiological model augmented by machine learning algorithm is proposed to study the effect of quarantine and isolation measures implemented in Wuhan on the reproduction number, R0. In order to model the behavior of the pandemic, an Adaptive Neuro Fuzzy Inference System is proposed in [478], which uses a flower pollination algorithm and salp swarm algorithm to optimize the model parameters.

Text processing: There exist substantial amount of information in texts that can be analyzed to collect data about the pandemic. A natural language processing algorithm combined with CT imaging is proposed in [479] to study the epidemic in the US. The algorithm uses natural language processing to analyze the CT imaging reports to correlate them with the incidence of official covid-19 cases and deaths in the US. A hybrid AI model for covid-19 prediction is presented in [480], in which first a traditional epidemic model is generated. Then, considering the prevention and control measures, a natural language processing along with a long short-term memory network are embedded into the model for prediction.

Cloud computing: Cloud computing provides a good platform for epidemiological algorithms as the capabilities of the cloud can provide large databases and connection among different models. To take advantage of this, a machine learning algorithm is proposed in [481] to predict the pandemic. The algorithm uses a mathematical model to analyze and predict the epidemic, and then a machine learning algorithm is used to predict the growth of the epidemic.

Managing the uncertainty: A machine learning algorithm is proposed in [482], to predict the number of daily cases, which captures uncertainty. The algorithm combines three machine learning algorithms, namely decision tree algorithm, support vector machine and Gaussian process regression. The model is built based on the projection of new cases, recovered cases, deceased cases, medical facilities, population density, number of tests conducted and facilities of services. These measures define a metric called criticality index, which is then used to classify the regions of the countries into high risk, low risk and moderate risk.

Other examples of the application of machine learning in epidemiology can be found in [483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494].

4.0.5. Epidemiology and Evolutionary Algorithms

In [495], a genetic algorithm is used with a cross-validation method to generate a model of the epidemic in Algeria. A multi-gene genetic programming algorithm is proposed in [496], as a model to predict covid-19 outbreak. In [497], a combination of virus optimization algorithm with ANFIS is proposed to investigate the effect of various climate-related factors and population density on the spread of the virus. In [498, 499], Genetic Programming is used to build a model of the pandemic. In [500], a surrogate-assisted prescription method is proposed to generate a large number of candidate strategies and evaluate them with predictive models. This way, the strategies can be customized for different countries.

It is very important to understand the transmission dynamics of the disease if one is to estimate the effectiveness of control policies in controlling the pandemic. In [501], a mathematical model of the transmission of the virus is considered and a multi-objective is proposed to achieve high-quality schedules for various factors including contact rate and transition rate. In order to build a model of the pandemic in Indonesia, a generalized Richards model is used in [502]. The model's parameters are optimized via Genetic Algorithms.

4.0.6. Monitoring the Pandemic:

Some research use AI to monitor the pandemic and its effect. In [503], a hybrid cellular automata is proposed to predict the effect of the pandemic in terms of deaths, number of people affected and recovery. In [504], a machine learning algorithm is proposed to study the effect of temperature, humidity and wind speed on the number of infected people. The authors suggest that there is a moderate inverse correlation between temperature and the daily number of infections. The effect of the pandemic on the tourism market is studied in [505]. In this work, a Long Short Term Memory neural network is calibrated for the properties of this pandemic.

4.1. Controlling the Pandemic

In order to control the pandemic, it is crucial to keep the reproduction rate small. In this section we perform a review on the research that use AI methods to control the pandemic and decrease the infection rate.

Contact tracing: In [506], machine learning techniques are used in developing an application for contact tracing. The application automatically records interactions between people and offers a self-assessment tool for monitoring the symptoms. In order to detect and prevent the spread of the pandemic and forecast the next epidemic and effective contact tracing, a machine learning modeling algorithm is proposed in [507].

Identifying covid-19 cases: Monitoring and inspecting the society is very important in controlling the spread of the disease. In [508], a call-based dialog agent is deployed for active monitoring in Japan and Korea. In [509], an AI based approach for optimized mobilization strategy for mobile assessment agents for the epidemics is presented. The model is trained by using data acquired from past mobile crowdsensing campaigns. A low cost blockchain and AI-coupled self-testing and tracking system for covid-19 is proposed in [510]. In [511], a machine learning algorithm is presented that is implemented on a mobile phone-based web survey to identify covid-19 cases. The method can reduce the spread of the virus. There are some indicators in the population that can be representative of infections in some areas. Monitoring these indicators is a good way of detecting small outbreaks. In [512], symptoms like diarrhea, nausea, conjunctivitis and loss of taste are used to cluster people into different groups and identify their risk of infection.

Testing for infection: According to WHO, testing is very important in the fight against the pandemic. To suppress the pandemic, a prompt action in identifying the suspected cases is important. In order to study the correlation between the number of swab tests and confirmed cases of infection, with attention to the sickness level, AI approaches are used in [513]. The authors report that there is correlation between the number of swab tests and daily positive cases, mild cases admitted to hospital, intensive care cases, recovery and death rates. In [514] it is suggested that social relationship between mobile devices can be used to help control the propagation of the disease. In this method, the differential contact intensity and the infectious rate in susceptible-exposed-infected-removed epidemic model is exploited to transform the optimization problem into minimum wight vertex cover problem in graph theory. In [515], in order to test people for covid-19 infection, immunochromatographic lateral flow assays (LFA) are analyzed via machine learning to present a proof-of-principle frame work that may be used to inform the pairing of LFAs to achieve better classification.

Risk assessment: In [516], an ANN is used to perform risk assessment of covid-19 in urban districts. The importance of employing AI-based search tools is discussed in [517] and it is argued that future research into the disease requires smart searching techniques. Using AI algorithms and using data from heterogeneous sources, an AI-based system is proposed in [518] which provides hierarchical community-level risk assessment to help in developing strategies for combating the pandemic. The system automatically predicts the risk assessment of a given area in a hierarchical manner, from state, county, city and specific location.

Social distancing: One of the most important measures for preventing the spread of the virus is social distancing. In order to monitor people to make sure they are following the guidelines in public places, a CNN is proposed in [519]. The algorithm checks people for symptoms like fever or cough. In [520], a machine vision algorithm is proposed which uses Al approaches to monitor people who do not obey social distancing rules. In [521], a deep learning framework is proposed for monitoring social distancing via surveillance video. In this algorithm, the YOLO v3 object detection model is used to segregate humans from the background and Deepsort method is used to track people. It is argued that social distancing measures show different consequences in different countries. To study this, a hybrid machine learning model called SIRNet is proposed in [522] to model the epidemic. In this method, spatio-temporal data from mobile phones are used as surrogate for physical distancing and a measure for social distancing. The work also uses population weighted density and other local data points. Reports suggest that social distancing and wearing face masks reduces the risk of transmission. In [523], machine vision and AI algorithms are used to monitor workers and detect violations. In this approach, deep learning and classic projective geometry techniques are combined.

Wearing facemask properly is very important in controlling the pandemic. In [524], a facemask wearing condition identification is proposed that consists of four steps, image pre-processing, face detection and crop, image super-resolution and facemask wearing condition identification. Public perception towards interventions like physical distancing should be studied to help authorities effectively manage the concerns. Social media reflect valuable information regarding the public opinion on the issue. In order to study this, deep learning based text classification models are presented in [525], for classifying social media content during the pandemic. The data are collected by analyzing Facebook comments.

Understanding the pandemic: In [526], it is argued that understanding the properties of other outbreaks like influenza can help better understand the behavior of the covid-19 pandemic. The authors explore performing sentinel syndromic surveillance for covid-19 using DNN. The approach is based on aberration detection utilizing auto-encoders7 that leverages symptom prevalence distribution to distinguish the outbreak. It is argued in [527], that AI systems were able to anticipate the pandemic in China before it caught the world by surprise. By a review on viral outbreaks during the last 20 years, the authors explore how early viral detection can be reduced using AI systems.

Battling against disinformation: Social media plays an important role during the pandemic as they provide a platform for sharing news and personal experience and viewpoints in real-time, globally which helps people build up their knowledge about the disease and the way they can confront the problems it causes. However, the existence of misinformation and social fatigue affect its usefulness. In [528], structural equation modeling and neural network techniques are used to investigate how motivational factors and personal attributes affect social media fatigue and sharing misinformation during the pandemic. A machine learning algorithm is used in [529] to analyze covid-19 online content around vaccination. The authors discover that the anti-vax community is performing less focused debate around the issue than the pro-vaccination community. The anti-vax community exhibits a wider range of topics so they can appeal to a broader range of people seeking guidance online. This makes the anti-vax community in a better position to attract support.

Since the spread of the pandemic, there has been an explosion in the spread of disinformation related to the disease. To manage this, an AI-based algorithm is developed in [530], to debunk disinformation. In [531], machine learning algorithm algorithm is used to develop a framework for detecting conspiracy theories. In order to fight fake news and conspiracies, in [532], a repository called CeCOVery is proposed to facilitate the studies around combating the misinformation. The work first investigates news publishers and builds a model based on multimodal information of news articles including textual, visual, temporal and network information. The model provides a model for predicting news credibility.

policy suggestion: In order to provide policy suggestion to fight the disease, a machine learning algorithm is proposed in [533] to identify structural breaks in detected positive cases dynamics with territorial level panel data. In [534], a neural network algorithm is used to model the behavior of the pandemic with respect to the governmental measures. Then, an optimization algorithm is proposed to find the optimal decision.

4.2. Managing the Effects of the Pandemic

The pandemic has caused a great deal of effect on many aspects of human life, economy, industry, etc. In some research, AI approaches are used to develop ways of managing the effects of the pandemic. In this section, we cover these research. In [535, 536, 537, 538, 539] the ways AI approaches can be used to manage the problems caused by the disease are over-viewed.

Utility services: The pandemic has caused unprecedented challenges for the utility and grid operators. Due to the lockdowns and restrictions, power consumption profiles around the world have shifted in magnitude and pattern. This has caused difficulties in load forecasting. Traditional algorithms employ weather, timing information and previous consumption levels as input variables; however, due to the pandemic, these measurements do not explain the new patterns. To capture the new behavior, mobility is used in [540] as a measure of economic activities. The work uses machine learning algorithms to build the predictive system. In [541], a comparative regressive and ANN model are developed to analyze the effect of covid-19 on the electricity and petroleum in China.

Helping organizations: In [542], AI tools are used to help charities deal with the problems they are faced during the pandemic. In [543], an AI algorithm is proposed to optimize the library services and resource allocation during the pandemic. The pandemic has made the justice system face difficulty in delivering the required service. Already, AI approaches like Ross intelligence, machine learning and natural language processing are widely used in developing systems like artificial lawyers. The new difficulties has increased the pressure for developing intelligent systems as help for the justice system. In [544], different ways in which AI can come to help to mange the problems caused by the pandemic are presented. A recurrent neural network is proposed in [545] for detection of fraud transactions during the pandemic.

Helping researchers: The pandemic has resulted in a great need for access to the latest scientific information. To study this, publicly available deep learning based commercial information retrieval systems to search biomedical research around covid-19 is proposed in [546].

Educational system: During the pandemic, the education system has been affected very significantly, and many countries have deployed new platforms to help students continue their educations. User satisfaction of these platforms is very important. In [547], an ANN is used to mode and forecast user satisfaction of the educational satisfaction in China.

Oil market: The pandemic has caused a chaotic behavior in the oil prices. To analyze the price of crude oil under the impact of the pandemic, an AI based method is proposed in [548]. Due to the pandemic, fuel demand plummeted and in some cases the price of oil future went negative. In [549], a machine learning based model is presented that uses information like travel and trip activities and fuel usage and builds a model to project the US medium-term gasoline demand and the impact of government interventions.

Psychological effects: The pandemic has caused great effect on psychological stressors including unemployment, fear of getting infected, hopelessness, helplessness, social isolation and inadequate psychological support. The impact of covid-19 on people's mental health is explored in [550] to assist policy makers to create actionable policies. In [551], AI-based approaches are proposed for managing the psychological effect of the pandemic. In order to understand the day to day living, activities, learning styles, and mental health of young students of India during the pandemic, a machine learning algorithm is used in [552]. In [553], machine learning algorithms are used to identify the factors that have significant impact on mental health during the pandemic. Using a Bayesian Network inference, key factors affecting mental health are identified. In another paper targeting the same problem [554], a method is proposed for the prediction of individuals at a higher risk of later chronic mental health disorders due to high distress during the pandemic. In [555], machine learning algorithms are used to study the effect of the pandemic on mental health of people.

Sport: In [556], a machine learning method is proposed that predicts the impact of the factors like presence or lack of fans, and the physical distancing on the performance of baseball teams.

Managing the economical impacts: In order to mitigate the economic impact of the lockdowns, a data driven dynamic clustering framework is presented in [557] for moderating the adverse economic impact of the covid-19 flare-up. The authors model the lockdown as a clustering problem and proposed a dynamic clustering algorithm for localized lockdown by taking into account the pandemic, economic and mobility aspects. In [558], data driven models are presented to learn fine-tune predictions for different countries that are used for epidemiological forecasting. The method uses deep learning estimation of the parameters of the disease in order to predict the cases and deaths and a genetic algorithm is used to find the optima trade-off between the constraints and objectives set by decision makers. In order to offer an understanding of how covid-19 will affect Brazil a neural regressor is proposed in [559].

Planing in hospitals: Decision making for kidney transplant during the pandemic is arguably a conundrum. A machine learning algorithm is proposed in [560] that performs the decision making process between immediate transplant versus delay-until-after-pandemic. Pathways used to deliver equipments for stroke patients are under intense pressure due to the pandemic. Therefore, the existing pathways should be reconfigured both within and between hospitals. In [561], an AI algorithm is proposed for Royal Berkshire Hospital to mange this problem.

Smart cities: In order to manage the difficulties that the pandemic causes for cities, some works have developed ideas in smart city developments. In [562], AI methods are used to analyze the virus outbreaks and methods are suggested on how smart city networks should perform towards enhancing standardization protocols for increased data sharing for better management of the pandemic. During the pandemic, the human activity within and between cities has changed dramatically. In order to understand such changes in the pattern, a deep learning algorithm is proposed in [563] that combines strategic location sampling and an ensemble of lightweight convolutional neural network. The model is generated to recognize specific elements in satellite images and compute economic indicators. In order to predict the effect of the pandemic on transportation trends a DNN is proposed in [564].

5. Pharmaceutical Studies

Finding an effective drug can help to decrease the mortality rate of the disease. Treatment approaches for the disease include three main options of repurposing, investigational therapies such as remdedivir and vaccine development. Repurposing drugs which already have shown few side effects for the treatment of the disease is an important and promising approach in developing new therapeutic strategies. In some research, AI approaches are used in pharmaceutical studies in battling covid-19. As the pandemic continues to progress, it is argued that the potentials of AI should be harnessed in the process of drug screening and repurposing [565, 566].

Drug repurposing: Among the most popular approaches is combination therapy based on drug repurposing. Multi-drug treatment is performed by selecting drugs based on their mechanism which is followed by a dose-finding to discover the drug synergy. Achieving this combination, however, is a challenge. To manage this, an AI based platform is proposed in [567] to analyze a 12 drug/doze parameter space in order to identify therapies that inhibit lung cell infection. Predicting interactions among heterogenous graph structured data has application in recommendation system and drug discovery and repurposing drugs for novel diseases. In [568] machine learning algorithms are used to discover new drugs.

In [569], the Naive Bayes algorithm is used to build a model for reporpusing drugs. Network medicine has been used in the past decade to develop and validate predictive algorithms for drug repurposing. This approach exploits the sub-cellular network based relationship between a drug target and the disease gene. In [570], an AI based algorithm is proposed that analyzes 6,340 drugs to discover their expected efficacy against SARS-CoV-2.

An integrative, network-based deep-learning methodology is proposed in [571] to identify repurposable drugs for the disease. The research provide a comprehensive knowledge graph that includes 15 million edges across 39 types of relationships connecting drugs, diseases, proteins, genes, pathways and expression from a large number of scientific publications. A network based deep learning framework is utilized and 41 repurposable drugs have been identified. The effectiveness of the drugs were then validated via clinical trials. The authors argue that the algorithms may not recommend specific drug, however, they provide a way of prioritizing drug research.

Discovering potential drugs: In order to find potential therapeutic drugs for the disease, in [572], a library of 1,670 compounds were processed via deep learning. A DNN was used in [573] to search for host-target acting antivirals among experimental and approved drugs with potential activity against the disease. The algorithm searches for gene expression signatures of molecular purturbations close to the SARS-CoV. In [574], AI methods are used to perform transcriptional analysis to identify potential antiviral drugs from natural products or FDA approved drugs. An AI platform is established in [575] to identify potential old drugs with antiviral properties against covid-19. The authors then test all AI predicted drugs against feline corona virus in vitro cell-based assay. They then feedback the assay results back to the AI system for relearning and generating a modified AI model to search for old drugs again.

To battle the pandemic, the most powerful super computer, SUMMIT has come to help in fight against the disease. It was used to identify existing small molecule pharmaceuticals which may have potential effect against the virus. In order to further improve the performance, in [576], it is demonstrated how Bayesian optimization can help to prioritize the calculations leading to accelerated identification of candidates with the same computational power. A data-driven drug repositioning framework is developed in [577], which applies machine learning to integrate and mine large-scale knowledge graphs to discover potential drug candidates against covid-19. An AI-based drug-repositioning strategy is proposed in [578] to build a learning prediction model and find the drugs that have potential in the treatment of the disease.

Studying immune system: In another work [579], in silico analysis of immune system protein interactome network, single-cell RNA sequencing of human tissues are performed with a neural network to discover potential therapeutic targets for drug repurposing against COVID-19. In [580] the study of finding peptides or antibody sequences is targeted to find possible drugs that can inhibit the viral epitopes of the disease. A machine learning algorithm is proposed in this work to predict the possible inhibitory synthetic antibodies for the corona virus. The authors collect 1933 virus-antibody sequences and their clinical patient neutralization response and trained a machine learning algorithm to predict the antibody response. They also use graph featurization with variety of ML methods to screen thousands of hypothetical antibody sequences to find 8 stable antibodies with potential capability to inhibit covid-19.

Herbal drugs: It is suggested that some herbal drugs can help treating the disease. In order to study the Indonesian herbal compound and their effectiveness on the drug, SVM, MLP and random forest algorithms are used in [581]. In this method, for a pharmacophore modeling approach, the structure-based method on the 3D structure of the virus mail protease is performed.

Studying drug molecule structure: In order to identify "progeny" drugs similar to the "parents" that are already tested for covid-19, an AI algorithm is proposed in [582], which assess similarity based on the molecular make-up and the context in which functional groups are arranged by three-dimensional distribution of pharmacophores. In [583], machine learning algorithms are used to analyze a group of 77 antiviral molecules and their structural information to identify potential therapeutics for managing the crisis. In another work [584], a Deep Learning Algorithm is used to identify molecule structures that are potential inhibitors against the virus.

In [585], an *in vitro* pharmacology of the treatment is performed which shows its effectiveness. Reliable molecule interaction data provide a basis, where drug protein-protein interaction networks establish important data resources. In [586], a deep learning algorithm is used to analyze these networks. The algorithm can predict unknown links between drugs and human protein that are targeted by the virus to bind.

Study of existing drugs: An AI-based binding affinity prediction is proposed in [587] to identify existing FDA approved drugs that can block the coronavirus from entering cells by binding to ACE2 or TMPRSS2. In [588], a pre-trained deep learning-based drug-target interaction model called molecule transformer-drug target interaction is used to identify commercially available drugs that can act on viral proteins of SARS-CoV-2 Baricitinib is approved for the treatment of rheumatoid arthritis and is predicted by AI algorithms to be effective on covid-19 patients due to its anti-cytokine effects.

Studying drug discovery techniques: In [589], a systematic study of AI based drug discovery techniques suitable for covid-19 is proposed. It is discussed in [590] how an AI assisted prediction can help develop new drugs for the disease. In another work [591], an LSTM model is trained to read the SMILES fingerprint of a molecule and to predict the IC50 of the molecule when binding to RdRp. The model is trained using IC50 binding data from the PDB database of 310,000 drug-like compounds from ZINC database. This system is used to find the candidate drug for controlling the virus.

Molecule design: A de novo molecular design strategy is proposed in [592], which uses AI algorithm to discover therapeutic biomolecules against covid-19. The method uses a Monte Carlo Tree search algorithm combined with a multi-task ANN surrogate model. In [593], a framework is proposed that combines adaptive pre-training of a molecular SMILES Variational Autoencoder and a multi-attribute controlled sampling scheme. The method uses guidance from attribute predictors trained on latent features. In this scheme, a protein molecule binding affinity predictor is used to generate novel and optimal drug-like molecules for unseen viral targets.

Text processing: In [594], a twitter data set of 424 million tweets of covid-19 chatter are analyzed via AI-based methods to identify potential treatments. In order to explore biomedical entities related to the disease, some topic specific dictionaries including human genes, disease, Protein Databank, drugs, drug side effects, etc. are integrated. The authors employ an automated literature mining and labeling system to measure the effectiveness of drugs against disease based on natural language processing [595].

Studying the side effect of drugs: In [596], an ontology-based side-effect prediction framework is used with DNN to evaluate the traditional Chinese medicine prescriptions that are officially recommended in China for the disease.

Studying the virus sequence: In order to discover the underlying association between viral proteins and antiviral therapeutics, an ANN is employed in [597] to build a model of the data in DrugVirus and National Center for Biotechnology Information database. The model uses virus protein sequences as inputs and antiviral agents deemed safe-in-human as output.

Studying the infection mechanism: In order to perform a rapid screening of possible therapeutic molecules, machine learning based models are combined with high fidelity ensemble docking simulations [598]. The screening is based on the binding affinity to either isolate the virus S-protein at its host receptor region or to the Sprotein-human ACE2 interface. This results in potentially limiting or disturbing the host virus interaction. The algorithm is applied to two drug datasets to find ligands capable of performing the mentioned process.

Studies suggest that the clinical characteristics of pregnant women are similar to those of non-pregnant patients. However, the disease can increase the risk of pregnancy complications, fetal distress and preterm delivery. In order to predict the pregnancy safety profile of potential covid-19 drugs, a machine learning model is built in [599] based on existing drug-related data sources with known pregnancy safety.

Vaccine studies: Machine learning techniques have also been used in vaccine development. In [600], Vaxign reverse vaccinology tool and the newly developed Vaxign-ML machine learning tool is used to predict covid-19 vaccine candidates. In [601], AI algorithms are used to study the mutation behavior of the virus for vaccine development. It is argued that bacille Calmette-Guerin (BCG) vaccination (a vaccine usually used against tuberculosis) may lessen the severity of covid-19. In [602] machine learning algorithms are used to analyze the existence of such correlation. The authors use k-means clustering and step wise linear regression.

6. Text Processing

A substantial amount of information is in the form of text data that can be exploited via text processing algorithms. In this section we review the works that use text processing techniques for covid-19 related subjects.

Text summarization: In [603], AI algorithms are used for automatic text summarization of covid-19 medical research articles. In a similar attempt, natural language processing techniques are combined with summarization in [604] for mining the available scientific literature. The system offers a query system for researchers to more easily access the information they require. In [605], it is argued that the rate of publication has far exceeded the time-consuming peer-review process. Thus, a natural language processing algorithm is proposed that summarizes long papers.

Research analysis: In order to filter efficiently the scientific bibliography for relevant literature around the disease, an active learning algorithm is proposed in [606] that classifies literature into relevant and non-relevant literature. In [607], using machine learning a bibliometric analysis is performed on publication outputs, countries, institutions, journals, keywords, funding and citation counts. The research performs an analysis on the research performed in the area.

Reviewing articles: In [608], a machine learning algorithm is proposed that rapidly surveys the abstract of the research around covid-19 and identifies research hotspots, areas warranting exploration and research overlap between covid-19 and other coronavirus diseases. As more research is performed around the disease, larger group of experts are monitoring, assessing, coding and summarizing new covid-19 publications. In [609], neural network algorithms are used to build a semi automatic screening of covid-19 publications.

Studying public awareness: Public response to the pandemic is important to be measured as it represents the awareness towards the problem. In this regard, Twitter data are an important source for public response monitoring as the reflect discussions, concerns and sentiments. In order to examine this, in [610] 4 million Twitter messages are analyzed via Latent Dirichlet Allocation. The discussion topics are categorized into five different themes. In order to identify public sentiment associated with the pandemic, machine learning algorithms are used to process covid-19 related Tweets in [611]. The Tweets are processed via natural language processing. In order to study Twitter user's psychological reactions to the disease, a machine learning algorithm is used in [612] to analyze 1.9 million Tweets.

In order to detect and characterize conversations on Twitter that are associated with the disease symptoms, experiences with access to testing and mentions of disease recovery, a machine learning algorithm is proposed in [613]. In this approach, Tweets with covid-19 related keywords are collected and analyzed via an unsupervised machine learning algorithm called the biterm topic model. An automated extraction of covid-19 related discussion system is proposed in [614] which processes social media and via a natural language processing method, extracts information from public opinions about the disease. The research uses LSTM for sentiment classification of covid-19 comments.

Improving social awareness: In the wake of the covid-19 outbreak, it is important to build interactive tools that can provide essential information such as covid-19 symptoms, treatment options, etc. In [615] an algorithm called COVID-Twitter-BERT algorithm is proposed which is a transformer-based model, and is pretrained on a large corpus of Twitter messages on the topic of covid-19. The model is used to analyze covid-19 content on Twitter. In [616], a neural text processing algorithm is proposed to make the information about the disease in different languages available to everyone. A chatbot is presented in [617] to provide assistance during the quarantine. The system uses NLP and machine learning algorithms that communicate with people to increase their consciousness toward the pandemic. The algorithm is capable of recognizing and managing stress.

Search engine: A search engine is proposed in [618, 619], that exploits the latest neural ranking models to provide information access to the open datasets.

Studying the pandemic: In [620] a transfer learning algorithm is used to study the problem of intent detection of user utterances. The authors focus on cross-lingual transfer learning for intent detection across English, Spanish, French and Spanglish (Spanish+English) languages. In [621], data mining and content analysis techniques are used to process the Chinese social media posts to develop a model that predicts the number of covid-19 cases.

Tackling misinformation: Using machine learning techniques, it is shown in [622] that malicious covid-19 content including hate speech, disinformation and misinformation spreads across social media platforms. The study provides a generalized form of the public health R0 predicting the tipping point for multiverse-wide viral spreading, which suggests new policy options to mitigate the global spread of malicious COVID-19 content without relying on future coordination between all online platforms. Fake news are spreading and acting as a plague to journalism and media. They poison the reliability of sources and affect the government policies. It is important for media, like social media to detect and remove them as soon as they are generated. To tackle this, in [623], an algorithm is developed that automatically detects covid-19 related fake news. The authors use a dataset of 299 fake and 100 truthful news and extract different features including linguistic inquiry and word count engine from the data. Then a decision tree classifier is used to classify the data.

Governmental policies: In order to analyze India's policy in controlling the pandemic, data were collected from the Press Information Bureau in the form of the press release of government programs, policies, plans and achievements [624]. A text corpus of 260,852 words was collected and an unsupervised machine learning modeling that uses Latent Dirichlet Allocation (LDA) algorithm is performed on the data. The findings suggest that the nudges from the Prime Minister of India was critical in creating social distancing norms across the nation.

7. Understanding the Virus

One important challenge in managing the pandemic is to understand the virus and its properties. Some research use AI methods in this area. In [625], Linear Regression, KNN and SVM are used to find the protein sequence of the virus. In order to identify an intrinsic SARS-CoV-2 genomic signature, a machine-learning-based alignment-free algorithm is used in [626]. The method combines a supervised machine learning algorithm with digital signal processing combined with a decision tree classifier. Understanding the mutation rate of the virus is very important as it provides insight about how effective and long lasting a possible vaccine will be. Using LSTM algorithm, the mutation rate of SARS-CoV-2 is studied in [627], where the algorithm is applied to a dataset collected from patients from different countries. The authors study the nucleotide and codon mutation separately. The analysis suggest that a large number of Thymine and Adenine are mutated to other nucleotide, while codons are not mutating that rapidly. The LSTM model is used to predict the mutation rate of the virus in future.

In is important to understand the behavior of the virus via studying its protease and glycosylated spike protein that outlines the fusion site between the virus and host cells. Nevertheless, the Heptad Repeat 1 domain on the spike protein is the region that shows fewer mutations and so is a good target for developing inhibitor drugs. To study this, a Siamese Neural Network (SNN) is proposed in [628] that distinguishes SARS-Cov-2 virus from two different virus family, HIV-1 and Ebola.

In order to identify the origin of the virus, an AI based approach is presented in [629]. In this work, more than 300 genome sequences of the virus cases are collected and an unsupervised clustering is applied. The algorithm suggests that all the virus genomes belong to a cluster that also contains bat and pangolin virus genomes.

8. Datasets

One important need in the research about the pandemic and the disease is to establish organized framework and datasets, so researchers can have access to the data collected around the world. One interesting work is presented in [630], where Instagram is used to share datasets. A set of 48262 CT scan images from 282 normal and 15589 patients are collected and shared in [631]. In [255], a clean and segmented CT dataset called Clean-CC-CCII is presented by fixing the errors and removing some noises in a large CT scan dataset CC-CCII with three classes: novel coronavirus pneumonia (NCP), common pneumonia (CP), and normal controls (Normal). After cleaning, the dataset consists of a total of 340,190 slices of 3,993 scans from 2,698 patients. In [632, 633], a benchmarking for covid-19 machine learning models is presented. A dataset of 6200 X-ray images is presented in [272]. An open research dataset is presented in [634, 635] to facilitate the development of text mining and information retrieval. In [636], a survey on public medical imaging datasets is presented. In [637], a public covid-19 X-Ray image data collection is presented in which the frontal and lateral view imagery and metadata such as the time since the first symptoms, ICU status, survival status, intubation status and hospital location are recorded. A survey on the existing open datasts are available in [638]. In [639] some open datasets for monitoring, modeling and forecasting the epidemic is provided. A set of CT images is collected and presented in [640]. In [290], a dataset of 13,975 CXR is presented.

Open data resources about the pandemic are overviewed in [641].

9. Conclusion Remarks

Until the time writing this paper, there is no effective drug or vaccine against the disease and due to the rapid increase in the number of cases and the huge economic impact it has left, there is a need for effective medicinal approaches. In this respect, early detection, prediction and treatment of covid-19 cases is crucial for alleviating the damage. Around the world, governments are taking drastic measures, with huge economic impacts, to relieve the effect of the pandemic. Artificial Intelligence approaches seem to provide promising solutions for many of the problems we face now.

In this paper we reviewed the application of AI in battling against the pandemic. Until now, AI approaches have achieved rather satisfactory results. However, the application of AI algorithms on covid-19 research is at its infancy and there is still much room for improvement and new areas that AI can be used in tacking the problem. In this section we review the challenges we believe these systems face and suggest ways of managing them. Because of the diversity of the areas in which AI has been used, such a conclusion would be long with lots of points. Thus we decided to organize them in bullet points.

- One problem in benefiting from AI systems is that they require a large body of data to provide accurate results. This is particularly true for algorithms like deep learning that can easily suffer from over-fitting. At the first step, the community should build a common platform for researchers to share the data. Also, it is important to define standards in data collection including data formats, type of data collected, labeling, codes, etc. This is particularly a problem where the hospitals do not disperse the data easily.
- The type and format of the already collected data can be significantly different from one another as different hospitals and agencies have different protocols for data collection. To build a single dataset, data fusion approaches should be adopted. As a line of future research, exploring different data fusion methods for the task is suggested.
- Testing for covid-19 is usually based on RT-PCR method which is not very accurate. As reviewed in this paper, there are other data like blood and urine tests, symptoms like fever, muscle ache, loss of smell, and CT and X-Ray imaging can be indicative of the disease. We suggest the development of ensemble methods that get as input every type of discrimin-

ative data from different tests for more accurate tests. This has not yet been employed in the literature.

- Until the problem of small datasets exist, new approaches for dealing with small datasets should be explored. For example, for problems like identifying patients via CT images, when there is not large enough datasets, researchers adopt pre-trained networks on general datasets. This results in diminished performance. While one solution could be deep domain adaptation, it has not been explored in the literature yet. Another example is to explore new or existing training approaches that are better at handling the over-fitting problems.

- In almost all the area that we studied, the datasets are growing steadily. Everyday new data and research output are emerging that, in some cases, are even in contrast with previous data. In this regard, using incremental learning is a useful approach. We suggest all the models should be implemented in an incremental way. This is specifically true for epidemic and CT/X-Ray image data. About the epidemic, the data are arriving from different countries with different policies every day. So models should be able to adapt themselves with new data. Similarly for CT/X-Ray images, the datasets are growing rapidly.

- We expect to see more AI approaches be adopted in the image acquisition process, to provide better scan quality and reduced radiation dosage inflicted on patients. This is important as more people at the hospitals require X-Ray imaging and thus the risk of exposure is higher than ever now. One approach, for example, is to measure the body parameters of a patient, like fat or muscle percentage and body thickness to adjust the amount of applied X-Ray to the patient.

- Many of datasets that are collected suffer from noise. The type of noise differs from application to application. For example in processing images, the CT images usually suffer from noise. This noise can be noise of the imaging devices, or noise in labeling the records. Voice signals collected from patients, like cough may suffer from noise. Or data collected about the number of cases are usually hugely effected by noise.The source of this noise is that many of patients are asymptomatic, so not all patients are detected and reported cases usually underestimate the true values. Testing techniques for covid-19 is also not very accurate so many of cases are misclassifed. Research in the field of noise reduction is crucial if successful AI algorithms are to be developed.

- There are many research showing that processing voice signals can be helpful in extracting valuable information about people [642, 643, 644]. To the best of our knowledge, there is not much work performed on processing voice signals in identifying covid-19 patients. Coughing is one of the main symptoms of the disease it seems that the characteristics of coughing in covid-19 patients is different from that of flu or other diseases. Surely processing cough voice signals for diagnosis and predicting the severity of a patient can be considered as a future work.

- Most of the works performed in epidemiology, take only some of the effective parameters into account. For example, they only consider weather, governmental policies, etc. There are many parameters that can affect the pandemic. A detailed study on the parameters that affect the reproductive rate should be performed. Then, in any study on epidemiology, these parameters should be considered for prediction and analysis.

- Many of the problems in machine learning are optimization problems. For example training in ANN and DNN is an optimization problem. Existing approaches use gradient decent methods which are prone to getting trapped in local optima. Global search algorithms can be of help as they are less likely to get trapped in local optima [645, 646, 647, 648]. As a line of future work, using global search algorithms for training these machines when solving covid-19 related problems is suggested.

- There are many optimization problems in solving the problems caused by the pandemic. There has been some works that use evolutionary algorithms to solve them. Studying the fitness landscape of these problems can be helpful to better understand these problems and thus develop more successful algorithms [649, 650, 651, 652]. Thus one area of research for future works can be studying the fitness landscape of these problems.

- The pandemic has caused a surge in xenophobia and hate against people of other races. This surely is a threat against human right that should be managed quickly. Understanding the dynamics of this phenomenon is another challenge that can be managed easier via AI approaches.

- Smart watches and wearable devices are widely used. These can provide an infrastructure for development of AI systems for diagnosis, monitoring and advisory systems. These devices can be used to measure data for symptoms like fever, oxygen level, cough, etc., or traveling history of people and collect them in a shared database. The database can then be used to train AI systems for diagnosis or providing clinical advise to people. The data can also be used for epidemiological reasons by providing early warning to people and authorities for countermeasures like quarantining and social distancing.

- All the approaches reviewed in this article use black box AI algorithms, and to the best of our knowledge, there is not much work on proposing explainable AI techniques. Explainable AI is when the designed system can provide information and insight on how the algorithm has reached the decision [653, 654]. This is particularly important in diagnosis where AI systems work as assistance to the practitioners. In this environment, the reason the AI algorithms believe a particular decision or diagnosis should be made is very important in informing the final decision maker as the system would work as a consultant.

- This pandemic will one day be over; however, its future impact on economy, global health, education, manufacturing, political relations, etc. will remain. It is important to know how the problems caused by the disease would look like in future to be able to plan strategies from now as they may be easier to cope with at their infancy. Until now, there is not much work in predicting these. AI approaches can be used in both prediction and suggestion of ways of handling the problems that future may throw at humanity.

- One important challenge is to fill the gap between the research and impact. There are many research and new ideas around developing new AI systems, but to see the implementation in real world is another matter. There requires to be more tight cooperation between the research and practitioners.

Although there are many interesting works that apply AI in handling the problems that the pandemic has caused, as mentioned here, there are still many areas that can be explored. This pandemic has provided a challenging test for AI to prove its practicality in unprecedented real-world problems. If AI become successful in solving important problems, it will gain more respect from the society.

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

none