# Artificial intelligence as a powerful tool in overcoming substantial health problems of the COVID-19 pandemic

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## SUMMARY

**Introduction** This review aims to investigate modern methods of applying artificial intelligence to diagnose SARS Cov-2 and predict the development of potential emergencies.

**Methods** The most commonly used electronic databases, such as Scopus and Medline during 2020, were searched. A narrative approach was used to synthesize the extracted data.

**Results** In this review paper, it has been shown that the application of artificial intelligence plays a significant role in virus diagnosis and prognosis in clinical trials. It allows resources to be used much more rationally, such as respirators, in hospitals, during the treatment of SARS Cov-2 and the prediction of possible mortality. The obtained results are from the analysis performed on 120 papers and studies that were electronically taken from papers published on Scopus and Pub Med line. Most commonly used artificial intelligence techniques are convolutional neural networks and machine learning.

**Conclusions** Included studies showed that artificial intelligence can significantly improve the treatment of SARS Cov-2, although many of the proposed methods have not yet been clinically accepted. In addition, more effort is needed to develop standardized reporting protocols or guidelines on applying artificial intelligence into conventional clinical practice. This technology is suitable for fast and accurate diagnosis, prediction and monitoring of current patients and prognosis of disease development in future patients.

**Keywords:** machine learning; artificial intelligence; radiology; chest X-ray; CT

## INTRODUCTION

Data from a large number of patients with COVID-19 can be integrated and analyzed using machine learning algorithms to have better understanding of the pattern of virus spread, improve diagnostic speed and accuracy, develop new practical therapeutic approaches, and identify the most vulnerable populations based on individual genetic and physiological characteristics. Machine learning techniques are used in the taxonomic classification of the COVID-19 genome, the CRISPR-based COVID-19 detection test, predicting the survival of severely ill COVID-19 patients, and identifying potential candidates for anti-COVID-19 drugs [1, 2, 3].

The recent discovery that more and more young adults are suffering from severe COVID-19 symptoms has challenged an earlier observation that older people are at higher risk for COVID-19, indicating urgent need for comprehensive risk assessment based on personalized genetic and physiological characteristics. The human enzyme for the conversion of angiotensin 2 (ACE2), expressed in the epithelial cells of the lung, small intestine, heart, and kidney, is the entry receptor for the glycoprotein SARS-CoV-2 spike. Some researchers believe that increased ACE2 expression, using drugs that stimulate ACE2 for treatment of hypertension and diabetes, worsens the clinical outcomes of COVID-19 infection [3, 4].

Accordingly, the biochemistry (ACE2 expression level) and clinical data (age, respiratory pattern, viral load, and survival) of patients with COVID-19 can be analyzed by machine learning approaches to predict risk based on ACE2. Genetic polymorphism that has been shown in ACE2, conditioned by various genetic variations in the human genome, affects the efficiency of virus binding; therefore, the analysis of machine learning of genetic variants in asymptomatic, mild or severe patients with COVID-19 is performed to classify and predict patient resistance to potential COVID-19 infection [2, 5].

Neural network classifiers have been developed for extensive screening of patients with COVID-19 based on their different respiratory patterns and for analysis of thoracic CT images based on machine learning to automatically detect infected patients and monitor them during disease development [2–5].

Chest X-ray and CT produce a large amount of data on COVID-19 very quickly, enabling the development of

machine learning algorithms, as well as other forms of artificial intelligence. Methods that are highly adapted to the application of artificial intelligence, especially when it comes to diagnostics, are observed in this paper. Also, huge data files originating from various countries of the world have led to rapid development of artificial intelligence applications, that aim to speed up diagnosis and help elucidate various factors that affect the rate of transmission of this disease and the severity of the expected clinical picture are particularly discussed. The availability of objective tools for rapid assessment of patient health helps health professionals make difficult decisions about allocating scarce resources. For COVID-19, training of algorithms for predicting outcomes such as mortality, admission to the intensive care unit or the need for mechanical ventilation had a significant clinical effect. Availability of multiple chest X-rays at an early stage of the patient's disease, with accompanying respiratory disorders, are the strongest predictor of long-term outcome diseases. The inclusion of sequential chest X-rays in training artificial intelligence models reveals many pictorial characteristics of disease progression, which are inaccessible to human eye [5, 6].

In addition, machine learning to detect drugs allows the design and creation of new compounds similar to drugs against SARS-CoV-2. It can point us to protein structures that could be the basis of COVID-19 drugs, greatly accelerating traditional experimental approaches and serving as valuable information for formulating the COVID-19 vaccine [7].

Artificial intelligence and machine learning help us identify people who are most at risk for coronavirus infection by integrating electronic health records with a wealth of "data that is personal in nature and speaks to patients' habits". They can also determine which infected patients are more likely to get a more severe form of infection [8].

Because the symptoms and development of COVID-19 disease vary significantly from patient to patient, a simple approach to treatment is not applicable. Machine learning techniques can help us determine the most effective treatment for each patient based on observation data from previous patients, as it helps us answer key questions about when to undertake a therapeutic procedure. Machine learning can help us choose specific treatments for specific subgroups of patients to understand which treatments are appropriate for the population as a whole [8, 9].

**Machine learning as a tool in protection against COVID-19**

As the main methods of diagnostic imaging of patients, chest X-ray and CT quickly produced a large amount of data on COVID-19, enabling the development of machine learning algorithms, increased due to the existence of a pandemic, which has led to numerous publications around the world reporting on the applications of artificial intelligence to all aspects of diagnosis and treatment of COVID-19 [10].

When applying artificial intelligence to COVID-19, research questions run the risk of focusing too much on creating new machine learning models without considering its practical application and potential biases. Occasionally, the speed and accuracy of machine learning algorithms are derived based on performance in clinical scenarios that do not reliably reflect clinical practice. Sometimes comparisons between algorithm and human performance are unbalanced. In most cases, computer is trained to detect a particular abnormality (e.g., parenchymal diseases associated with COVID-19), while a radiologist is usually responsible for detecting any abnormality (such as pulmonary nodules or pulmonary emboli). Machine-based CT analysis is a promising COVID-19 screening tool and sometimes exceeds the reliability of PCR tests [11, 12].

Studies conducted during the pandemic were characterized by a high prevalence of the disease and the nature of the disease in selected participants, whose severity of the disease justified hospital admission and CT assessment. Ideally, algorithms should be trained to recognize the full spectrum of diseases, including asymptomatic and early-stage cases, so that machine-assisted CT interpretation can be reliably applied to real-world data. Further, consensus must be reached on the best data labeling strategy and whether to include only patients with real-time PCR-positive SARS-CoV-2 infection. It should be decided whether the data labeling should contain multidisciplinary information such as cough or fever, how the participant's exposure to an infected household member changes the training algorithm, etc. In most cases, machine-learning algorithms develop on retrospective, clinically indicated data that are often imperfect. Additionally, it is necessary to include the noise effect to improve the algorithm's clinical applicability [13, 14].

Without any doubt, COVID-19 offers many exciting opportunities for applied artificial intelligence research. As we learn more about the history of COVID-19, it is becoming increasingly clear that the disease is progressing in stages. The need to prevent deterioration and personalize preventive interventions has emerged as a priority. Currently, research on images focuses on diagnosis based on the appearance after the disease progresses. Detection of the disease in the earliest stages, when initiating appropriate therapy is most effective, would be useful to develop a prognostic tool, for many lung diseases, especially in combination with clinical data, which is especially important for patients who need intensive care and support for ventilation [15, 16].

An untapped resource in COVID-19 patients is the availability of chest X-rays at multiple time points in the early stages of the patient's disease. In other respiratory disorders, short-term disease behavior is the strongest predictor of long-term outcome. By including sequential chest X-rays in model training, new imaging features of disease progression can be detected, including those inaccessible to human eye. In general, although patients with comorbid diseases represent a population at high clinical risk, it is currently not possible to identify patients without underlying health problems but who also often develop similar disease progression. The availability of objective tools for rapid assessment of the patient's condition would help

healthcare professionals make difficult decisions about allocating scarce resources [17, 18].

Machine learning algorithms are often modular, which means that new algorithms generated during this pandemic could be successfully repurposed for other lung diseases in the future. There will always be a balance of risk and speed, and the key to this balance is defining the needs for which the solutions will have the most significant clinical value. With the right collaboration between clinical expertise and machine learning expertise, the current public health crisis could mark the beginning of a decade when artificial health intelligence is fulfilling its broad, transformative clinical impact [18, 19].

## Advantages of application of artificial intelligence in COVID-19 diagnostics

The main advantage of machine learning is its ability to "learn" how an individual's characteristics (risk factors), along with clinical and social information, can be mapped into personalized risk predictions. Although standard epidemiological approaches, such as Cock's model of proportional hazards, are not able to effectively combine data from different data sources and modalities (demographic, social, longitudinal, image, multi-omics), modern neural network-based learning techniques can easily and efficiently provide personalized risk predictions, updating them and improving the possibilities of their use. Such risk prediction mechanisms can be used to prevent, monitor and detect disease [20].

For people who are already infected with SARS-CoV-2, it is crucial to anticipate the risk of adverse events (including death) and the dynamics of the necessary health resources to provide appropriate care to patients. Key risk factors are the patient's age and / or the presence of comorbidities, such as hypertension, cystic fibrosis, transplant-related immunosuppression, and chemotherapy for cancer. Current risk assessment methods for infected patients use only a few factors (assessment of clinical weakness, number of comorbidities, previous therapeutic procedures, and administrative data from previous hospital admissions, to assess which patients are most at risk. These relatively simple approaches may be appropriate in the acute stages of an epidemic. However, they fail to capture and explain subtle interactions between age, specific comorbidities (including duration), assessments of the extent of organ dysfunction, and the impact of other relevant health factors [21, 22].

Reliance on such measures often leads to discovering previously undetermined, completely new risk factors - that is especially important for diseases that little is known about. These methods provide increasingly accurate subtypes of COVID-19 disease as more data are collected. They can define an estimate of the probability with which a patient may experience various adverse events and change that probability over time, allowing for improved prediction accuracy compared to conventional epidemiological methods [23].

As mentioned, patients diagnosed with COVID-19 have many possible disease outcomes in terms of incubation time and changes in lung oxygen capacity, and the development of disease severity. It provides a way to predict the dynamics of the patient's disease progression and an understanding of how certain events (worsening of symptoms) can abruptly change the dynamics of the disease. This is essential for rational use of systems that enable dynamic management of limited health resources [24, 25].

When it comes to patients, it is essential to know which patients require early admission to the hospital, when a patient can safely leave intensive care or be discharged from the hospital. Such timely admission and discharge questions are often answered based on simple basic rules (e.g., examining the latest measurements for several selected variables and making decisions based on limit values). However, such decisions should include data from the history of each patient. Using all available observations at any time, artificial intelligence, has the possibility of a deeper understanding of the patient's condition, and it can participate in making such a decision, predicting the patient's future health needs, pointing to significant predictors of the patient's treatment outcome (specific comorbidities that are likely to worsen the patient's prognosis with COVID-19) [26, 27].

Monitoring and collecting health data is expensive because it takes a lot of time and staff engagement, although not all data is equally valuable. Therefore, it is necessary to set priorities, what we must actively measure, when it should be measured, and on which patients and the monitoring of each patient should be active and transparent. Active reading of data and their appropriate selection by importance enable institutions to dynamically allocate hospital resources depending on the needs of their patients. This, in turn, allows physicians to make competent decisions about delaying treatment for conditions that are not immediately life-threatening so that resources can be used for critically ill patients with COVID-19 [28, 29].

Models based on artificial intelligence make it possible to monitor and determine the effects of existing medical treatments of individuals, given their specific features, which include existing comorbidities, creating conditions for choosing the best approach to treatment for each patient, which includes the use of mechanical ventilation and potentially new therapeutic treatments. Models based on Gaussian processes of contradictory generative network and deep neural network can help in experimental treatment phases, based on observational data, without resorting to randomized trials [30, 31].

They answer questions "what would happen to a given patient if mechanical ventilation were delayed for a few hours?" or "What would be the outcome of treatment if the appropriate experimental care procedure has been applied a week earlier? This can help us learn the best treatment plan for each individual when it comes to available health resources. This is not just about which intervention should be applied for each patient individually, but also about when a given patient needs a specific intervention, which is extremely important, given the limited available resources [32, 33].

Using longitudinal patient observation data, the counterfeit recurrence network is learned to predict counterfeit

health pathways according to different management plans for each individual. Such predictions can be made dynamically by modeling and updating the patient's condition over time to account for all past medical events. This way, it is possible to determine the time frame during which the intervention would be most effective and select a specific sequence of interventions that would result in the best outcome for each patient. In addition, this method can show when interventions, such as a mechanical ventilator, are not necessary for the patient and for how long their use can be delayed without significant deterioration in the patient's health [34, 35, 36].

Recently, improving the design of adaptive clinical trials has shown that their efficiency and effectiveness can be significantly improved through machine learning. Customizable ML-enabled clinical trials in recruiting patients in groups (instead of all at once), monitoring its effect on each group before recruiting the next group, so that instead of randomly recruiting patients, machine methods the studies make it possible to recruit subjects from the subgroups, more suitable for a particular type of treatment, thus requiring much fewer patients to check the effectiveness of treatment with a given drug. Another important application of ML in the field of RCT is a post-hoc analysis of clinical trials and in particular, identification of subpopulations that show the most similar response to a given type of treatment, which facilitates the treatment of specific subpopulations and understanding treatments that might be appropriate for the population as a whole [37, 38].

The problem of biased machine learning models can be solved by transfer learning methods, which implicitly deal with uncertainty in predicting individuals from populations not used for training. International cooperation could create an extensive data set containing data from multiple infected populations, and a unique two-step risk assessment model can be trained for such a data set and applied worldwide. Transfer learning models work well for disease prognosis in different countries or health systems [39].

Transfer learning is desirable for transferring models between populations and updating machine learning models for a given population over time. It shows how the disease develops within a given population over time, linking it to certain specifics of the patients themselves, using successive data series developed by Bayesian optimization technique to update the model with new information. When we provide information-based information to decision-makers based on artificial intelligence systems, it is important to determine what we know reliably and what we do not know. For this purpose, a technology has been developed to systematically quantify uncertainties in predictions, which follow from the machine-learning model. All data entered must include a confidence assessment so that decision-makers know when and for which patients they can trust the predictions provided by the artificial intelligence system and when they should be careful about the information obtained. Quantifying uncertainty in predicting outcomes at the patient level is crucial for hospitalization management and for making optimal therapeutic decisions. The obtained confidence interval in machine learning should cover the true outcome [40–48].

## CONCLUSIONS

The application of methods based on artificial intelligence can be achieved through three levels of human-machine interface: Interface at the individual level, implies the existence of mobile applications powered by GPS, which individuals install on their mobile phones. These applications can be used to target social distancing by informing individuals that they are in high-risk geographic locations where a significant number of COVID-19 cases have been diagnosed or where a significant number of virus carriers are currently present. The application of this system can be primarily based on software applications, which can be quickly connected to GP patient registries held in the NHS.

For public health risk assessments, the existing hospital EHR infrastructure can be supplemented with risk modeling applications that show alert clinicians to new risks in patients in each hospital. Such applications can be used for remote diagnosis and care of self-isolated persons with evident disease symptoms. The application of models based on artificial intelligence in hospitals relies on the existing hardware infrastructure to connect input data streams with software (driven by machine learning models). It shows the risks for patients at the clinical level.

At the national level, the artificial intelligence-human interface enables government officials and decision-makers to continuously update the latest epidemiological data on COVID-19, with a geographically stratified overall risk assessment and hospital occupancy rate for the entire population. This application can be directly linked to the NHS patient registration database and other applications to collect data on the risk to which a given population is exposed, enabling administrators to make selective strategic decisions about which locations to lock and which hospitals need more funding.

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# Veštačka inteligencija kao moćno sredstvo u prevazilaženju zdravstvenih problema u toku pandemije bolesti COVID-19

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**KRATAK SADRŽAJ**

**Uvod** Cilj ovog rada bio je da istraži savremene metode primene veštačke inteligencije u dijagnozi virusa SARS Cov-2 i da predvidi razvoj potencijalnih hitnih stanja.

**Metode** Pretražene su najčešće korišćene elektronske baze podataka, npr. Scopus i Medline, tokom 2020. godine. Za sintezu dobijenih podataka korišćen je narativni pristup.

**Rezultati** U ovom preglednom radu pokazalo se da primena veštačke inteligencije igra veoma važnu ulogu u dijagnozi i prognozi virusa u kliničkim ispitivanjima. Omogućava da se resursi (kao što su respiratori u bolnicama) koriste mnogo racionalnije tokom lečenja SARS Cov 2 i predviđanje mogućeg mortaliteta. Rezultati su dobijeni nakon analize izvedene na 120 radova i studija koje su elektronski preuzete iz radova objavljenih u bazama podataka Scopus i Pub Medline. Najčešće korišćene tehnike veštačke inteligencije su konvolucione neuronske mreže i učenje uz pomoć računara.

**Zaključci** Obuhvaćene studije pokazale su da veštačka inteligencija ima potencijal da značajno poboljša lečenje SARS Cov-2, iako mnoge od predloženih metoda još uvek nisu klinički prihvaćene. Iz toga sledi da je potrebno mnogo više napora za razvijanje standardizovanih protokola izveštavanja ili smernica o tome kako primeniti veštačku inteligenciju na konvencionalnu kliničku praksu. Ova tehnologija je pogodna za brzu i tačnu dijagnozu, predviđanje i praćenje pacijenata, odnosno prognozu razvoja bolesti kod budućih pacijenata.

**Ključne reči:** učenje uz pomoć računara; veštačka inteligencija; snimanje; RTG snimanje grudnog koša; CT

## UVOD

Podaci velikog broja pacijenata sa bolešću COVID-19 mogu se integrisati i analizirati uz pomoću algoritama na računarima kako bi se bolje razumeo obrazac širenja virusa, poboljšala brzina dijagnostike, razvili novi efikasni terapijski pristupi i identifikovali najugroženiji pripadnici populacije na osnovu individualnih genetskih i fizioloških karakteristika. Tehnike mašinskog učenja koriste se u taksonomskoj klasifikaciji genoma COVID-19, testu otkrivanja bolesti COVID-19 zasnovanog na detekcionom testu CRISPR, u predviđanju preživljavanja teško bolesnih pacijenata sa bolešću COVID-19 i u identifikovanju potencijalnih kandidata za lekove protiv bolesti COVID-19 [1, 2, 3].

Ranije zapažanje da su stariji ljudi pod većim rizikom od bolesti COVID-19 ponovo je postalo upitno nedavnim otkrićem da sve više mladih pati od ozbiljnih simptoma bolesti COVID-19, što ukazuje na hitnu potrebu za sveobuhvatnom procenom rizika na osnovu personalizovanih genetskih i fizioloških karakteristika. Ljudski enzim za konverziju angiotenzina 2 (ACE2), izražen u epitelnim ćelijama pluća, tankog creva, srca i bubrega, ulazni je receptor za glikoproteinski SARS-CoV-2 protein. Neki istraživači veruju da povećana ekspresija ACE2, do koje dolazi korišćenjem lekova koji stimulišu ACE2 za lečenje hipertenzije i dijabetesa, može pogoršati kliničke ishode infekcije COVID-19 [3, 4].

Shodno tome, biohemijski rezultati (nivo ekspresije ACE2) i klinički podaci (starost, respiratorni obrazac, virusno opterećenje i preživljavanje) pacijenata sa bolešću COVID-19 mogu se analizirati učenjem uz pomoć računara i predvideti rizik na osnovu ACE2. Pokazalo se da genetski polimorfizam ACE2, uslovljen raznim genetskim varijacijama u ljudskom genomu, utiče na efikasnost vezivanja virusa, pa se analizom uz pomoć računara kod asimptomatskih i pacijenata sa blagom i teškom kliničkom slikom može predvideti otpornost pacijenata na moguću infekciju COVID-19 [2, 5].

Na osnovu različitih respiratornih obrazaca, kao i analize torakalnih CT snimaka zasnovanih na mašinskom učenju, razvijeni su klasifikatori neuralne mreže za opsežni skrining pacijenata sa bolešću COVID-19, kako bi se automatski otkrili zaraženi pacijenti i nadgledali tokom razvoja bolesti [2–5].

U ovom radu uočeno je da RTG i CT grudnog koša daju vrlo brzo veliku količinu podataka o bolesti COVID-19, omogućavajući razvoj algoritama računarskog učenja kao i drugih oblika veštačke inteligencije, prilagođenih za brzu dijagnostiku. Takođe, posebna pažnja je posvećena ogromnim datotekama sa podacima poreklom iz različitih zemalja sveta koje su dovele do brzog razvoja aplikacija veštačke inteligencije, sa ciljem ubrzanja dijagnoze i pomoći u rasvetljavanju uticaja različitih faktora koji utiču na brzinu prenosa bolesti i težinu očekivane kliničke slike. Dostupnost objektivnih alata za brzu procenu zdravlja pacijenta pomaže zdravstvenim radnicima da donesu pravilne odluke o raspodeli oskudnih resursa. Za COVID-19, algoritmi kao što su smrtnost, prijem u jedinicu intenzivne nege ili potreba za mehaničkom ventilacijom imaju značajan klinički efekat. Dostupnost višestrukog rendgenskog snimanja grudnog koša u ranoj fazi bolesti, sa pratećim respiratornim poremećajima, najsnažniji je prediktor dugoročnih ishodnih bolesti. Uključivanje sekvencijalnih rendgenskih snimaka grudnog koša u modele veštačke inteligencije otkriva mnoge karakteristike progresije bolesti, koje su nevidljive ljudskim okom [5, 6].

Pored toga, učenje uz pomoć računara omogućava i njihov dizajn, ali i stvaranje novih jedinjenja i sličnih lekova protiv SARSCoV-2. Može nas uputiti na proteinske strukture koje mogu biti osnova lekova koji mogu ubrzati tradicionalne eksperimentalne pristupe i pružiti dragocene informacije za formulaciju vakcine protiv bolesti COVID-19 [7].

Veštačka inteligencija i mašinsko učenje mogu pomoći u identifikaciji ljudi koji su najviše izloženi riziku od infekcije koronavirusom integrišući elektronske zdravstvene kartone sa brojnim podacima lične prirode koji govore o navikama pacijenata. Veštačka inteligencija i mašinsko učenje mogu pomoći da se utvrdi kod kojih pacijenata je veća verovatnoća da će dobiti teži oblik infekcije [8].

Budući da se simptomi i razvoj bolesti COVID-19 uveliko razlikuju od pacijenta do pacijenta, jednostavan pristup lečenju nije primenljiv. Tehnike mašinskog učenja mogu pomoći da se odredi najefikasniji tretman za svakog pacijenta na osnovu podataka posmatranja prethodnih pacijenata, jer pomažu da se odgovori na ključna pitanja o tome kada treba preduzeti terapijski postupak. Mašinsko učenje nam može pomoći da odaberemo specifične tretmane za određene podgrupe pacijenata da bismo razumeli koji su terapijski postupci prikladni za populaciju u celini [8, 9].

### Računarsko učenje kao sredstvo za zaštitu od bolesti COVID-19

Kao glavne metode za postavljanje dijagnoze, rendgen i CT grudnog koša brzo su proizveli veliku količinu podataka o bolesti COVID-19 i omogućili razvoj algoritama mašinskog učenja, povećanih zbog postojanja pandemije, što je dovelo do brojnih publikacija širom sveta o primeni veštačke inteligencije na sve aspekte dijagnoze i lečenja bolesti COVID-19 [10].

Kada primenjuju veštačku inteligenciju na bolest COVID-19, istraživačka pitanja rizikuju da se previše usredsrede na stvaranje novih modela mašinskog učenja, pri čemu ne uzimaju u obzir njegovu praktičnu primenu i potencijalne pristrasnosti. Povremeno se brzina i tačnost algoritama mašinskog učenja izvode na osnovu performansi u kliničkim scenarijima koji ne odražavaju potpuno kliničku praksu. Ponekad su poređenja između algoritma i ljudskih karakteristika neuravnotežena. U većini slučajeva, računar je obučen za otkrivanje određene abnormalnosti (npr. parenhimske bolesti povezane sa bolešću COVID-19), dok je radiolog obično odgovoran za otkrivanje poremećaja (kao što su plućni čvorovi ili plućne embolije). Mašinska CT analiza je obećavajući alat za skrining bolesti COVID-19 i ponekad premašuje pouzdanost PCR testova [11, 12].

Studije sprovedene tokom pandemije pokazale su visoku prevalencu bolesti i prirodu bolesti kod izabranih učesnika čija je težina bolesti zahtevala prijem u bolnicu i CT procenu. U idealnom slučaju, algoritme treba prilagoditi za prepoznavanje čitavog spektra oboljenja, uključujući asimptomatske slučajeve i slučajeve u ranoj fazi, kako bi se interpretacija CT uz pomoć računara mogla pouzdano primeniti na podatke u realnom svetu. Dalje, mora se postići konsenzus o tome koja je najbolja strategija odabira podataka i da li treba uključiti samo pacijente sa pozitivnim PCR testom na infekciju SARS-CoV-2. Treba odlučiti da li podaci treba da sadrže multidisciplinarne informacije kao što su prisustvo kašlja ili temperature, i kako izloženost učesnika studije menja algoritam zaraženom članu domaćinstva. U većini slučajeva algoritmi računarskog učenja se razvijaju na osnovu retrospektivnih kliničkih podataka, koji su često nesavršeni. Pored toga, neophodno je uključiti i efekat buke kako bi se poboljšala klinička primenljivost algoritma [13, 14].

Nesumnjivo, COVID-19 nudi mnoge mogućnosti za primenjena istraživanja veštačke inteligencije. Kako sve više saznajemo o istoriji bolesti COVID-19, postaje sve jasnije da bolest napreduje u fazama. Potreba za sprečavanjem pogoršanja i personalizacijom preventivnih mera pojavila se kao prioritet. Trenutno se istraživanja fokusiraju na dijagnozu zasnovanu na izgledu nakon napredovanja bolesti. Otkrivanje bolesti u najranijim fazama, kada je započinjanje odgovarajuće terapije najefikasnije, bilo bi korisno za razvoj prognostičkih alata za mnoga plućna oboljenja, što je posebno važno za pacijente kojima je potrebna intenzivna nega [15, 16].

Neiskorišćeni resurs kod pacijenata sa bolešću COVID-19 je dostupnost rendgenskog snimanja grudnog koša u više vremenskih intervala u ranim fazama bolesti. Kod ostalih respiratornih poremećaja kratkotrajni tok bolesti je najsnažniji prediktor ishoda oboljenja. Uključivanjem sekvencijalnih rendgenskih snimaka grudnog koša u model, mogu se otkriti nove karakteristike napredovanja bolesti, uključujući i one nedostupne ljudskom oku. Generalno, iako pacijenti sa komorbiditetima predstavljaju populaciju sa visokim kliničkim rizikom, trenutno nije moguće identifikovati pacijente bez osnovnih zdravstvenih problema, kod kojih se često razvija slična progresija bolesti. Dostupnost objektivnih alata za brzu procenu stanja pacijenta pomogla bi zdravstvenim radnicima u donošenju teških odluka u situacijama sa oskudnim resursima [17, 18].

Algoritmi računarskog učenja su često modularni, što znači da bi se novi algoritmi generisani tokom ove pandemije mogli uspešno prenameniti za druge plućne bolesti u budućnosti. Kao i uvek, postoji ravnoteža rizika i brzine, a ključ za optimizaciju ove ravnoteže je definisanje potreba za rešenjima koja će imati najveću kliničku vrednost. Uz pravilnu saradnju kliničkih eksperata i stručnjaka za mašinsko učenje, trenutna kriza javnog zdravlja bi mogla označiti početak kada veštačka zdravstvena inteligencija ispunjava svoj široki, transformativni klinički uticaj [18, 19].

### Prednosti primene veštačke inteligencije u dijagnozi bolesti COVID-19

Glavna prednost učenja uz pomoć računara je njegova mogućnost da „nauči" kako se osobine pojedinca (faktori rizika), u kombinaciji sa kliničkim i socijalnim informacijama, mogu preslikati u personalizovana predviđanja rizika. Iako standardni epidemiološki pristupi, poput Kokovog modela proporcionalnih opasnosti, nisu u stanju da efikasno kombinuju podatke iz različitih izvora i modaliteta (demografski, socijalni, longitudinalni, slikovni), savremene tehnike učenja zasnovane na neuronskim mrežama mogu lako i efikasno pružiti personalizovana predviđanja rizika, ažurirajući ih i poboljšavajući mogućnosti njihove primene. Takvi mehanizmi predviđanja rizika mogu se koristiti za sprečavanje, praćenje i otkrivanje bolesti [20].

Za ljude koji su već zaraženi SARS-CoV-2, važno je predvideti rizik od neželjenih događaja (uključujući smrt), kao i dinamiku potrebnih zdravstvenih resursa, kako bi se pacijentima pružila odgovarajuća nega. Ključni faktori rizika su starost pacijenta i/ili prisustvo komorbiditeta, kao što su hipertenzija, cistična fibroza, imunosupresija povezana sa transplantacijom i hemoterapija kod obolelih od raka. Trenutne metode procene rizika za zaražene pacijente koriste samo nekoliko faktora – procena kliničkog stanja, broja komorbiditeta, prethodnih terapijskih postupaka i administrativnih podataka iz prethodnih prijema u bolnice. Ovi relativno grubi pristupi su korisni u akutnim

fazama epidemije, iako ne uspevaju da obuhvate i objasne suptilne interakcije između godina starosti, specifičnih komorbiditeta (uključujući trajanje), procene obima disfunkcije organa i uticaja drugih relevantnih zdravstvenih faktora [21, 22].

Oslanjanje na takve mere često dovodi do otkrivanja ranije neodređenih, potpuno novih faktora rizika – što je posebno važno za bolesti o kojima se malo zna. Ove metode pružaju mogućnost otkrivanja bolesti COVID-19 ukoliko je više prikupljenih podataka. Oni mogu definisati procenu verovatnoće za različite neželjene reakcije i promeniti tu verovatnoću tokom vremena, omogućavajući efikasnija predviđanja u poređenju sa konvencionalnim epidemiološkim metodama [23].

Kao što je pomenuto, pacijenti sa dijagnostikovanom bolešću COVID-19 mogu imati veliki broj mogućih ishoda bolesti, vezano za vreme inkubacije i promenu kapaciteta plućnog kiseonika, odnosno razvoja i toka bolesti. Nove metode ne pružaju samo mogućnost predviđanja dinamike napredovanja bolesti već i razumevanje kako određeni događaji (pogoršanje simptoma) mogu naglo promeniti dinamiku bolesti. Ovo je neophodno za racionalno funkcionisanje sistema sa ograničenim zdravstvenim resursima [24, 25].

Kada je reč o pacijentima, važno je znati koji pacijenti zahtevaju rani prijem u bolnicu, kada on može bezbedno napustiti intenzivnu negu ili biti otpušten iz bolnice. Na takva pitanja o pravovremenom prijemu i otpustu često se daje odgovor na osnovu jednostavnih osnovnih pravila (npr. najnovija merenja za nekoliko izabranih faktora i donošenje odluka na osnovu graničnih vrednosti), iako bi takve odluke trebalo da uključuju podatke iz zdravstvene istorije svakog pacijenta. Koristeći sva dostupna zapažanja u bilo kom trenutku, veštačka inteligencija bi, zbog mogućnosti dubljeg razumevanja stanja pacijenta, mogla učestvovati u donošenju takve odluke, uz predviđanje budućih zdravstvenih potreba pacijenta i ukazivanje na važne prediktore ishoda lečenja pacijenta (specifični komorbiditeti koji će verovatno pogoršati prognozu pacijenta sa bolešću COVID-19) [26, 27].

Nadgledanje i prikupljanje zdravstvenih podataka je skupo, jer oduzima puno vremena i angažovanja osoblja, a svi podaci nisu jednako vredni. Stoga je neophodno odrediti prioritete, šta se mora aktivno meriti, kada to treba meriti i na kojim pacijentima, uz aktivno praćenje svakog pacijenta. Aktivno čitanje podataka i njihov odgovarajući odabir omogućavaju institucijama da dinamički raspoređuju bolničke resurse u zavisnosti od potreba pacijenata. To omogućava lekarima da donose kompetentne odluke o odlaganju lečenja za stanja koja nisu odmah opasna po život, čime se resursi mogu koristiti za kritično bolesne pacijente sa bolešću COVID-19 [28, 29].

Modeli zasnovani na veštačkoj inteligenciji omogućavaju praćenje i utvrđivanje efekata postojećih medicinskih tretmana, uključujući postojeće komorbiditete, čime se stvaraju uslovi za izbor najboljeg pristupa lečenju za svakog pacijenta, i eventualnu upotrebu mehaničke ventilacije i potencijalno novih terapijskih mogućnosti. Modeli zasnovani na Gausovim procesima generativne kontradiktorne mreže i duboke neuronske mreže mogu pomoći u eksperimentalnim fazama lečenja, samo na osnovu podataka posmatranja, i bez randomiziranih ispitivanja [30, 31].

Oni odgovaraju na pitanja poput „šta bi se dogodilo sa datim pacijentom ako bi se mehanička ventilacija odgodila na nekoliko sati?" ili „Kakav bi bio ishod lečenja da je odgovarajući eksperimentalni postupak primenjen nedelju dana ranije?" Ovo nam

može pomoći da odlučimo koji je najbolji plan lečenja za svakog pojedinca u skladu sa dostupnim zdravstvenim resursima. Ovde se ne radi samo o tome koju intervenciju treba primeniti za svakog pacijenta pojedinačno već i o tome kada je određenom pacijentu potrebna specifična intervencija, što je izuzetno važno, s obzirom na ograničene resurse [32, 33].

Koristeći podatke longitudinalnog posmatranja pacijenta, mreža je naučena da predviđa puteve neadekvatnog lečenja u skladu sa različitim planovima za svakog pojedinca. Takva predviđanja se mogu dinamički davati modeliranjem i ažuriranjem stanja pacijenta tokom vremena, uzimajući u obzir informacije o prošlim medicinskim događajima. Na ovaj način je moguće odrediti vremenski okvir kada bi intervencija bila najefikasnija, odnosno odabrati određeni redosled intervencija koji bi rezultirali najboljim ishodom za svakog pacijenta. Pored toga, ovaj metod može pokazati kada intervencije, poput mehaničkog ventilatora, nisu neophodne za pacijenta i koliko dugo se njihova upotreba može odložiti, bez značajnog pogoršanja zdravstvenog stanja pacijenta [34, 35, 36].

Nedavni rad na poboljšanju dizajna adaptivnih kliničkih ispitivanja pokazao je da se njihova efikasnost i delotvornost mogu značajno poboljšati primenom mašinskog učenja. Prilagodljiva klinička ispitivanja omogućavaju upotrebu mašinskog učenja u regrutovanju pacijenata u grupe (umesto svih odjednom), nadgledanje efekta na svaku grupu, pre nego što se regrutuje sledeća grupa, tako da mašinske metode umesto slučajnog regrutovanja pacijenata omogućavaju regrutovanje najpogodnijih ispitanika, zahtevajući tako mnogo manje pacijenata za proveru efikasnosti lečenja određenim lekom. Druga važna primena mašinskog učenja u polju RCT je post-hoc analiza kliničkih ispitivanja, i posebno identifikacija subpopulacija koje pokazuju najsličniji odgovor na određenu vrstu lečenja, čime se olakšava lečenje i razumevanje terapijskog postupka, koji bi mogao biti prikladan za stanovništvo u celini [37, 38].

Problem pristrasnosti modela mašinskog učenja može se rešiti metodama učenja koje se implicitno bave neizvesnošću predviđanja kod pojedinaca iz populacija koji nisu učestvovale u obuci. Međunarodna saradnja mogla bi stvoriti skup podataka iz više zaraženih populacija, a jedinstveni model procene rizika u dva koraka mogao bi odabrati ove podatke i primeniti ih širom sveta. Modeli transfera učenja dobro funkcionišu u prognozi toka bolesti u različitim zemljama ili zdravstvenim sistemima [39].

Transfer učenja nije poželjan samo za prenos modela informacija između populacija već i za ažuriranje mašinskog učenja za određenu populaciju tokom vremena. Pokazuje kako se bolest razvija u određenoj populaciji tokom vremena, povezujući je sa određenim specifičnostima samih pacijenata, i koristeći serije podataka razvijene u skladu sa Bajesovom tehnikom optimizacije kako bi se model ažurirao novim informacijama. Važno je utvrditi šta pouzdano znamo a šta ne znamo kada donosiocima odluka pružamo informacije zasnovane na informacijama zasnovanim na sistemima veštačke inteligencije. U tu svrhu je razvijena i tehnologija za sistematsko kvantifikovanje neizvesnosti u predviđanjima, na osnovu modela mašinskog učenja. Svi uneti podaci moraju da sadrže procenu poverenja, tako da donosioci odluka znaju kada i za koje pacijente mogu da veruju predviđanjima koja pruža sistem veštačke inteligencije, a kada treba da budu oprezni u vezi sa dobijenim informacijama. Kvantifikovanje nesigurnosti u predviđanju ishoda presudno je

za upravljanje hospitalizacijom, ali i za donošenje optimalnih terapijskih odluka. Dobijeni interval poverenja u učenju uz pomoć računara treba da obezbedi pravi ishod [40–48].

## ZAKLJUČCI

Primena metoda zasnovanih na veštačkoj inteligenciji može se postići kroz tri nivoa interfejsa čovek–računar. Interfejs na individualnom nivou podrazumeva postojanje mobilnih aplikacija koje pokreće GPS, a koje pojedinci instaliraju na svoje mobilne telefone. Ove aplikacije mogu se koristiti za obezbeđivanje socijalnog distanciranja obaveštavanjem pojedinaca da se nalaze na visokorizičnim lokacijama gde je dijagnostikovan značajan broj slučajeva COVID-19 ili gde je trenutno prisutan značajan broj nosilaca virusa.

Za procenu rizika po javno zdravlje postojeća bolnička infrastruktura može se dopuniti aplikacijama za modeliranje rizika koje pokazuju i upozoravaju kliničare na nove rizike kod pacijenata u svakoj bolnici. Takve aplikacije mogu se koristiti za daljinsku dijagnozu i negu samoizolovanih osoba sa evidentnim simptomima bolesti. Primena modela zasnovanih na veštačkoj inteligenciji u bolnicama oslanja se na postojeću hardversku infrastrukturu za povezivanje ulaznih podataka sa softverom (vođenim modelima mašinskog učenja). Ovaj model prikazuje rizike za pacijente na kliničkom nivou.

Na nacionalnom nivou veštačka inteligencija – ljudski interfejs omogućava vladinim službenicima i donosiocima odluka da kontinuirano ažuriraju najnovije epidemiološke podatke o bolesti COVID-19, sa geografski stratifikovanom procenom rizika i stopom popunjenosti bolnica. Ova aplikacija se može direktno povezati sa bazom podataka o registraciji pacijenata i drugim aplikacijama za prikupljanje podataka o mogućem riziku kojem je populacija izložena, omogućavajući administratorima da donesu pravilne strateške odluke o tome koje lokacije treba zaključati i kojim bolnicama je potrebno više sredstava.