

**Can AI help in the fight against COVID-19?**

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**Abstract**

Artificial intelligence (AI) is playing several roles in healthcare responses to COVID-19. AI has helped map pandemic spread, forecast effects of different public health strategies, and trace contacts of confirmed cases. AI can facilitate earlier diagnosis by helping design rapid virus detection assays and analyse medical imaging data from suspected cases. It may identify patients at risk of clinical deterioration and poor outcomes, and pinpoint existing drugs for repurposing to treat the disease, propose new compounds for development, and suggest immunogenic viral proteins as targets for vaccines. Further research will likely accelerate emergence of effective AI-mediated responses to COVID-19.

**Can AI help in the fight against COVID-19?**

*Artificial intelligence is being used in several different ways to curb the current pandemic while demonstrating its potential to be even more effective for the next one*

The COVID-19 pandemic has accelerated efforts to incorporate artificial intelligence (AI) into clinical care at a time when, in many countries, health care systems are facing unprecedented strain on their resources. Prior to COVID-19, AI was already being widely exploited in healthcare,<sup>1</sup> and reviews are emerging of how it may assist in efforts to combat the current pandemic.<sup>2-5</sup> We describe several applications of AI relevant to COVID-19, some having immediate clinical application, others awaiting further refinement and evaluation.

**Detecting outbreaks, tracing contacts and shaping public health responses**

The AI-automated HealthMap system at Boston Children’s Hospital first alerted the world about the novel coronavirus on December 30, 2019, with a Canadian-based AI model, Blue Dot, issuing a similar alert a day later. Researchers warned of the top 20 destination cities for passenger arrivals from Wuhan to which the disease could spread.<sup>6</sup> These AI-enabled early warning systems use natural language processing (NLP) to scan social media, online news articles and government reports for signs of emerging pandemics to help inform governments and agencies such as the World Health Organization. AI-assisted analysis and modelling have also helped reconstruct the progression of an outbreak, elucidate transmission pathways,

identify and trace contacts, and determine real or expected impacts of various public health control measures (Box 1).<sup>7-11</sup>

How data are collected, and how these algorithms are deployed, raise difficult issues of consent, privacy, ethics and trade-offs between public and private good. Some countries, like Taiwan, have mandated a top down approach to data harvesting. Others, including Australia, encourage individuals to voluntarily download apps to input symptoms and COVID-19 status and permit health authorities access to identify potential contacts. However, the efficacy of app-mediated contact tracing depends on the level of population uptake, its ability to accurately detect infectious contacts, and the extent of adherence to self-isolation by notified contacts.<sup>12</sup> Expert position statements around design, scope, security and usage of such apps aim to prevent ‘mission creep’ towards unauthorised surveillance of society at large.<sup>13</sup>

### **Screening for people who might be infected**

Detecting COVID-19 in most health systems currently involves testing symptomatic patients presenting to stand-alone fever clinics, general practices or emergency departments. This takes time, consumes personal protective equipment and testing reagents, and poses transmission risk to staff. Digital symptom checkers soliciting information about symptoms and risk factors may screen out persons with very low likelihood of COVID-19 who do not require testing. In one pre-clinical study using hypothetical cases, an AI-powered chatbot identified patients with COVID-19 with sensitivity, specificity and overall diagnostic accuracy of 97%, 96% and 96% respectively.<sup>1</sup> However, a side by side test of eight different chatboxes on the same set of symptoms produced conflicting results,<sup>15</sup> suggesting other forms of data may also be needed.

Data from phone hotlines used to pre-screen based on travel history and symptoms,<sup>16</sup> and from sensors (cameras, microphones, temperature and inertial sensors) embedded within smartphones can all be used to detect COVID-19.<sup>17</sup> Neural networks embedded in cameras can distinguish patterns of tachypnoea due to COVID-19 from those caused by influenza or the common cold.<sup>18</sup> AI-powered thermal-scanning face cameras, capable of screening up to 200 people per minute, are being used by some Australian private hospitals to remotely

detect people with fevers, sweating and discolouration, and prevent them entering public spaces.<sup>19</sup>

### **Facilitating earlier diagnosis**

Diagnosing COVID-19 in sick patients presenting to hospital is currently performed by reverse transcriptase-polymerase chain reaction (RT-PCR) testing of nasopharyngeal and throat swabs. However, initial tests may only be 70% sensitive and turnaround times can be 24 hours or more.<sup>20</sup> ML models combined with virus detection systems using CRISPR (a tool which uses an enzyme to edit genomes by cleaving specific strands of genetic code) can rapidly design SARS-CoV-2 assays which have high sensitivity and speed.<sup>21</sup> AI has also been used to design, within a few weeks, point of care immunoassays for detecting viral antigens within 20 minutes, and prototype testing kits are in development.<sup>22</sup>

For hospitalisations where RT-PCR testing is unavailable, untimely, or yields negative results among patients highly suspected of suffering COVID-19 pneumonitis, deep learning algorithms applied to imaging data captured via chest X-rays or computed tomography (CT) chest scans may help early diagnosis. Studies suggest such cases demonstrate particular image patterns which may, combined with PCR testing, improve sensitivity to more than 90%.<sup>23,24</sup> However, radiological appearances of COVID-19 can overlap with other forms of lung inflammation, imaging can be insensitive or misleading in mild or asymptomatic cases,<sup>25</sup> and CT scanning creates a transmission risk. Hence the Royal Australian and New Zealand College of Radiology, and peer societies overseas, do not recommend CT scanning, including AI applications, to screen for COVID-19, or to diagnose it as a first-choice test.<sup>26</sup> For patients with lower respiratory tract illness who pose diagnostic uncertainty, deep learning algorithms applied to chest X-rays may be more feasible and impose less risk (Box 2).<sup>27-30</sup> However, current algorithms may perform poorly on the 80% of COVID-19 cases which are mild and under-represented in the data used to train and test these algorithms.

### **Predicting risk of deterioration and poor outcomes**

Predictive models able to identify, on admission, patients likely to deteriorate and require respiratory support can assist triage and resource allocation decisions. While older age, male gender, and certain comorbidities (hypertension, cardiovascular disease, diabetes) portend

worse outcomes,<sup>31</sup> these factors do not necessarily predict outcomes at the level of the individual, especially in younger patients. Some ML algorithms can more accurately estimate risk of death, development of acute respiratory distress syndrome (ARDS), and duration of hospitalisation (Box 3).<sup>32-36</sup>

### **Augmenting remote monitoring and virtual care**

Patients diagnosed with COVID-19 but not requiring hospitalisation can be monitored remotely at home using wearable devices measuring temperature, blood pressure, and oxygen levels, and transmitting this data to central virtual care units,<sup>37</sup> as exist in some Australian hospitals. AI-assisted analysis alerts staff to worsening status with activation of outreach care or patient recall for admission.

### **Developing potential treatments and vaccines**

As no effective treatments for COVID-19 currently exist, ML-based repurposing frameworks have used algorithms to identify baricitinib (used in rheumatoid arthritis)<sup>38</sup> atazanavir (anti-human immunodeficiency virus drug)<sup>39</sup> and afatinib (used in lung-cancer)<sup>40</sup> as potential treatments. Deep learning-based algorithms have helped design six new molecules that could halt SARS-CoV-2 replication,<sup>41</sup> and identify 10 promising agents from among 4,895 drugs.<sup>42</sup> Algorithms using NLP applied to the PubMed database have identified a poly (ADP-ribose) polymerase 1 (PARP1) inhibitor (CVL218) as a potential candidate, currently undergoing clinical testing.<sup>43</sup>

In expediting vaccine development, a deep learning system predicted targetable protein structures of SARS-CoV-2 within weeks, compared with months normally taken using traditional experimental approaches.<sup>44</sup> AI has identified viral protein epitopes most likely to be immunogenic, but not cross-reacting with human proteins,<sup>45</sup> while a reverse vaccinology tool integrated with ML has identified genes that code for potential eipitopes.<sup>46</sup>

AI-powered knowledge graphs can interrogate thousands of research papers and public documents to link genetic and biological properties of virus-caused diseases with composition and actions of existing drugs. The COVID-19 Open Research Dataset (CORD-19) contains over 29,000 articles about SARS-CoV-2 and other coronaviruses,<sup>47</sup> and is linked with several

ongoing Google Kaggle challenges that daily attract dozens of questions from multiple research teams.

### **Assisting hospital responses**

AI mapping tools can track hospital bed capacity and location, number and utilisation of ICU and hospital beds across the US.<sup>48</sup> Another tool tracks numbers of ventilated patients and uses modelling software to predict breaking points for healthcare networks,<sup>49</sup> estimating a shortage of 9,100 ICU beds and 115,000 non-ICU beds for routine care at the peak of the pandemic. At the front line, autonomous AI robots can transport drugs around the hospital and disinfect patients and hospital areas by emitting UV light, reducing interpersonal contact and saving medical and ancillary staff.<sup>5</sup>

### **Cautions and limitations**

While AI and ML can support COVID-19 responses across various domains, most applications have not reached operational maturity. The speed of research means many reports are pre-prints awaiting peer review, although still attracting media coverage and clinician adoption prior to proper evaluation. Most ML models have relied on Chinese data, limiting generalizability to other populations. Those trained on limited and unrepresentative data are susceptible to overfitting and can perform poorly on real-world datasets. Many diagnostic and prognostic ML models published to date are poorly reported, lack external validation, and have high risk of bias.<sup>50</sup>

Overcoming these constraints requires scalable approaches to data sharing. The 4CE international consortium is assembling electronic health data from over 96 countries for rapid visualisation of regional differences and global commonalities.<sup>51</sup> Such endeavours require balancing data privacy with public health concerns, and collaboration between clinicians, data scientists and policy-makers across international borders and between private and public sectors.

**Conclusion**

It is still too early to tell if—and to what extent—AI will impact on the COVID-19 outbreak. While it may not help much during the present pandemic, it may certainly help with the next one.

**Box 1. Public health applications**

- Baidu Inc's AI-mediated analysis of real-time mobile phone data in Wuhan, along with detailed case data including travel history, helped elucidate the role of case importation on transmission in cities across China and showed how the drastic quarantine and lockdown control measures implemented in China substantially mitigated the spread of SARS-CoV-2.<sup>7</sup>
- In Taiwan, the government utilized its rigid household registration system and mobile phone data to build an algorithm that tracked individuals based on their recent travel history.<sup>8</sup> Individuals identified as high risk were quarantined at home and tracked through their mobile phone to ensure compliance during the 14-day incubation period.
- The AI-enabled Australian Census-based Epidemic Model (ACEMod) has used data on age, occupation, gender, risk factors and contact rates from COVID-19 cases in predicting the likely impact of various public health control measures.<sup>9</sup> It indicated a combination of international arrival restrictions, case isolation and social distancing for at least 13 weeks, with compliance rates 80% or above, was the best approach to suppressing the pandemic.
- An AI vendor in the US is analysing a de-identified healthplan dataset of 30 million patients using more than 5000 variables, including lifestyle and socioeconomic factors, to create lists of people who should be contacted proactively to warn them of their vulnerability to COVID-19, and to create heat maps for local health authorities to use to prioritize healthcare resources and deploy preventive interventions.<sup>10</sup>
- ML models have assessed the infectious risk of a given geographical area at the community level by analysing large scale, real-time data on numbers of cases and deaths, demographic data, traffic density and social media data e.g. Reddit

posts.<sup>11</sup> The models estimate a risk index for that area which individuals and relevant authorities can use to implement appropriate mitigation strategies.

**Box 2. Diagnostic applications**

- A deep learning algorithm trained on 16,756 chest X-rays across 13,645 patients showed a diagnostic accuracy for COVID-19 of 92%.<sup>27</sup> Other algorithms developed using 5,941 chest X-rays across four classes (normal, bacterial pneumonia, COVID-19 pneumonia and non-COVID viral pneumonia) have yielded diagnostic accuracy of 90%.<sup>28</sup>
- Using deep learning algorithms trained on CT data, one study of only 312 cases achieved sensitivity, specificity and area under the curve (AUC) for COVID-19 of 94%, 95% and 0.98 respectively in an independent validation dataset of 1,255 cases.<sup>29</sup> In an accompanying reader study involving five radiologists, only one was slightly more accurate than the algorithm which was also twice as fast as the radiologists.
- Using data from 4,356 chest CT exams of 3,322 patients, a deep learning algorithm distinguished between COVID-19 and non-COVID pneumonia in independent test sets with a per-exam sensitivity, specificity and AUC of 90%, 96%, 0.96 and 87%, 92%, 0.95 respectively.<sup>30</sup>

**Box 3. Prognostic applications**

- In one study of 53 patients from two hospitals in Wenzhou, investigators used clinical and laboratory data to train an algorithm that identified mildly elevated alanine aminotransferase, the presence of myalgias, and an elevated haemoglobin, in this order, as being most predictive (70% to 80% accuracy) of subsequent onset of ARDS.<sup>32</sup>
- In another study of 133 patients, multivariate logistic regression identified age >55years, hypertension, low serum albumin, lymphopenia, elevated high-sensitivity C-reactive protein (hsC-RP) and progressive consolidation on chest CT scans as predictive of ARDS.<sup>33</sup> By combining clinical and temporal CT data, deep learning models outperformed the regression model (AUC of 0.954 versus 0.893).
- In regard to mortality risk, ML tools applied to 404 patients in Wuhan selected three biomarkers from a pool of 300 features as predicting high risk of mortality with more than 90% accuracy: elevated lactic dehydrogenase (measure of cell injury), lymphopenia (measure of cellular immunity), and raised hsC-RP (measure of inflammation).<sup>34</sup> In another study, neural networks trained on 42 clinical and demographic factors demonstrated 94% accuracy in predicting mortality.<sup>35</sup>
- In identifying patients at risk of long-term hospitalisation, a ML model trained on CT imaging data was able to identify such patients with predictive accuracy of 95%.<sup>36</sup>

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