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INTERVIEW

How could artificial intelligence aid in the fight against coronavirus?

An interview with Dr Hadi M Yassine and Dr Zubair Shah by Felicity Poole, Commissioning Editor

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1. Do you believe that artificial intelligence (AI) is the key to a cure for the coronavirus?

Dr Hadi: Artificial intelligence (AI) is one of the means or avenues to understand the virus and develop preventative and control measures. This includes but is not limited to: the usage of mathematical modeling to understand virus transmission, structural biology to determine virus structure and develop vaccines, computational biology to understand virus evolution, as well as docking studies to screen for drugs and inhibitors.

Dr Zubair: AI has the potential to help in all the stages of healthcare, from syndromic surveillance through to rapid diagnosis tests, and faster drug development. AI-based systems are already being deployed to diagnose coronavirus infection in China. A system named 'Coronavirus Chest CT Smart Evaluation System' developed by YITU technologies for the Shanghai Public Health Clinical Center (SPHCC) can now diagnose the suspected cases within seconds. AI may also help determine which patients should be prioritized for treatment. A population-wide mortality rate of 3% conceals the fact that young healthy people are much less likely to die than older people who may also have preexisting respiratory conditions. Machine learning methods can be trained to quickly learn which factors predict a higher risk of mortality, as well as the interventions and population-level controls, led to reduced harm. AI-based methods incorporating genetic, biological and environmental data could ultimately aid in the discovery of a cure for the coronavirus.

2. What is in-silico screening, and why is it particularly important in the case of the coronavirus outbreak?

Dr Zubair: In-silico is a term commonly used to refer to 'performed through computer simulation' rather than as part of a biological experiment. In-silico screening utilizes sophisticated computer modeling to simulate a biological experiment for medical analysis. Given the urgency of the situation due to the coronavirus outbreak, in-silico screening has fast-tracked the testing of various strategies for identifying effective drug treatment options. Researchers are using computational models for repurposing drugs by studying the drug-target interaction to recognize drugs that could act on viral proteins of COVID-19. The drugs that target relatively generic parts of various coronaviruses (i.e. Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS) and SARS-CoV-2) could be extremely effective and recommended for testing through randomized controlled trials. Currently, patients with the coronavirus infection are treated using repurposed drug Kaletra combined with other repurposed drugs, which are known to target parts of the replication machinery of other viruses similar to coronavirus as the World Health Organization (WHO) has noted clinical benefits in such combination [1].

Dr Hadi: Screening for antiviral drugs can be done using one of two main methods: Either using an *in vitro* system (cell culture) to robotically screen for thousands of compounds that can inhibit virus growth; or utilizing a solved viral protein structure and specific computer programs to screen for drugs that can bind the viral proteins (typically an active domain) and potentially inhibit the virus replication. Still, predicted anti-viral drugs must be tested in vitro and in vivo before testing them in clinical trials.

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3. How can techniques such as artificial intelligence and in-silico screening be applied to vaccine development for COVID-19?

Dr Zubair: In this difficult time of emergency, each promising technique, including AI and in-silico screening, must be utilized to expedite the drug discovery struggle against COVID-19. AI can quickly search large databases for drugs already available in the market that can be used against coronavirus or can assist in developing a new one in a short space of time. Insilico Medicine, which is specialized in AI-based drug discovery and development, used its AI-powered generative chemistry models to find hundreds of new drug-like compounds and molecules, which will be tested to ascertain their possible potential as medications for treating coronavirus infections. Their model generated these molecule structures in just four days. The scalability and speed of AI are crucial for accelerating the development of vaccines and drug trials.

Dr Hadi: A vaccine can be developed using different approaches, one of which is structure-based vaccine development. Previously, scientists used to grow the virus in cell culture or animals, then chemically inactivate it and used it as vaccine. Such treatment could alter the nature of the virus, which might induce wrong antibody responses and could cause more harm than good. To induce appropriate immune responses, i.e. antibodies that can neutralize the virus, we must first understand the target of these antibodies on the virus. This could be partially achieved by understanding the structure of the viral proteins, typically the surface ones that are used by the virus to bind and infect cells. Solved structures will reveal the charecterestics of the antigenic sites and functional domains on the surface glucoproteins (Spike protein in case of coronaviruses). Such information could help in designing a stable protein (or a protien subunit), which could then be mounted on a specific platform (nanoparticles) to be used as a vaccine.

4. How has monitoring and surveillance of disease outbreaks changed in recent years, and what does this mean for disease modeling?

Dr Hadi: According to some reports, more than 50% of emerging or reemerging infectious diseases are of zoonotic origin; i.e. transmitted to humans from animals, either directly or through intermediate hosts. This includes avian influenza, SARS/MERS/SARS-2 coronaviruses, Nipah virus and many others. Such pathogens are now being investigated using what we call "one health approach"; i.e. at the human-animal-environment interphase. Accordingly, viruses are surveyed and studied in their natural hosts, whether in birds in the cases of influenza viruses, or in bats in case of coronaviruses. These viruses might not be 100% identical to those isolated from human, however, sequence analysis can help in identifying factors that contribute to virus transmission from one host to another. For example, you can compare the sequence of the virus in human to that in a bat to determine the differences in certain functional sites (e.g. receptor binding domain, protease cleavage sites and others) that could influence virus transmission.

Dr Zubair: Until recently, surveys, registries, and information from health departments were the common means for public health surveillance. However, this has started to change, surveillance systems are now being designed to use large scale, publicly available, self-reported data sources such as social media, news sources, blogs, opinions, and other information sources. There is now enough evidence that the results produced by monitoring such sources are at least as good as results produced by using surveys, registries, and health departments reports. Modern surveillance systems now powered by AI and big data analytics using these sources extract important signals that are indicators of population-level health outcomes. It is something that costs less, is much faster, and much broader than what we can get from traditional surveillance systems, which can be resource-intensive and relatively slow to report.

AI also presented a new paradigm for epidemiology, complementing the previous disease modeling methods. Mathematical models were used to project the progression of infectious diseases to identify the likely outcomes of an outbreak. While the efficacy of these models mostly depends on the supplied parameters, the control response strategies for the outbreak may also make a significant difference to the spread of disease. Machine learning-based approaches are not only predicting more realistic parameters for disease modeling but also identifying best response strategies. For instance, AI-based models are now being used to identify at-risk populations or people who should be screened first, while also considering various scenarios and diseases AI can also find an optimal-mix of targets for public health communications to minimize the likely impact of the epidemic on the overall population [2].

5. What is the relevance of artificial intelligence and big data analytics in situations such as the recent coronavirus outbreak, and how can they help us prepare for future viral outbreaks?

Dr Hadi: It is proposed that every 100 years, a major pandemic will occur and claim the lives of thousands if not millions. In 1918, a major influenza pandemic (Spanish flu) resulted in the death of about 50 million people globally. Now, we are facing another pandemic with the SARS-2 coronavirus. Can these pandemics be predicted? Maybe! Predicting when such a 'zoonotic' disease will initiate an outbreak remains challenging; however, some studies suggests that AI could play a role in this regard. Using mathematical modeling, researchers were able recently to pinpoint, with 90% accuracy, the rodent species that are known to carry pathogens that can transmit to humans. A more complex algorithm may be used to predict the underlying dynamics of virus evolution and immune response to viral changes. For example, computation biology has been used to study HIV evolution in single patients, as well as the parallel evolvement of antibody responses to the virus in the elite controllers: 'are a group of people living with HIV who spontaneously control HIV viral load below the limit of detection for long periods of time in the absence of antiretroviral therapy'

Dr Zubair: Modern technologies such as AI and big data analytics is going to be a giant firewall against disease outbreaks and epidemics due to its potential for rapid detection, screening, and diagnosis. On 31 December 2019, a tech company specializing in AI-based infectious disease surveillance identified the coronavirus outbreak in Wuhan, hours after the earliest cases diagnosed by local hospitals, but far before an official announcement was made by Chinese authorities and the World Health Organization (WHO). The key to technology is big data. They employed machine learning and NLP techniques to crawl data from thousands of sources such as social media, news sources, digital media, airline ticketing data, public health reports, and population demographics, processing and synthesizing these data every 15 minutes to generate consolidated reports. When it comes to outbreak detections, AI-based models can be developed and trained to analyze massive amounts of data from heterogeneous sources, taking on a task that typically requires human experts to work tirelessly around the clock and with incredible speed. This is the real strength of AI-based methods, making analysis more efficient and scalable, complementing and learning from human intelligence to support timely decision-making. As with coronavirus, AI is likely to play a critical role in the early detection of future outbreaks to stop or limit spread and save lives.

6. How has social media impacted the recent coronavirus outbreak, and can it be used to benefit public health?

Dr Hadi: Social media is a double-edged sword. Still, international organizations (the WHO and others), local institutions (ministries) and individual scientists have been trying their best to deliver the correct information.

Dr Zubair: Social media can play an important role as a source of data for detecting outbreaks but also in understanding public attitudes and behaviors during a crisis, as a way to support crisis communication and health promotion messaging. In this digital era, information, especially on social media, flows faster than the disease spreads. Although its data is noisy and biased, important signals can be extracted from the social media that are indicators of public health outcomes. Examples that are validated against outcome data include infectious diseases like influenza, cholera and even cardiovascular mortality. Social media *is* a double-edged sword. While it can support rapid communications and surveillance, it is also used to disseminate fake news and misinformation. Studies with poor clinical evidence receive more responses in the media than studies with high-quality evidence [3]. Misrepresentation of lower-quality evidence in media can have negative effects on health decisions [4] and opinions developed by misinformation can remain for years even after providing contradictory evidence [5]. Social media can be used to spread rumors, persuade and manipulate the public, and cyberbullying leading to depression, anxiety, social isolation, and suicide. An article published in the *Science* journal investigated the spread of true and false news online and found that lies spread much faster than the truth [6]. Rumors can have a significant impact on society. Rumors of coronavirus have fueled panic-buying in many countries. Fake news sparked fears of coronavirus in India. Many people who were exposed to social media posts claiming coronavirus was the result of failed bioweapon experiments may now believe this conspiracy. A woman received treatment after eating 1.5kgs of garlic to avoid contracting the coronavirus. A small town in Ukraine was also torn apart by rumors of coronavirus, leading to mass chaos during which nine police officers were injured and five people were officially charged, and 25 were arrested for rebelling.

7. What are some of the downsides of using artificial intelligence and what are some of the challenges around data protection?

Dr Hadi: For the most part, AI findings must be validated in the lab as well as in animals. Furthermore, whatever works in animals won't necessarily work in humans. Accordingly, vaccines and drugs are initially tested in mice followed by none-human primates before

testing in human. In humans, drugs and vaccines are tested in different phases clinical trial to evaluate safety, immunogenicity and efficay.

Dr Zubair: It mostly depends on where AI is being used or which field to consider. Technology has transformed the way we live our lives, ranging from the way we interact with friends and loved ones to the what and how we purchase and seek out information. Social media is everywhere and unavoidable and is designed to be compelling largely because of AI-based attention capturing algorithms. The growing influence of technology has started to impact our various activities, especially in children who are now playing games on a computer that are based on AI and are quite addictive, in favor of physical activity. Adults aren't unimpacted either, Fear Of Missing Out or FOMO is just one perpetuation of technology. Social isolation that is largely due to technological intervention in our lives has reached an all-time high. Digital addiction is now officially considered a mental disorder by the WHO. Over-trust and reliance on technology are stimulated traits that becoming embedded in our personalities. Most of these problems are due to the design of these technologies that may be somehow linked to artificial intelligence.

AI-based algorithms need complete, accurate, clean, and multifaceted data for model training to produce any useful results. To this end, AI presents a new set of challenges about security and data privacy. When it comes to healthcare, handling gigabytes of data by these disparate AI-based systems is uncharted territory. High-profile data breaches have a much wider financial and reputational impact on stakeholder profiles.

8. What do you think the next decade holds for the use of artificial intelligence in your research fields?

Dr Hadi: It is hard to answer this question at this point. In my lab, we focus mostly on wet lab work more than AI. Still, we do use AI in various field, including, virus evolution (influenza and coronaviruses), docking studies to find anti-viral drugs, and modeling of mutations that can influence vaccine efficacy (e.g. rotavirus). This field is still very much in its infancy in the State of Qatar, and we need to do a lot in terms of capacity building before we can achieve high levels of performance.

Dr Zubair: AI-based systems are already being used in the diagnosis of several health conditions including detecting lung cancer and strokes using CT scans, detecting lesions in skin images, evaluating the risk of sudden cardiac death using cardiac MRI images and electrocardiograms, and discovering indicators of diabetic retinopathy using eye images. In the future, we may witness much more than this, including fully autonomous health bots that can offer diagnosis and treatments, ranging from prescriptions to surgeries. AI-powered diagnostic products are growing and becoming cheaper. Companies will install such systems in public places such as shopping malls, stadiums, and airports under the pay-per-use business model. Nanox, a global company specialized in AI-based imaging systems, has already announced the mass deployment of its products. They have launched a digital X-ray device accompanied by AI-based software and are offering it on a pay-per-scan business model. With AI, big data technologies and advancement in computational powers, data from such systems with mass deployment accompanied by the Internet of things (IoT) and social media data, will give rise to large-scale surveillance systems that can predict outbreaks much faster, allowing better control, strategy formulation, resource allocations, and impact management, which will eventually make preventive healthcare common practice.

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Declaration of Interest

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Dr Zubair Shah received a M.S. degree in computer system engineering from Politecnico di Milano, Italy, and a PhD degree from the University of New South Wales, Australia. He has been a Research Fellow from 2017-2019 at Australian Institute of Health Innovation, Macquarie University, Australia. Dr Shah is currently an Assistant Professor at the Division of ICT, College of Science and Engineering, Hamad Bin Khalifa University, Qatar. His expertise is in the field of artificial intelligence, big data analytics and its application to health informatics. His research is focused on health informatics, particularly to public health using social media data (e.g., Twitter) and news sources to identify patterns indicative of papulation level health. He has developed vaccine surveillance system for Australian

Twitter users using social media data and designed algorithms to identify health-related misinformation on social media and its effect on papulation health. Dr. Shah's contribution in the field also includes the development of methods to identify current events on Twitter in near real-time. He has published his work in various IEEE Transactions and A-tier international journals and conferences.

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