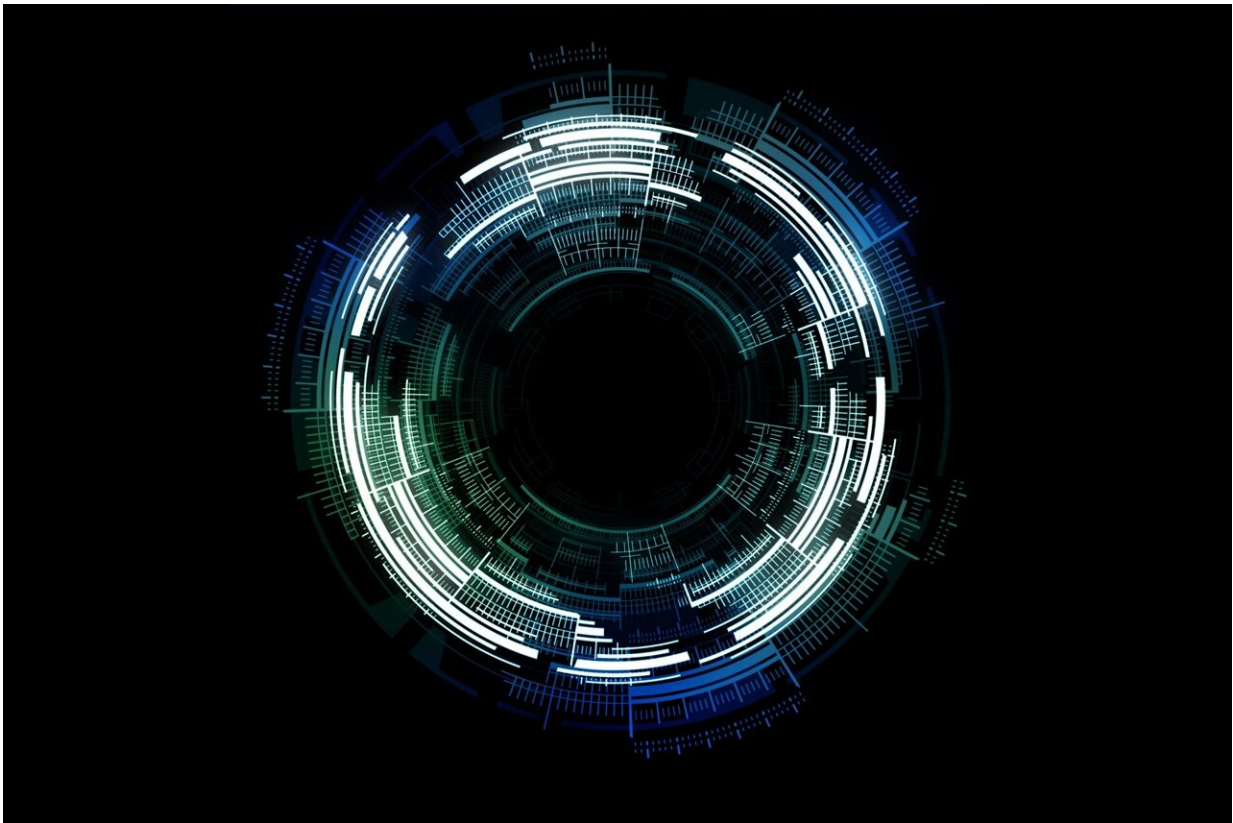


Machine learning uncovers the best drug combos to prevent COVID recurrence

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A groundbreaking machine-learning study has unmasked the best drug combinations to prevent COVID-19 from coming back after an initial infection. It turns out these combos are not the same for every patient.

Using real-world data from a hospital in China, the UC Riverside-led study found that individual characteristics, including age, weight, and additional illness determine which [drug combinations](#) most effectively reduce recurrence rates. This finding has been [published](#) in the journal *Frontiers in Artificial Intelligence*.

That the data came from China is significant for two reasons. First, when patients are treated for COVID-19 in the U.S, it is normally with one or two drugs. Early in the pandemic, doctors in China could prescribe as many as eight different drugs, enabling analysis of more [drug](#) combinations. Second, COVID-19 patients in China must quarantine in a government-run hotel after being discharged from the hospital, which allows researchers to learn about reinfection rates in a more systematic way.

"That makes this study unique and interesting. You can't get this kind of data anywhere else in the world," said Xinping Cui, UCR statistics professor and study author.

The study project began in April 2020, about a month into the pandemic. At the time, most studies were focused on death rates. However, doctors in Shenzhen, near Hong Kong, were more concerned about recurrence rates because fewer people there were dying.

"Surprisingly, nearly 30% of patients became positive again within 28 days of being released from the hospital," said Jiayu Liao, associate professor of bioengineering and study co-author.

Data for more than 400 COVID patients was included in the study. Their average age was 45, most were infected with moderate cases of the virus, and the group was evenly divided by gender. Most were treated with one of various combinations of an antiviral, an anti-inflammatory, and an immune-modulating drug, such as interferon or hydroxychloroquine.

That various demographic groups had better success with different combinations can be traced to the way the virus operates.

"COVID-19 suppresses interferon, a protein cells make to inhibit invading viruses. With defenses lowered, COVID can replicate until the [immune system](#) explodes in the body, and destroys tissues," explained Liao.

People who had weaker immune systems prior to COVID infection required an immune-boosting drug to fight the infection effectively. Younger peoples' immune systems become overactive with infection, which can lead to excessive tissue inflammation and even death. To prevent this, [younger people](#) require an immune suppressant as part of their treatment.

"When we get treatment for diseases, many doctors tend to offer one solution for people 18 and up. We should now reconsider age differences, as well as other disease conditions, such as diabetes and obesity," Liao said.

Most of the time, when conducting drug efficacy tests, scientists design a clinical trial in which people having the same disease and baseline characteristics are randomly assigned to either treatment or control groups. But that approach does not consider other medical conditions that may affect how the drug works—or doesn't work—for specific sub-groups.

Because this study utilized real-world data, the researchers had to adjust for factors that could affect the outcomes they observed. For example, if a certain drug combination was given mostly to older people and proved ineffective, it would not be clear whether the drug is to blame or the person's age.

"For this study, we pioneered a technique to attack the challenge of confounding factors by virtually matching people with similar characteristics who were undergoing different treatment combinations," Cui said. "In this way, we could generalize the efficacy of treatment combinations in different subgroups."

While COVID-19 is better understood today, and vaccines have greatly reduced [death rates](#), there remains much to be learned about treatments and preventing reinfections. "Now that recurrence is more of a concern, I hope people can use these results," Cui said.

Machine learning has been used in many areas related to COVID, such as disease diagnosis, vaccine development and drug design, in addition to this new analysis of multi-drug combinations. Liao believes the technology will have an even bigger role to play going forward.

"In medicine, [machine learning](#) and [artificial intelligence](#) have not yet had as much impact as I believe they will in the future," Liao said. "This project is a great example of how we can move toward truly personalized medicine."

More information: Song Zhai et al, Learning from real world data about combinatorial treatment selection for COVID-19, *Frontiers in Artificial Intelligence* (2023). [DOI: 10.3389/frai.2023.1123285](https://doi.org/10.3389/frai.2023.1123285)

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