Drug promoted by Trump as coronavirus 'game changer' increasingly linked to deaths

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For two months, President Trump repeatedly pitched hydroxychloroquine as a safe and effective treatment for coronavirus, asking would-be patients "What the hell do you have to lose?"

Growing evidence shows that, for many, the answer is their lives.

Clinical trials, academic research and scientific analysis indicate that the danger of the Trump-backed drug is a significantly increased risk of death for certain patients. Evidence showing the effectiveness of hydroxychloroquine in treating covid-19 has been scant. Those two developments pushed the Food and Drug Administration to warn against the use of hydroxychloroquine outside of a hospital setting last month, just weeks after it approved an emergency use authorization for the drug.

Alarmed by a growing cache of data linking the anti-malaria drug to serious cardiac problems, some drug safety experts are now calling for even more forceful action by the government to discourage its use. Several have called for the FDA to revoke its emergency use authorization, given hydroxychloroquine's documented risks.

"They should say, 'We know there are harms, and until we know the benefits, let's hold off,' " said Joseph Ross, a professor of medicine and public health at Yale University, who added that the original authorization may have been warranted but new evidence has emerged about the drug's risks.

"I'm surprised it hasn't been revoked yet," said Luciana Borio, who served as director for medical and biodefense preparedness of the National Security Council and was acting chief scientist at the FDA.

Testimony this week from a former top vaccine official removed from his post last month further highlighted allegations that Trump's White House pressured government scientists to quickly sign off on the untested drug in March, at the same time the president was pitching it as a "game changer."

Rick Bright, former director of the Biomedical Advanced Research and Development Authority, told Congress on Thursday that political pressure forced "dozens of federal scientists" to spend a harried 48-hour stretch rushing to put together a protocol for approving hydroxychloroquine for widespread use in covid-19 patients. Ultimately, that approach wasn't taken. The FDA issued an emergency authorization for hospitalized covid-19 patients who cannot participate in a clinical trial.

In his whistleblower complaint, Bright said he was removed from his position in part because of his reluctance to promote the use of chloroquine and hydroxychloroquine, because they had not been tested and deemed safe for treating covid-19.

“It’s important to use available clinical data,” Bright told lawmakers. “And if we know there are potential risks, we need to make sure that we are cognizant of those risks and make sure those drugs are used in a very safe and controlled manner.”

The White House did not respond to requests for comment. Health and Human Services Secretary Alex Azar attacked Bright on Thursday, saying “his allegations do not hold water.”

In a recent interview, FDA Commissioner Stephen Hahn denied that he was pressured to authorize hydroxychloroquine: “I can assure you 100 percent that the president has never pressured me to make a decision regarding any regulatory aspect of the FDA’s work.”

The FDA said in a statement Friday that it is continuing to evaluate its emergency use authorization for chloroquine and hydroxychloroquine, as it does with all such authorizations for drugs to ensure their continued safety.

"In general, the FDA may revise or revoke an EUA under certain circumstances, including information related to linked or suspected adverse events, newly emerging data that may contribute to revision of the FDA's initial conclusion that a product may be effective against the particular threat or a material change in the risk/benefit assessment based on evolving understanding of the disease or condition," the statement said.

Trump has continued to promote hydroxychloroquine without reservation while attacking those who question its effectiveness. He has described Bright as a "disgruntled employee" who is resisting the proposed treatment without cause.

"So we have had some great response, in terms of doctors writing letters and people calling on the hydroxychloroquine," Trump told reporters Thursday. "And this guy is fighting it. There's no reason to fight it. There's no reason. But more importantly than that, we've had tremendous response to the hydroxy."

But doctors, health experts and officials from Trump's own administration say the evidence does not back up the president's positive assertions. Those assertions, which Trump has claimed are partly based on "a feeling," could be costing lives, they said.

Yogen Kanthi, assistant professor in the division of cardiovascular medicine at the University of Michigan, said that it has been clear that the combination of hydroxychloroquine and azithromycin — used to treat bacterial infections — could lead to cardiac arrhythmias, which cause the heart to beat irregularly or too fast or slow. Many patients hospitalized for covid-19 had underlying cardiovascular disease that put them at higher risk for arrhythmias, "so it shouldn't be surprising we saw an increase in death," he said.

"The question has been answered that if you have the infection and it's significant enough to be in the hospital, the drug doesn't seem to do anything for you," he said. "It may be the horse is out of the barn."

Many hospitals have stopped using the drug outside of clinical trials.

"We no longer are keeping large quantities and have returned most of it," said Nishaminy Kasbekar, director of pharmacy for the Penn Presbyterian Medical Center in Philadelphia. "I think they should revoke the EUA because clearly based on the data it is no longer considered a treatment for covid."

Some doctors, including one in Texas who is also a Republican committeeman, have continued to give the drug to coronavirus patients — with mixed results.

A study of Veterans Affairs patients hospitalized with the coronavirus found no benefit and higher death rates among those taking hydroxychloroquine, researchers said last month.

More than 27 percent of patients treated with hydroxychloroquine died, and 22 percent of those treated with the combination therapy died, compared with an 11.4 percent death rate in those not treated with the drugs, the study said.

The National Institutes of Health announced Thursday that it had begun a clinical trial of 2,000 adults to determine if the combination of hydroxychloroquine and azithromycin — the cocktail touted by Trump — works as a therapeutic for those with coronavirus.

"Although there is anecdotal evidence that hydroxychloroquine and azithromycin may benefit people with COVID-19, we need solid data from a large randomized, controlled clinical trial to determine whether this experimental treatment is safe and can improve clinical outcomes," Anthony S. Fauci, the nation's top infectious disease expert, said in a statement.

While Fauci has cautioned against drawing broad conclusions from anecdotal evidence, Trump's promotion of the drug has been almost exclusively based on personal stories he has heard — often on cable news. He has largely ignored scientific studies to pitch the drug without caveat.

In a tweet shared 102,800 times and liked 384,800 times on March 21 Trump claimed that "HYDROXYCHLOROQUINE AZITHROMYCIN, taken together, have a real chance to be one of the biggest game changers in the history of medicine."

He invited several recovered coronavirus patients to the White House last month, including some who said hydroxychloroquine saved their lives.

From mid-March through early April, Trump touted the drug as a potential panacea while downplaying any potential risks.

"The nice part is it's been around for a long time, so we know that if things don't go as planned, it's not going to kill anybody," he told reporters on March 19.

The president's associates, including Fox host Laura Ingraham and his personal attorney, Rudolph W. Giuliani, have also pushed the drug as a treatment for covid-19 in private Oval Office meetings and phone calls.

Some Republican lawmakers have continued to promote hydroxychloroquine while attempting to defend Trump's handling of the coronavirus pandemic, which has killed more than 86,000 Americans.

"When you're the physician at the bedside, and there is a medication that has promise, and that has a safety profile that we understand — doctors will use this medication offline," Rep. Larry Bucshon (R-Ind.) told Bright during Thursday's hearing. "That's what's happening. Whether that's right or wrong, it might take us years to prove, but in the meantime, people can die."

The Trump administration deployed tens of millions of doses of the drug from the Strategic National Stockpile as the president promoted the FDA's emergency use authorization. His repeated statements that the drug had been fully "approved" by the FDA in record time added to the false sense that hydroxychloroquine had been vetted and declared safe for use, experts said.

While the FDA didn't intend for the authorization to signal an endorsement, many physicians and patients interpreted it that way, especially with "political figures saying the FDA had approved the drug," said Jesse Goodman, former chief scientist at the FDA and now a Georgetown University professor.

"There's a misperception out there that the EUA means that the FDA has approved the drug," said Aaron S. Kesselheim, a professor of medicine at Harvard Medical School. "That's wrong, of course, but it's a widespread misconception driven by irresponsible statements from certain politicians and members of the media."

Goodman and Kesselheim are among a growing number of medical experts calling for the FDA to revoke its emergency use authorization for hydroxychloroquine in light of new evidence about its risks.

While an emergency use authorization is not a full-fledged approval by the FDA, it allows unapproved drugs and devices to be used during a public health emergency. The standard for an emergency authorization is that the agency "determines that the known and potential benefits of the medical products for their intended uses outweigh their known and potential risks," according to the agency.

Mark McClellan, who was FDA commissioner during President George W. Bush's administration, said he disagreed with calls to revoke the authorization. He called for it to be strengthened with additional warnings about side effects for those with heart disease, adding that removing the emergency authorization could create access issues for people who need the drug for ailments other than covid-19. In weeks before the Veteran's Administration study was released in late April, there was a steady stream of warnings from different physician groups about the potentially deadly side effects of hydroxychloroquine. On Apr. 8, the United States' three cardiology medical groups urged "caution" in using the combination. On Apr. 21, a National Institutes of Health panel recommended against using hydroxychloroquine with azithromycin due to potential toxic effects.

While hydroxychloroquine is approved by the FDA to treat malaria, rheumatoid arthritis and lupus, some medical groups have long voiced concern that using it for coronavirus patients was particularly risky.

Several studies have been published since then that support those initial findings. Doctors in Brazil stopped a trial of chloroquine, closely related to hydroxychloroquine, after 11 patients died. They reported in JAMA Open Network on April 24 that in 81 patients, those who took high doses of the drug had a 3.6-fold higher death rate as compared to a lower dose group.

Brazil's top health official resigned Friday following reported disagreements with President Jair Bolsonaro over the efficacy of the anti-malarial drug in curbing the rapid rise of coronavirus in Latin America's largest country.

The departure of the oncologist Nelson Teich, who resigned less than one month after becoming health minister, came as Bolsonaro has followed Trump's lead in wagering heavily on the drug. He has ordered its mass production despite serious questions over its side effects and its effectiveness in a country that now has the worst outbreak in the Southern Hemisphere.

Many public health officials have called for Trump to defer to his medical experts, a push that intensified last month after the president pondered aloud whether light or disinfectant could be used internally to kill the coronavirus.

"Data-free advocacy for projects rarely turns out well," said Peter Lurie, a former top FDA official and president of Center for Science in the Public Interest who has criticized the promotion of hydroxychloroquine by politicians. "This was a product that never had a solid basis for believing it worked, and the data that has since emerged are not encouraging. The best thing to do is to leave drug review to the experts. That goes for hydroxychloroquine, it goes for bleach and it goes for ultraviolet light as well."

Terrence McCoy contributed to this report.