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Don’t rush to deploy COVID-19 vaccines and drugs without sufficient safety guarantees

We must urgently develop measures to tackle the new coronavirus — but safety always comes first, says Shibo Jiang.

Shibo Jiang

Around the world, I am seeing efforts to support ‘quick-fix’ programmes aimed at developing vaccines and therapeutics against COVID-19. Groups in the United States and China are already planning to test vaccines in healthy human volunteers. Make no mistake, it’s essential that we work as hard and fast as possible to develop drugs and vaccines that are widely available across the world. But it is important not to cut corners.

Vaccines for measles, mumps, rubella, polio, smallpox and influenza have a long history of safe use and were developed in line with requirements of regulatory agencies.

I have worked to develop vaccines and treatments for coronaviruses since 2003, when the severe acute respiratory syndrome (SARS) outbreak happened. In my view, standard protocols are essential for safeguarding health. Before allowing use of a COVID-19 vaccine in humans, regulators should evaluate safety with a range of virus strains and in more than one animal model. They should also demand strong preclinical evidence that the experimental vaccines prevent infection, even though that will probably mean waiting weeks or even months for the models to become available.

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That is time well spent. Work with the SARS virus shows that worrying immune responses were seen in ferrets and monkeys, but not in mice. Also, some viral protein fragments can elicit more potent or less risky immune responses than others, and it makes sense to learn this in animal studies before trying them in people.

Governments are understandably desperate for anything that would forestall the deaths, closures and quarantines resulting from COVID-19. But combating this disease demands a vaccine that is safe and potent. The fatality rate is low (3.4% by the World Health Organization’s latest estimate, although this is highly uncertain), yet transmission rates are high and the spread is difficult to track. That means many people — perhaps the majority in hotspots — would need to be vaccinated to stop the spread and prevent deaths. By contrast, Ebola virus has very high fatality rates (averaging around 50%, but varying from 25% to 90%), yet is less contagious, so vaccination can be more targeted.

Decades ago, vaccines developed against another coronavirus, feline infectious peritonitis virus, increased cats’ risk of developing the disease caused by the virus (T. Takano *et al. J. Vet. Med. Sci.* **81**, 911–915; 2019). Similar phenomena have been seen in animal studies for other viruses, including the coronavirus that causes SARS (Y. W. Kam *et al. Vaccine* **25**, 729–740; 2007).

Regulators must continue to require that vaccine developers check for potentially harmful responses in animal studies. They must also be careful to assess healthy human volunteers for antibodies against any coronaviruses before enrolling them in safety trials. Funders should beware of hype, and release more grants for appropriate tests for coronavirus drug and vaccine development.

China is advancing several COVID-19 vaccines of different types, and has announced plans to have products in human tests or emergency use in healthy people in April. My worry is that this could mean a vaccine is administered before its efficacy and safety have been fully evaluated in animal models or clinical trials. And in the United States, the biotechnology company Moderna in Norwood, Massachusetts, has shipped an experimental vaccine based on messenger RNA to the US National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, for testing in a clinical trial. The mRNA-based platform for delivering vaccines has been shown to be safe in humans, but this COVID-19 vaccine has not. The NIAID argues that the risk of delaying the advancement of vaccines is much higher than the risk of causing illness in healthy volunteers, but I worry that vaccine developers will rush in too hastily if standards are lowered.

More than 100 COVID-19 treatments are listed in China’s public clinical-trials registry. Most of these involve a drug that has already been approved for another disease. That means that they do not act specifically against human coronaviruses and have not been tested in COVID-19 animal models, even though that would usually be required by Chinese regulators. What is

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more, trials done to gain approval of the treatment for other diseases often do not consider combinations with other drugs. The potential for synergistic toxicity needs to be assessed before such ‘old’ drugs enter COVID-19 treatment regimes.

Another factor should also be considered: the potential for emerging and re-emerging coronaviruses to cause future outbreaks. The virus behind COVID-19 might well mutate in ways that would make previously effective vaccines and antivirals useless. Therefore, any regulatory agency considering ways to accelerate treatments into testing should also weigh up how likely these drugs are to work beyond this particular coronavirus.

Testing vaccines and medicines without taking the time to fully understand safety risks could bring unwarranted setbacks during the current pandemic, and into the future. The public’s willingness to back quarantines and other public-health measures to slow spread tends to correlate with how much people trust the government’s health advice. A rush into potentially risky vaccines and therapies will betray that trust and discourage work to develop better assessments. Despite the genuine need for urgency, the old saying holds: measure twice, cut once.

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