We can expect more COVID drugs next year, but we've wasted so much time getting here

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Credit: AI-generated image (disclaimer)

Several COVID drugs are in the pipeline for 2022, some you can potentially take at home, others for use in hospital.

It's taken almost two years of the pandemic to get here.

However, as we argue in our paper, with more and larger collaborations, and focusing on repurposing the right drugs, we could have developed effective COVID drugs at scale, earlier.

Here's what we can do better for the next pandemic.

First, some good news

One recent study found a commonly prescribed drug for depression, fluvoxamine, given to people diagnosed with COVID-19 reduced their chance of symptoms deteriorating, needing to go to hospital, and dying.

There are four powerful features of this study. It was based on:

- **an existing human drug:** drugs designed for another purpose can have extra therapeutic benefits. We also didn't have to design a drug from scratch and knew a lot about tolerated doses, side-effects and drug interactions, over many years of people taking it
- **earlier observation and data:** the drug was chosen based on prior data showing people taking the same or similar drugs for depression did better with COVID-19 infection
- **a large population:** the study included enough people to give meaningful results
- **an international collaboration:** it is unclear why were there not many, thorough, studies of this type implemented at the very start of the pandemic. Collaboration helps with quicker recruitment and broader input into trial design.

However, this example is the exception rather than the rule when it comes to finding COVID drugs. And during the pandemic, we've had several missteps.

We missed an early opportunity

We can treat COVID with one of two broad strategies. One is to target or immobilize the virus itself. The other is to "treat the host." This involves treating the body's overwhelming response to the virus and the cause of most death and disease. Fluvoxamine mentioned above is an example of the latter.

However, we didn't see any major strategy to "treat the host" in the early part of the pandemic, except with the decades-old corticosteroid drugs dexamethasone and budesonide.

Focusing more on "treating the host" would have bought us time to produce vaccines and antiviral drugs, which typically take longer to develop.

> the medical establishment is too busy figuring ways of treating the #COVID virus and not treating the host
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> — iMikeofStaff (@IeriStaff) April 13, 2020

"Treating the host" is hardly radical. We've been doing this with existing medicines for infectious diseases for years.

In fact, we knew early on that we respond to COVID-19 in much the same way to being infected with other viral infections that can overwhelm the body, such as influenza and Ebola.

That's not the only mis-step.

We backed a few wrong horses

It's inevitable some existing drugs trialed initially for COVID-19 would fall by the wayside and never be used clinically. But we backed some of the wrong drugs, at the wrong doses. According to basic research and clinical knowledge of how drugs work in the body, this should have been obvious from the start.

Over a century after doctors unsuccessfully tried to treat the Spanish flu with quinine and its derivatives, history was repeating itself. We were asking if the related drug hydroxychloroquine could be used to treat COVID-19.

Researchers around the world conducted multiple trials with hydroxychloroquine, even after some others reported a lack of efficacy.

In the first year of the pandemic, hydroxychloroquine was tested in about 250 studies involving nearly 89,000 people, despite evidence it does not help.

If we are to repurpose existing drugs, this needs to be based on our experience of that drug in humans with COVID-19, such as in the fluvoxamine example. Alternatively, the drug needs to fit with what we know about how the virus causes disease and how the infection develops in humans.

If we are to repurpose drugs identified solely on cell-based laboratory studies, this must also be based on what we know about how the human body handles the drug and how the drug works in the body. We also need the relevant quality mathematical models to get the dose right for the early phase human studies.

Using such basic approaches to drug development, which we've known about for years, we could have foreseen that ivermectin and hydroxychloroquine would prove to be ineffective—before larger scale

human trials were ever allowed to be conducted.

We also backed too many small trials

During the pandemic, there have been an estimated 2,800 clinical trials for COVID drugs with fewer than 300 reported.

In one database of COVID-19 trials, 40% said researchers were enrolling fewer than 100 patients, a sample size generally too small to be useful.

For us to get a better idea if a COVID drug is safe and effective, we need larger, collaborative trials.

For example, the RECOVERY trialenrolled about 45,000 people at 180 sites to test a range of potential COVID therapies. It showed the repurposed drug dexamethasone reduced death rates, changing standard practice.

How could we do better next time?

We need to start thinking about ways of developing drugs for the early part of the next pandemic, considering what we've learned from this one.

This is essential if we are to have a range of safe, effective, cheap and available therapies for treating the host, to buy time to develop vaccines and antivirals.

We now know from global experiences the importance of rational choice of drugs for testing. We also know the importance of large clinical trials that come from major, international collaborations.

We also need to co-ordinate research efforts nationally, rather than

compete for research dollars with other groups. Doing research in a pandemic is not like doing research in non-pandemic times. So this means countries such as Australia need to have their own center for pandemic preparedness or center for disease control to co-ordinate research and funding priorities.

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