

3 September 2020

## **BRIEF19**

*A daily review of covid-19 research and policy.*

### **RESEARCH BRIEFING**

#### **A primer on vaccine development.**

There is no definitive treatment for covid-19. Below we discuss one of several promising vaccines and then provide a glossary of terms.

The pharmaceutical company Astra-Zeneca begins the Phase 3 trial of its vaccine, AZD1222, against SARS-CoV-2 this week. The aim of the trial is to evaluate whether AZD1222 prevents symptomatic covid-19 in humans. The trial is funded by the National Institutes of Health and aims to enroll 30,000 adults across the United States. AZD1222 is also being evaluated in Phase 2/3 trials in the United Kingdom and Brazil as well as a Phase 1/2 trial being conducted in South Africa.

AZD1222 uses another type of virus, called adenovirus, to cause our body to manufacture the Spike protein of SARS-CoV-2, the virus that causes covid-19. Scientists switched out the usual content of adenovirus for the Spike protein. SARS-CoV-2 uses the Spike protein to enter into human cells. The rationale underlying AZD1222 is that the immune response the body mounts against the Spike protein ferried by adenovirus will also neutralize the Spike protein when it appears as part of a full SARS-CoV-2 viral particle.

In a recent [experiment](#), six rhesus monkeys who received one dose of the experimental vaccine did not develop pneumonia despite infection with SARS-CoV-2. After two doses 35 human participants in a Phase I/2 trial of AZD1222 in the UK were tested and were found to have developed antibodies. None of the human test subjects experienced an allergic reaction to the vaccine nor did any other serious adverse events occur.

While our best way out of the covid-19 pandemic is likely through a safe and effective vaccine, vaccines are not panaceas. First, not everyone can receive them. Those who must take medications to suppress the immune system, for example recipients of transplants or those with autoimmune conditions, are caught in a catch-22. The medications they take to stave off organ rejection (which work by immune suppression) may also prevent vaccines from working. On the other hand, if organ transplant recipients do not take these medications their underlying conditions may worsen. A second problem is that older individuals may require more doses of a vaccine because their immune systems do not react as robustly as those of younger individuals. The risk of side effects grows with the number of doses of the vaccine. Finally, if a virus mutates enough scientists may need to update the vaccine. Despite these limitations an effective vaccine can halt SARS-CoV-2 by preventing the spread of disease that we witnessed this year.

#### Trial Glossary:

*Phase 1 Clinical Trial:* A trial in humans designed to answer whether the treatment is safe. A trial progresses from preclinical trials to a phase I clinical trial if the treatment has been shown to have been safe and effective in animals.

*Phase 2 Clinical Trial:* A trial in humans designed to answer whether the treatment is effective. It often also gauges the range of doses that are the most therapeutic with the least side effects.

*Phase 3 Clinical Trial:* A trial in humans designed to determine whether the treatment is more effective than the treatments that are available. Phase 3 trials are also able to assess for adverse effects that are too rare to occur in the smaller Phase 1 and 2 trials. If drug causes a rash in 1 out of 100 people, a trial that studies 80 people may not identify the rash as a side effect of that drug.

—Michael Chary, MD PhD

## **POLICY BRIEFING**

### **Insurance alternative not paying off.**

In April, as millions of Americans faced the loss of employer-provided health insurance due to unemployment, the Trump administration considered reopening enrollment periods for Affordable Care Act plans. Instead they [decided](#) to allocate CARES Act funding to reimburse hospitals at Medicare rates for treating uninsured patients admitted for treatment of covid-19, with the caveat that hospitals would not be allowed to charge the patients for any remaining balance not deemed to have been covered (similar to a practice known as “balance billing”).

Now, a new [analysis](#) by *The New York Times* shows that the program is not the silver bullet it was touted to be. In some cases it is as simple as the hospital deciding not to participate, while in others it is the lack of an official covid-19 diagnosis or other primary cause as the reason for the hospitalization; it should be noted that while hospitalization and clinic appointments are covered by the plan, the program does not reimburse outpatient prescriptions, nor treatment of chronic conditions that may exacerbate the effects of the covid-19. Regardless of the reason, it has meant big bills for as many as forty percent of affected patients.

The Kaiser Family Foundation has estimated hospital costs for uninsured care may reach \$41.8 billion, an astronomical number compared to the \$584 million in care that has been reimbursed so far. Many hospital executives have stated the majority of their possible claims sit unsubmitted due to inconsistencies between internal billing processes and program requirements, or concomitant conditions affecting the reason for hospitalization, and there has been little explanation of why different regions around the country have received vastly different rates of reimbursement. While the process is murky, it is clear that more needs to be done to support the uninsured during this time of increased medical need. *Various.*

—Joshua Lesko, MD

*Kimi Chernoby, MD, JD, Policy Section Editor. Joshua Niforatos, MD Research Section Editor Frederick Milgrim, MD, Kate Taylor, Editors-at-Large. Kane Elfman PhD, Publishing and Design. Jeremy Samuel Faust MD MS, Editor-in-Chief.*

<http://www.brief19.com/>

Twitter: [@brief\\_19](#)

[submissions@brief19.com](mailto:submissions@brief19.com)

*Brief19 is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health policy, and public policy.*