White paper

What challenges is the vaccine industry facing when dealing with the flu and COVID-19?

Authors

Lisa Kierstead, Executive Director,
PPD Laboratory services Vaccine Sciences Lab

Fall marks the beginning of the "flu season," the period during the year when influenza (flu) viruses are in increased circulation and cause illness at higher rates than usual.

The season also marks the increased circulation of other respiratory viruses, namely SARS-CoV-2, which causes COVID-19, and respiratory syncytial virus (RSV).

In the US, the flu or respiratory virus season typically begins in the fall and peaks in the winter, usually between December and February, but it can last as late as May.

Influenza results in thousands of deaths in the US each year. The Centers for Disease Control and Prevention (CDC) estimates that 12,000 to 52,000 people died of the flu in the US annually between 2010 and 2020.

The best way to prevent the flu is by getting vaccinated every year. The CDC and the World Health Organization (WHO) recommend annual flu vaccination for most people, especially those at high risk of serious complications, like pregnant women, elderly individuals, children and people with certain chronic health conditions.

As a newer virus that triggered a global pandemic, recommendations around COVID-19 vaccination are continually evolving and adapting, particularly in the context of emerging new variants of SARS-CoV-2. The US Food and Drug Administration (FDA) approved new updated COVID-19 vaccines from both Pfizer-BioNTech and Moderna that target the Omicron XBB.1.5 subvariant, which is currently the dominant subvariant in the US and other countries.

The flu vaccine is updated annually to target the most common strains predicted to circulate that season.

And now, RSV vaccines will also be available for the first time this fall. In May, the FDA approved GSK's Arexvy as the first RSV vaccine, which was shortly followed by the approval of Pfizer's RSV vaccine Abrysvo. Both are approved for adults 60 years of age and older, as older adults are at a higher risk of complications from RSV infection. Abrysvo received expanded approval as a maternal RSV vaccine in August to help prevent RSV in infants.

In this Spotlight feature, Xtalks spoke with Lisa Kierstead, PhD, Executive Director, PPD™ Laboratory services Vaccine Sciences lab, to learn more about navigating the respiratory virus season this year. Dr. Kierstead shed light on the similarities and differences between influenza and COVID-19, including the viruses' biology and the current recommendations for vaccination. Also, she spoke about some of the challenges that the vaccine industry is currently facing in dealing with the flu and COVID-19.

Dr. Lisa Kierstead, Executive Director, PPD Laboratory services Vaccine Sciences Lab

Dr. Kierstead joined PPD Laboratory services Vaccine Sciences Lab in 2009 and is currently an executive director of the vaccine sciences lab. She has 23 years of experience working with clients to move vaccine candidates through the clinical development pipeline, including regulatory submission. She specializes in infectious disease and oncology, including dengue, norovirus, pneumococcus, meningococcus and melanoma.

The current climate of COVID-19

While the WHO downgraded the COVID-19 pandemic in May 2023 to it no longer being a global emergency and the US federal COVID-19 public health emergency (PHE) declaration ended during the same month, cases of COVID-19 began rising during the summer of this year. Both hospitalizations and deaths associated with COVID-19 have been trending upward since mid-July.

The biggest challenge with COVID-19 is that there is a lot that remains unknown for a virus that is only about four years old. This includes the emergence of new variants and vaccination strategies.

As the virus keeps mutating, there are challenges associated with COVID vaccination. While variants are arising relatively quickly, the good news is that most appear to be offshoots of the Omicron subvariant X.BB.1.5 for which there are now updated vaccines that target it.

Dr. Kierstead explained that while vaccination against Omicron XBB.1.5 may be effective against other Omicron-related variants that may arise, we just don't know with any certainty.

Nonetheless, she says, "Just because we have variants popping up doesn't mean the vaccine won't be effective against those strains that pop up. We have the variant that's been selected, but we will just have to wait and see."

Even more good news is that mRNA-based vaccines can be updated relatively quickly and easily, which has been demonstrated by vaccine makers.

The X.BB.1.5 variant was selected in June and within a few months, both Pfizer-BioNTech and Moderna were able to get vaccines for it to market by September, which Dr. Kierstead says is "astonishingly fast."

There is a lot of risk in doing this work, she says, as mutations and the emergence of new variants are unpredictable. It worked in the favor of vaccine makers that X.BB.1.5 remains the dominant variant.

Influenza versus COVID-19: Virology and vaccines

Influenza versus SARS-CoV-2 virology

Viruses contain genetic material that can either be RNA or DNA. Both influenza and SARS-CoV-2 have RNA as their genetic material. An RNA genome enables the genetic material to mutate more rapidly. This is why both viruses are constantly mutating, as we see with the emergence of new variants of SARS-CoV-2 and influenza, explains Dr. Kierstead. This necessitates the need for an annual influenza vaccine targeting the specific strains in circulation for that year, and updated COVID vaccines as well.

The difference between the two viruses is that influenza is a single-stranded negative-sense RNA virus while SARS-CoV-2 is a positive-sense single-stranded RNA virus. This means COVID-19 can replicate as soon as it gets into a host cell, making its cycle of replication faster than influenza.

As respiratory viruses, infection with the flu or COVID result in respiratory symptoms.

Another shared characteristic of both viruses is that they both infect multiple species. Flu can infect birds and pigs and COVID-19 can infect cats, dogs and multiple other species.

Vaccination recommendations

While Viruses contain genetic material that can either be RNA The flu and COVID vaccines have similar recommendations, both are advised for individuals six months of age and older. However, while COVID vaccination begins with a primary series of two to three doses (for the Moderna and Pfizer-BioNTech vaccines, respectively) followed by boosters, vaccination for influenza does not involve primary dosing.

The updated X.BB.1.5 COVID vaccine can be given as a primary series for those who have never been vaccinated against COVID or as a booster. The CDC recommends one dose of the newly updated shot. In contrast, influenza vaccines are annual vaccines.

Given evidence of immunity waning after about six months of a COVID shot, COVID boosters continue to be recommended every six months to one year. It remains to be seen whether COVID vaccination could turn into annual vaccinations like influenza in the long term, as it appears the virus isn't going anywhere any time soon.

Vaccine composition and technology

The flu and COVID vaccines don't have many similarities. Flu vaccines are generally whole inactivated or attenuated viruses that are typically produced in egg or cell culture-based manufacturing processes, explains Dr. Kierstead.

There are four main types of influenza viruses: A, B, C and D. Influenza A and B viruses are the ones that cause seasonal flu epidemics each year. Each type can have multiple strains, and these strains can change from year to year. This is why a new flu vaccine is formulated each year to best match the anticipated circulating strains.

COVID-19 vaccines from Pfizer-BioNTech and Moderna are mRNA-based vaccines that encode for the spike protein located on the surface of the SARS-CoV-2 virus. There are other types of COVID vaccines as well, including an adenoviral vector (AAV)-based one from AstraZeneca and a protein-based vaccine developed by Novavax. The use of AstraZeneca's vaccine has been discontinued in some places like the UK due to the risk of rare, but serious blood clots.

Several companies including Pfizer-BioNTech and Moderna are now developing mRNA-based influenza vaccines. Some of the vaccines are already in clinical trials, including a universal influenza vaccine developed by researchers at the National Institute of Allergy and Infectious Diseases' (NIAID) Vaccine Research Center (VRC), part of the National Institutes of Health (NIH). The NIH says a universal vaccine could eliminate the need to develop annual vaccines and could offer more durable, long-term protection.

The number of variants or strains that the flu versus COVID vaccines target also differs. The flu shot is typically quadrivalent, meaning it targets four different seasonal variants of influenza as recommended by the WHO, whereas the COVID vaccines, including the newest updated one, is monovalent. However, last fall, vaccine makers developed a bivalent COVID booster targeting two different Omicron variants (BA.4 and BA.5), which has now been discontinued.

Correlates of protection for the Flu and COVID-19

A correlate of protection, or surrogate of protection, is data that correlates with protection from either infection or symptoms.

Dr. Kierstead says universal correlates of protection are challenging to establish.

"We do have some, what we call legacy vaccines, that do have correlates of protection," she explains. "A couple of examples are measles, which has been around for a very long time, and pneumococcus." For measles, the correlate of protection is having a certain concentration of antibodies in your system that will generally provide protection from getting measles infection.

"The challenge to correlates of protection is that they don't always hold true," says Dr. Kierstead. This is because there are various factors that play into determining them, she explains, including differences in population demographics around the world and the complex nature of certain pathogens. For example, there are more than 90 different types of pneumococcus strains. This is why a single value for a correlate of protection cannot hold true for every case. Hence there's a lot of complexity around establishing them.

For both the flu and COVID, no single value has been established as a correlate of protection. For the flu, for example, if an individual has a certain level of antibodies against hemagglutinin (HA) as determined by a hemagglutination inhibition assay, it is assumed that they will have protection against the flu. However, this is a generality and is not universally accepted, explains Dr. Kierstead.

For COVID, it is much the same case. While levels of neutralizing antibodies can be used to determine protection, it is not a defined universal criterion. It is taken simply as a correlation between antibodies that function in a certain capacity and protection from COVID.

Vaccination challenges

Influenza and COVID-19 vaccinations both share the common challenge that both viruses tend to mutate. Influenza doesn't mutate as quickly as SARS-CoV-2, but we know that new COVID variants keep popping up, says Dr. Kierstead.

Every year, the seasonal flu strains are defined and selected for the Northern and Southern Hemisphere by the WHO in conjunction with influenza experts. Once selected, vaccine manufacturers will generate the vaccine with the relevant strains.

One challenge Dr. Kierstead says is that sometimes the vaccine may not be effective against the circulating strains. She explains this could be the result of one or two things. One, perhaps they selected the wrong strain to generate the vaccine. Secondly, the flu vaccine, on average, is known to be between 50 to 65 percent effective in preventing infection even if the right strains have been selected.

There are continuing discussions around these challenges. "Some experts may say that the production processes for flu vaccines may need to be reassessed and improved as the vaccines have been around for a long time," says Dr. Kierstead.

New technologies like mRNA-based vaccines could perhaps be more effective, with the advantage that they can be produced faster than traditional cell- or egg-based flu vaccines.

One of the main challenges around COVID vaccination is that the virus is continually mutating with variants arising at a relatively quick pace. Although a challenge to the industry, it is a matter of closely monitoring the emergence of new variants and selecting the right variants to target.

Progress and future of COVID vaccination

As Dr. Kierstead mentioned previously, the industry has been quite proactive in handling COVID with respect to vaccines.

Dr. Kierstead says she's impressed by how "nimble" vaccine manufacturers have been in responding to the appearance of new variants of concern and "being proactive."

"Even before the XBB variant was selected for the September/October vaccination this year, manufacturers were being proactive and already running clinical studies with that variant to see if their vaccine was effective," she explains. "That's one of the things I find extremely impressive."

There is also now funding from the Department of Health and Human Services for what "they're calling next-generation COVID vaccines," says Dr. Kierstead. These next-gen vaccines are specifically looking at novel approaches, which are different than the ones we've seen for COVID vaccines so far.

"There's been a lot of good progress as far as COVID-19 vaccinations go," she says.

While the flu and COVID-19 have many differences, both respiratory viruses can have serious negative impacts on the health and well-being of the populations they affect and on healthcare systems. Vaccination is an important tool to help reduce these impacts.

Despite differences in biology, epidemiology and vaccines, there are similarities in the approaches that can be employed to help mitigate the spread and impact of the flu and COVID-19.

To explore more about vaccines development and our Vaccines Sciences lab go to: **https://www.ppd.com/our-solutions/ppd-laboratories/vaccine-sciences-lab/**

This article was created in collaboration with PPD Laboratory services and the Xtalks editorial team.