Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	Pfizer Inc.
Vaccine Studied:	Influenza Modified RNA (modRNA) Vaccine
Protocol Number:	C4781004
Dates of Study:	12 September 2022 to 12 March 2024
Title of this Study:	A Study to Evaluate the Safety, Tolerability, and Immunogenicity of a Modified RNA Vaccine Against Influenza [A Phase 3, Randomized, Observer-Blinded Study to Evaluate the Efficacy, Safety, Tolerability, and Immunogenicity of a Modified RNA Vaccine Against Influenza Compared to Licensed Inactivated Influenza Vaccine in Healthy Adults 18 Years of Age or Older]
Date(s) of this Report:	29 October 2024

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is influenza?

Influenza is also known as the flu. It is caused by a virus that infects the respiratory system. This includes the nose, throat, and lungs. Symptoms include runny or stuffy nose, sore throat, cough, headache, fever, chills, and muscle pain or body aches. Many people with influenza will have mild illness. Some people can become seriously ill and may die.

What is a vaccine?

A vaccine can help prevent an infection or a disease. It works by helping the body fight off germs. One of the ways to potentially help prevent influenza is to be vaccinated. Antibodies are proteins that fight germs and infections to help prevent disease. After a person gets a vaccine, the body's response includes making antibodies. This is called an antibody response.

What is an influenza vaccine?

Hemagglutinin (HA) is a protein that is made by the influenza virus that is important for how the virus works. The influenza virus can mutate (change) the form of HA it makes. This means each year different strains (types) of the influenza virus may become widespread worldwide.

There are 4 types of influenza viruses, types A, B, C, and D. Influenza A and B viruses cause seasonal epidemics of disease in humans. Within these 2 main types, there are lots of different varieties of the virus. The study vaccine contains ribonucleic acid (RNA) that is found in different type A and/or B influenza viruses. RNA is present in all living cells, and it helps the cell make proteins. RNA is also present in some viruses where it carries genetic information rather than deoxyribonucleic acid (DNA). DNA is used in human cells to carry genetic information.

Each year, the World Health Organization (WHO) tries to predict what influenza types are likely to be most common that year. The vaccines are then made to target these or similar types.

What vaccines were tested in this study?

The investigational vaccine used in this study was a 4-part (quadrivalent) influenza modified RNA vaccine (qIRV) that targets 2 type A and 2 type B influenza viruses.

Some participants also received licensed 4-part (quadrivalent) influenza vaccine (QIV). The licensed QIV vaccine used in this study is approved by health authorities.

What was the purpose of this study?

The main purpose of this study was to see if the qIRV vaccine used in this study was at least as good as, or better at stopping participants from catching influenza than the licensed QIV vaccine.

Researchers wanted to know:

- **Did the participants who received qIRV have fewer influenza-like illness or laboratory confirmed influenza than those receiving licensed QIV?**
- **Did participants have any local reactions (any redness, swelling, or pain at the injection site) within 7 days of being given the vaccines?**
- **Did participants have any systemic events (any high temperature or fever, tiredness, headache, chills, vomiting, loose stools, new or worsening muscle pain,**

or new or worsening joint pain) within 7 days of being given the vaccines?

- **Did participants who received qIRV have any medical problems or serious medical problems after being given the qIRV vaccine?**

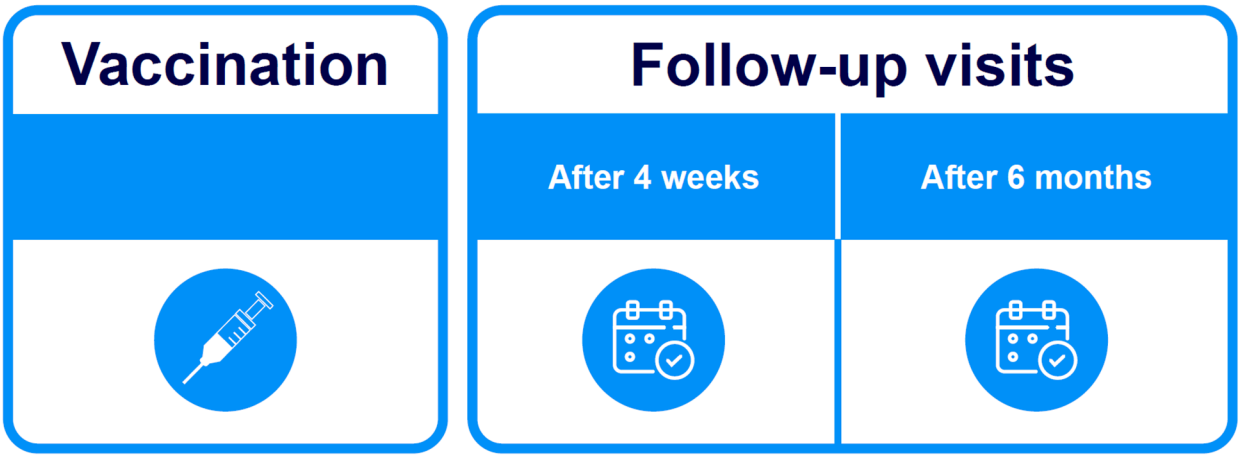
What happened during the study?

How was the study done?

Researchers tested the qIRV on a group of study participants over 18 years old. When looking at the results, the researchers split the participants into 2 groups. The first group was participants aged 18-64 years old, and the second group was participants aged over 65 years old. In both groups the researchers wanted to find out if vaccination with qIRV was better than or the same as vaccination with licensed QIV. Researchers also wanted to know if vaccination with qIRV was safe and well tolerated.

Each participant was given 1 vaccination with either qIRV or licensed QIV. Following vaccination, all participants were asked to complete an electronic diary. They were asked to record details of any influenza-like illness. If the participant recorded an influenza-like illness, a swab was taken from their nose to check if they had influenza. Study visits are shown in Figure 1.

Figure 1: Study Diagram



To look at the safety and tolerability of the vaccines, the researchers looked at whether there were any “local” reactions to the vaccine. A local reaction is something that is seen at the site where the injection of the vaccine was given and can include pain at the injection site, swelling, and/or redness. The researchers also looked at whether there were any “systemic events” or reactions to the vaccine. Systemic means something that affects the whole body or specific parts of it like the head or joints. Systemic events were reactions that participants may have had after they had been given the vaccine. These could have included having a fever or high temperature, tiredness, headache, vomiting, loose stools, chills, new or worsening muscle pain, and new or worsening joint pain. The researchers also asked participants about their health and how they were feeling.

Researchers then compared the results of study participants given qIRV to the results of study participants who were given licensed QIV.

The study researchers did not know who received which vaccine. This is known as an “observer-blinded” study. Study participants were assigned to each group by chance alone.

Where did this study take place?

The Sponsor ran this study at 310 locations in 6 countries, 1 in the northern hemisphere, and 5 in the southern hemisphere.

When did this study take place?

It began 12 September 2022 and ended 12 March 2024.

Who participated in this study?

The study included participants over 18 years old who met the inclusion/exclusion criteria for things such as age and prior vaccinations:

- A total of 19567 men participated
- A total of 26028 women participated
- All participants were between the ages of 18 and 97 years

Of the 45595 participants who received 1 dose of a vaccine, 2593 left the study before the study was finished. The most common reason for leaving the study was that the participant was lost to follow-up. This means that the study center was not able to contact the participant.

How long did the study last?

Study participants were in the study for approximately 6 months. The entire study took 18 months to complete.

When the study ended in March 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did the participants who received qIRV have fewer influenza-like illness or laboratory confirmed influenza than those receiving licensed QIV?

The number of influenza-like illnesses varied depending on which vaccine the participant received and how old they were.

What was the safety and tolerability of the vaccines?

Not all participants who were vaccinated completed the study diary. This meant that safety information on local reactions and systemic events was not available for some participants.

The researchers also asked participants about any medical problems they had after the vaccinations. Medical problems are discussed in the next section of this document.

Did the participants who received qIRV have fewer influenza-like illness or laboratory confirmed influenza than those receiving licensed QIV?

18-64 years old

Researchers found that participants receiving qIRV had less laboratory-confirmed influenza than those receiving licensed QIV.

Over 65 years old

Researchers found that qIRV did not work better than licensed QIV at stopping participants from getting laboratory confirmed influenza.

Based on these results, the researchers have decided that the results are

not likely the result of chance. Researchers found that participants aged 18-64 receiving qIRV had less laboratory-confirmed influenza than those receiving licensed QIV, but qIRV may not work better than licensed QIV in participants over 65 years old.

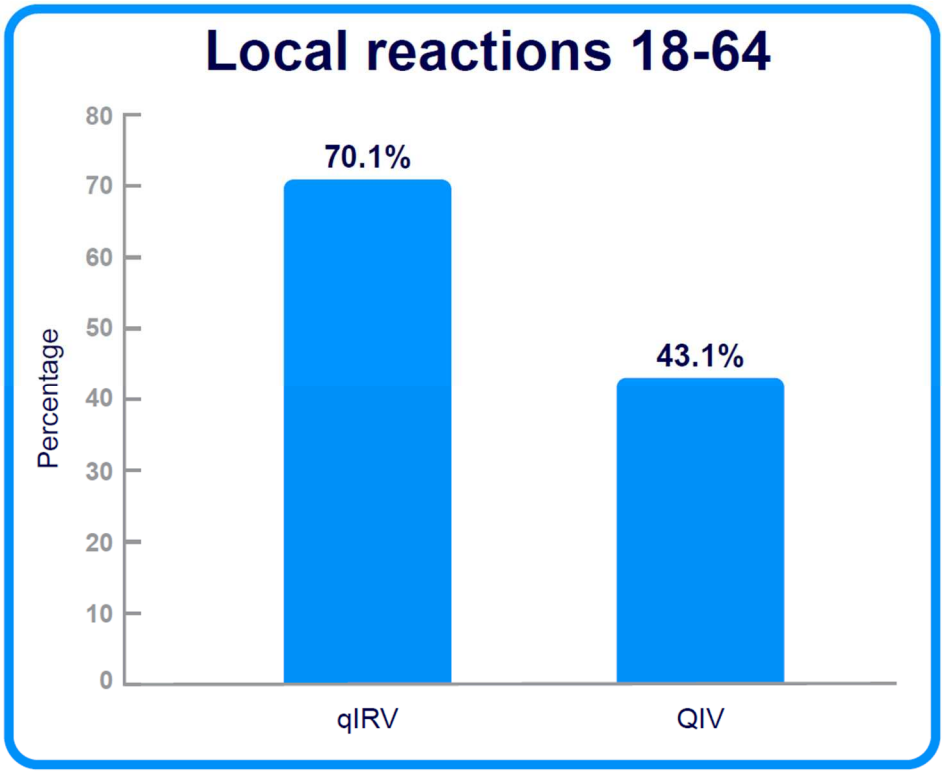
Did participants have any local reactions within 7 days of being given the vaccines?

A local reaction was pain at the injection site, swelling, and/or redness.

18-64 years old

The percentage of participants aged 18-64 years old who reported any local reactions within 7 days of either vaccine is shown in Figure 2.

Figure 2: Percentage of Participants Aged 18-64 Years Old With Any Local Reactions Within 7 Days of Either Vaccination

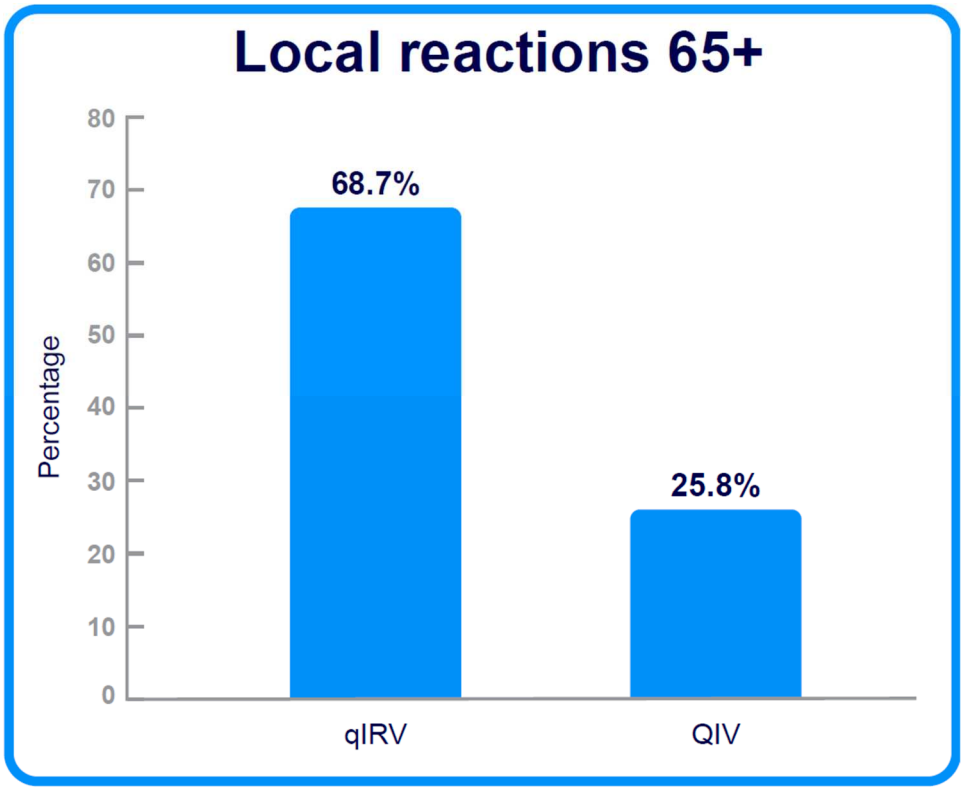


The most frequently reported local reaction in both vaccine groups was pain at the injection site.

Over 65 years old

The percentage of participants over 65 years old who reported any local reactions within 7 days of either vaccine is shown in Figure 3.

Figure 3: Percentage of Participants Over 65 Years Old With Any Local Reactions Within 7 Days of Either Vaccination



The most frequently reported local reaction in both vaccine groups was pain at the injection site.

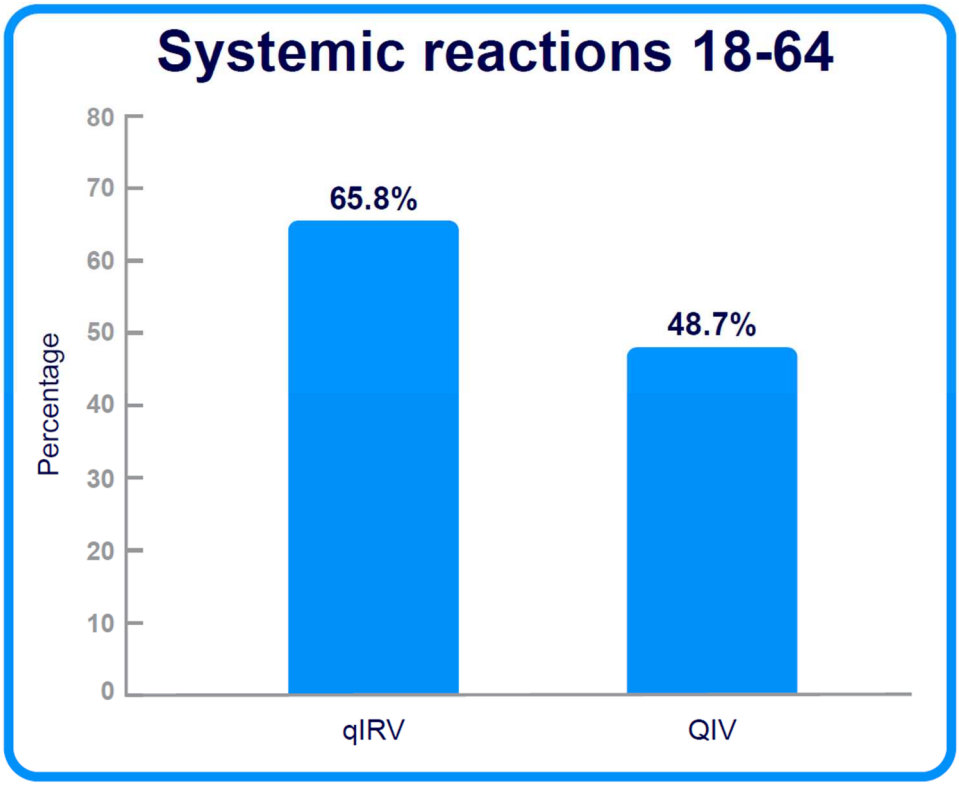
Did participants given the vaccines have any systemic events within 7 days of being given the vaccines?

Systemic events were fever or high temperature, tiredness, headache, vomiting, loose stools, chills, new or worsening muscle pain, and/or new or worsening joint pain.

18-64 years old

The percentage of participants aged 18-64 years old who reported any systemic reactions within 7 days of either vaccine is shown in Figure 4.

Figure 4: Percentage of Participants Aged 18-64 Years Old With Any Systemic Reactions Within 7 Days of Either Vaccination

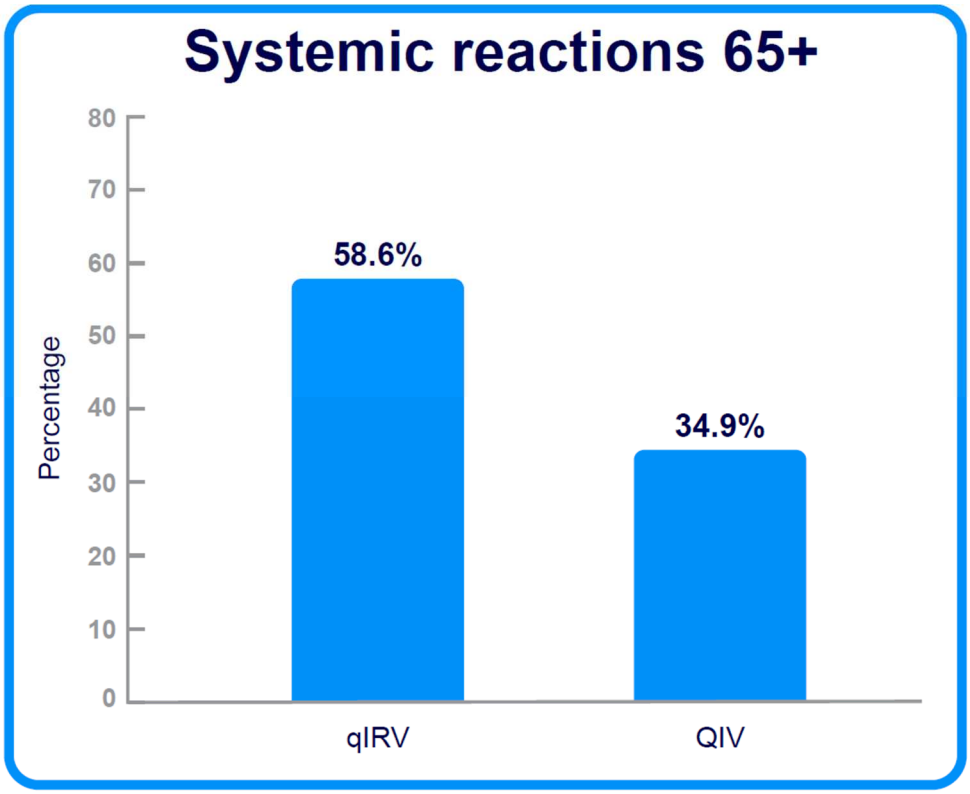


The most commonly reported systemic reaction in both vaccine groups was fatigue, followed by headache.

Over 65 years old

The percentage of participants over 65 years old who reported any systemic reactions within 7 days of either vaccine is shown in Figure 5.

Figure 5: Percentage of Participants Over 65 Years Old With Any Systemic Reactions Within 7 Days of Either Vaccination



The most commonly reported systemic reaction in both vaccine groups was fatigue, followed by headache.

There were more local and systemic reactions reported in the qIRV vaccine group than the licensed QIV vaccine group across both age groups. This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

18-64 years old

A total of 1069 out of 18388 (5.8%) participants aged 18-64 years old in this study had at least 1 medical problem. These medical problems were reported within 4 weeks of vaccination. Three (3) participants left the study due to medical problems.

Over 65 years old

A total of 1972 out of 27168 (7.2%) participants aged over 65 years old in this study had at least 1 medical problem. These medical problems were reported within 4 weeks of vaccination. Seventeen (17) participants left the study because of medical problems.

Overall

In this study, the medical problems were grouped into “tiers”. This was done because the study included lots of participants and there were lots of

medical problems reported to the researchers. Most of the medical problems were not thought related to any of the vaccines used in this study.

Tier 1 events included severe allergic reactions, autoimmune disorders (where the immune system accidentally attacking your body instead of protecting it), inflammation of the heart muscle or lining, or any major heart or blood vessel problem. No medical problem was reported by more than 0.1% of participants in either age group. In addition, most of the medical problems reported in participants over 65 years old, were consistent with medical problems that may occur in this age group.

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

18-64 years old

A total of 176 participants (less than 0.1%, or 176 out of 18388 participants) had serious medical problems. One (1) participant had serious medical problems that the study doctors thought were linked to the vaccine they were given. This participant was given qIRV and had a vaccination site reaction and a severe allergic reaction (anaphylactic shock).

There were 16 participants 18-64 years old who died during the study. Researchers do not believe any of the deaths reported by participants were related to study medications.

Over 65 years old

A total of 614 participants (2.2%, or 614 out of 27168 participants) had serious medical problems. Three (3) participants had serious medical

problems that the study doctors thought were linked to the vaccine they were given.

- One (1) participant who was given qIRV had a stroke and died. This may have been related to study drug or to a recent blood infection and dehydration that the participant experienced immediately before the stroke.
- One (1) participant who was given licensed QIV had a condition where the liver enzymes in your blood are temporarily increased.
- One (1) participant who was given licensed QIV had nausea and vomiting. This resulted in the participant being admitted to hospital.

There were 95 participants over 65 years old who died during the study. Researchers do not believe any of the deaths reported by participants except the stroke were related to study medications. Researchers believed that the stroke may have been related to study drug, though it could have also been caused by other factors.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4781004

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT05540522**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!