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 vaccine 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:	BioNTech SE
Sponsor Agent:	Pfizer Inc.
Vaccine Studied:	Combination COVID-19 and Influenza modRNA Vaccine (PF-07926307)
Protocol Number:	C5261001
Dates of Study:	28 October 2022 to 28 December 2023
Title of this Study:	A Study to Learn About Combined Modified RNA Vaccine Candidates Against COVID-19 and Influenza in Healthy Adults [A Phase 1/2 Master Protocol to Evaluate the Safety, Tolerability, and Immunogenicity of Combined Modified RNA Vaccine Candidates Against COVID-19 and Influenza in Healthy Individuals]
Date of this Report:	11 November 2024

– Thank You –

If you participated in this study, Pfizer, the Sponsor Agent, 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 are influenza (flu) and coronavirus disease 2019 (COVID-19)?

Flu and COVID-19 are contagious illnesses. **Flu** is caused by influenza viruses. **COVID-19** is caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Some symptoms of flu and COVID-19 are the same. Symptoms can include runny or stuffy nose, sore throat, cough, headache, fever, chills, and muscle or body aches. Most people with flu or COVID-19 have a mild illness, but both flu and COVID-19 virus can cause serious illnesses, especially in older adults, and may lead to death.

What is a modified RNA (modRNA) vaccine?

A **modified RNA (modRNA)** vaccine uses a small piece of messenger RNA (also called mRNA) to help the body make a protein that the immune system can recognize and use to fight off a virus.

The modRNA vaccines tested in this study are listed below.

Influenza Modified RNA (flu modRNA) vaccine

The **flu modRNA vaccine** is an injectable vaccine that researchers think can help protect against flu illnesses.

The flu modRNA vaccines tested in this study were investigational, which means they are not approved for use outside of research studies. These study vaccines are listed below:

- **"bIRV flu vaccine"** is the bivalent **flu modRNA** vaccine. "Bivalent" means it was designed to target 2 different flu virus strains.
- **"tIRV flu vaccine"** is the trivalent **flu modRNA** vaccine. "Trivalent" means it was designed to target 3 different flu virus strains.
- **"qIRV flu vaccine"** is the quadrivalent **flu modRNA** vaccine. "Quadrivalent" means it was designed to target 4 different flu virus strains.

BNT162b2 COVID-19 vaccine

BNT162b2 (also called Comirnaty®) is an injectable modRNA vaccine that can help protect people of different ages against COVID-19 illness.

In this study, the bivalent form of BNT162b2 was designed to target 2 strains of the COVID-19 virus: Omicron BA.4/BA.5 and original (also called "wild-type") strains. At the time of this study, health authorities in the United States (US) and other countries have authorized this bivalent form of BNT162b2 vaccine for people 6 months of age and older.

The bivalent **BNT162b2** vaccine is called **"COVID vaccine"** in this summary.

Flu modRNA plus BNT162b2 combination vaccine

Researchers think that the combination of flu modRNA vaccine plus BNT162b2 vaccine can help protect against flu and COVID-19. Giving the flu modRNA and BNT162b2 vaccines as 1 shot would need fewer healthcare visits and injections compared to giving the 2 vaccines separately.

The flu and COVID-19 viruses can circulate at the same place and time and are likely to have peak circulation in winter. Because of this, it might be possible in the future to schedule the flu and COVID-19 vaccinations at the same time of the year.

The combination of **flu modRNA** vaccine plus **BNT162b2** vaccine given together as a single shot is called **"flu plus COVID combination (combo) vaccine"** in this summary. This combination vaccine tested in this study was investigational, which means it is not approved for use outside of research studies.

What was the purpose of this study?

The main goal was to find out if the combination of flu and COVID vaccines (in different dose levels) is safe in healthy participants, and if it can help to protect against flu and COVID-19 virus.

Researchers checked the participants' overall health and heart health during the study. Participants had different tests during the study such as blood tests to measure the **troponin I** levels and electrocardiogram (**ECG**) tests.

- **Troponin I** is a protein found in the heart muscles. High troponin I levels in the blood could mean there is injury or damage to the heart.
- An **ECG** measures the electrical activity of the heart.

Researchers also checked if participants had any local or systemic reactions within 7 days after vaccination.

- **Local reactions** are the body's response at the injection site (spot in the arm where the study vaccine was injected). These can include injection site redness, swelling, or pain.
- **Systemic reactions** are symptoms that affect the whole body or specific parts of the body like the head or joints. These can include fever, tiredness, headache, chills, vomiting, diarrhea, new or worsened muscle pain, or new or worsened joint pain.

Researchers wanted to know:

- **How many participants had any local reactions (injection site redness, swelling, or pain) within 7 days after vaccination?**
- **How many participants had any systemic reactions (fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain) within 7 days after vaccination?**
- **How many participants had high troponin I levels within 7 days after vaccination?**
- **How many participants had new abnormal ECG findings within 7 days after vaccination?**
- **How many participants had medical problems within 1 month after vaccination?**
- **How many participants had serious medical problems within 6 months after vaccination?**

Researchers also checked the participants' levels of antibodies before and after vaccination in this study. **Antibodies** are proteins that can fight off infections and help prevent disease. Antibodies can tell us about the body's immune response. An **immune response** is the body's ability to find and fight germs that cause diseases.

Results of participants' immune response to the study vaccines are not included in this report because that was not the main focus of the study. These results may be found in the links on the last page of this report.

What happened during the study?

How was the study done?

This study had 2 parts: **Substudy A** and **Substudy B**. Participants joined only 1 part of the study. All participants in each substudy got 1 dose of their assigned study vaccines.

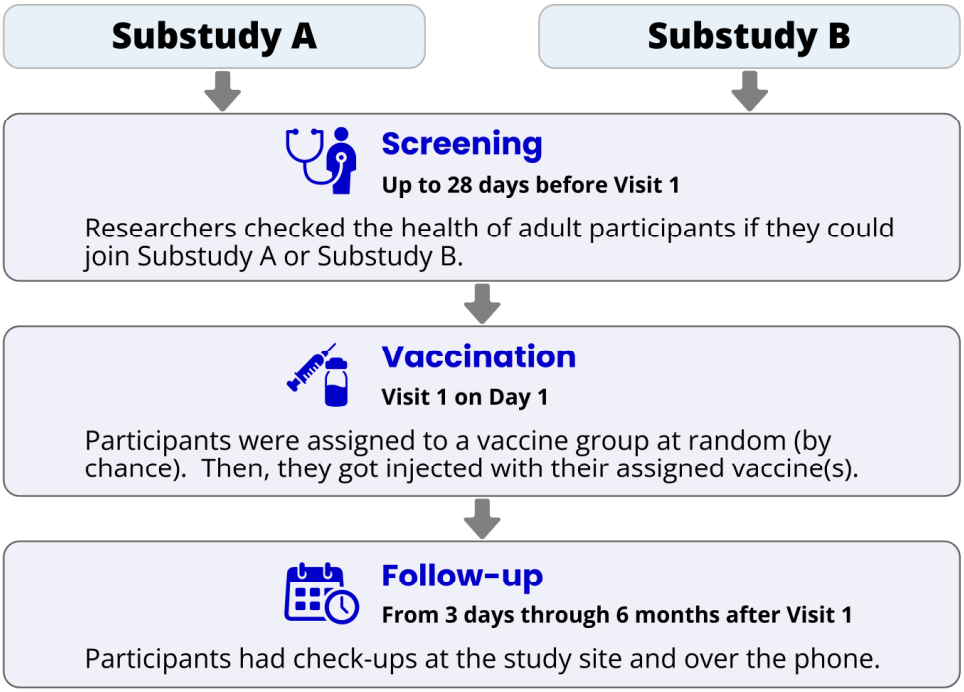
In this study, some participants also received 1 dose of a **licensed quadrivalent influenza vaccine** (or **QIV)**. Licensed QIV is approved by health authorities in the US and other countries for use in people of different ages, from children to older adults. Licensed QIV is designed to target 4 different flu virus strains.

Health authorities from different countries recommend people get a **flu vaccine** every year. Flu viruses constantly change (mutate), which leads to new strains of the flu virus.

Each year before flu season starts, scientists check which flu strains are likely to be circulating that year, so that the flu vaccines can be made to protect against these most common flu strains.

Figure 1 below shows how the study was done in both substudies.

Figure 1. What happened in Substudy A and Substudy B?



Researchers took samples of blood from participants during the study. Researchers also checked the participants' health during the study and asked them how they were feeling.

In this study, participants who had high troponin I levels, abnormal ECG results, or symptoms that suggest possible myocarditis or pericarditis had additional check-ups at the study site.

- **Myocarditis** is an inflammation (or swelling) of the heart muscle. This heart condition can make it harder for the heart to pump blood.
- **Pericarditis** is an inflammation of the lining around the heart (called the pericardium).

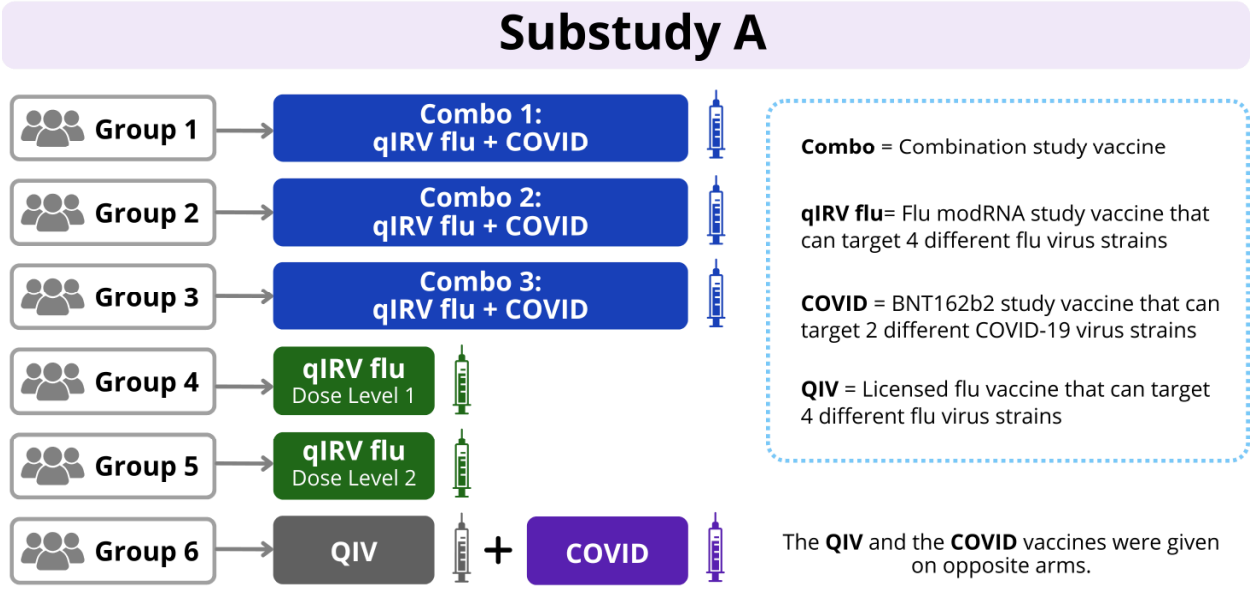
Participants had follow-up checks at the study site and over the phone from 3 days through 6 months after vaccination.

Substudy A:

Substudy A was an **open-label** study. This means that participants and researchers knew which vaccines participants got during the study.

Participants were divided into 2 age groups: **18 years through 64 years of age** and **65 years of age and older**. Researchers used a computer program to randomly assign participants per age group to 1 of 6 vaccine groups by chance. Figure 2 below shows the vaccine groups in Substudy A for both age groups.

Figure 2. Which vaccines were given in Substudy A?

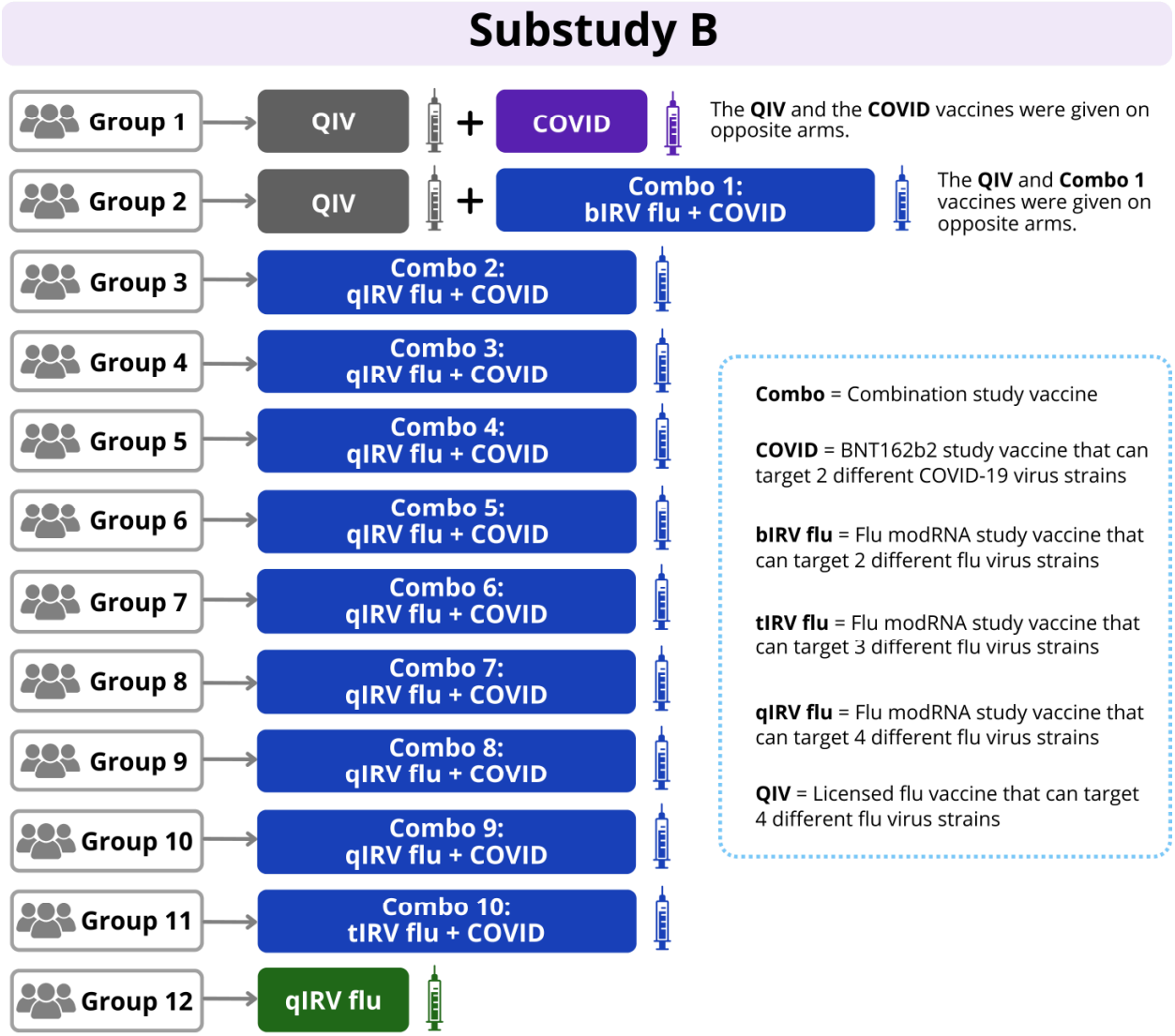


Substudy B:

Substudy B was a **single-blind** study. This means that researchers knew which vaccines participants got during the study, but participants did not know.

Participants in Substudy B were **18 years through 64 years of age**. Researchers used a computer program to randomly assign participants to 1 of 12 vaccine groups by chance. Figure 3 below shows the vaccine groups in Substudy B.

Figure 3. Which vaccines were given in Substudy B?



Where did this study take place?

This study ran at 41 locations in the US.

When did this study take place?

Substudy A began on 28 October 2022 and ended on 23 August 2023.
Substudy B began on 25 May 2023 and ended on 28 December 2023.

Who participated in this study?

Substudies A and B included healthy adults at least 18 years of age.

Substudy A:

Participants **18 years through 64 years of age** must have received at least 3 doses of 30 micrograms of BNT162b2 COVID-19 vaccine before joining this study. They must have not received a flu vaccine in the last 6 months before joining this study.

- Participants **65 years of age or older** must have received a flu vaccine for the current flu season at least 4 months before joining this study. They must have also received 4 or 5 doses of an modRNA COVID-19 vaccine before joining this study.

Substudy B:

- Participants **18 years through 64 years of age** must have received at least 3 doses of US-authorized modRNA COVID-19 vaccines before joining this study. They must have not received a flu vaccine in the last 6 months before joining this study.

A total of 379 participants joined **Substudy A**, and 633 participants joined **Substudy B**. Table 1 below shows how many participants took part in each substudy.

Table 1. Number of participants who took part in the study			
	Substudy A		Substudy B
	18 years through 64 years of age	65 years of age and older	18 years through 64 years of age
Started the study	182 participants	197 participants	633 participants
Got the study vaccine	180 out of 182 participants (98.9%)	All 197 participants (100%)	632 out of 633 participants (99.8%)
Finished the study	175 out of 182 participants (96.2%)	196 out of 197 participants (99.5%)	617 out of 633 participants (97.5%)
Did not finish the study	5 out of 182 participants (2.7%)	1 out of 197 participants (0.5%)	15 out of 633 participants (2.4%)

Among participants in either substudy who did not finish the study (Table 1), the most common reasons were:

- They did not want to continue with the study.
- They could not be contacted for a check-up.

Substudy A:

- **18 years through 64 years of age group:** Out of 180 participants who got the study vaccine, 84 men (46.7%) and 96 women (53.3%) participated. Participants were between 18 and 63 years of age.
- **65 years of age and older group:** Out of 197 participants who got the study vaccine, 98 men (49.7%) and 99 women (50.3%) participated. Participants were between 65 and 86 years of age.

Substudy B:

- **18 years through 64 years of age:** Out of 632 participants who got the study vaccine, 248 men (39.2%) and 384 women (60.8%) participated. Participants were between 18 and 64 years of age.

How long did the study last?

Each participant was in the study for about 6 months. The entire study took about 14 months to complete.

When the study ended in December 2023, the Sponsor Agent began reviewing the information collected. The Sponsor Agent then created a report of the results. This is a summary of that report.

What were the results of the study?

How many participants had any local reactions (injection site redness, swelling, or pain) within 7 days after vaccination?

Researchers checked how many participants recorded on their electronic diary or app in their phone whether they had any local reactions (such as injection site redness, swelling, or pain) within 7 days after vaccination. Then, researchers calculated the percentage of participants with local reactions.

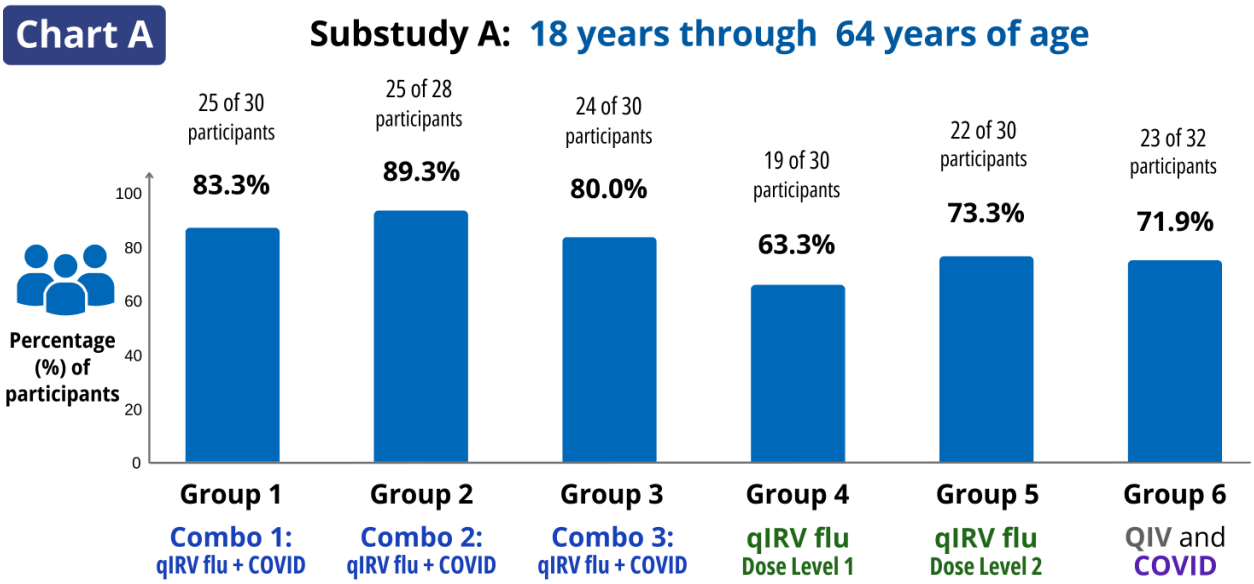
Percentage is used to compare proportions or parts of a whole. For example, if 20 out of 100 people had local reactions, that means 20% of people had local reactions.

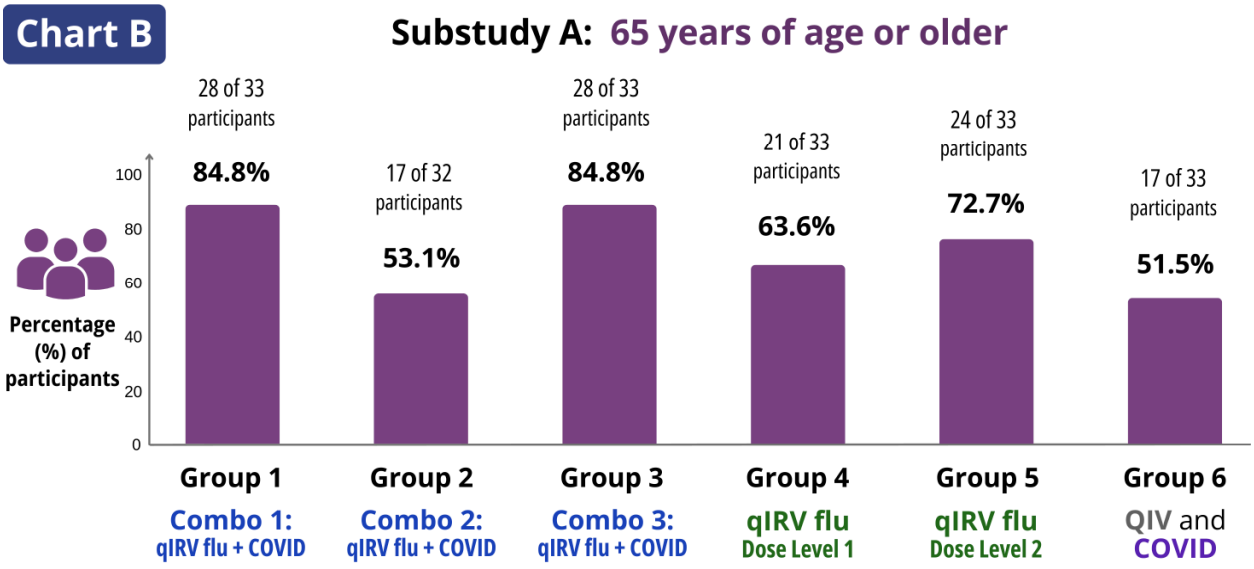
Substudy A:

The charts in Figure 4 below show how many participants in each age group had any local reactions within 7 days after vaccination in Substudy A.

- **18 years through 64 years of age:** **Chart A** shows that **63.3%** to **89.3%** of participants across the 6 groups had any local reactions within 7 days after vaccination.
- **65 years of age and older:** **Chart B** shows that **51.5%** to **84.8%** of participants across the 6 groups had any local reactions within 7 days after vaccination.

Figure 4. How many participants had any local reactions within 7 days after vaccination in Substudy A?





In both age groups of Substudy A:

- Most local reactions were mild or moderate in severity.
- The most common local reaction within 7 days after vaccination was pain at the injection site.

Substudy B:

The charts in Figure 5 below show how many participants had any local reactions within 7 days after vaccination in Substudy B.

- **Chart A** (Groups 1 to 6) and **Chart B** (Groups 7 to 12) show that **58.6%** to **82.8%** of participants across the 12 groups had any local reactions within 7 days after vaccination.

Figure 5. How many participants had any local reactions within 7 days after vaccination in Substudy B?

Chart A **Substudy B: 18 years through 64 years of age – Groups 1 to 6**

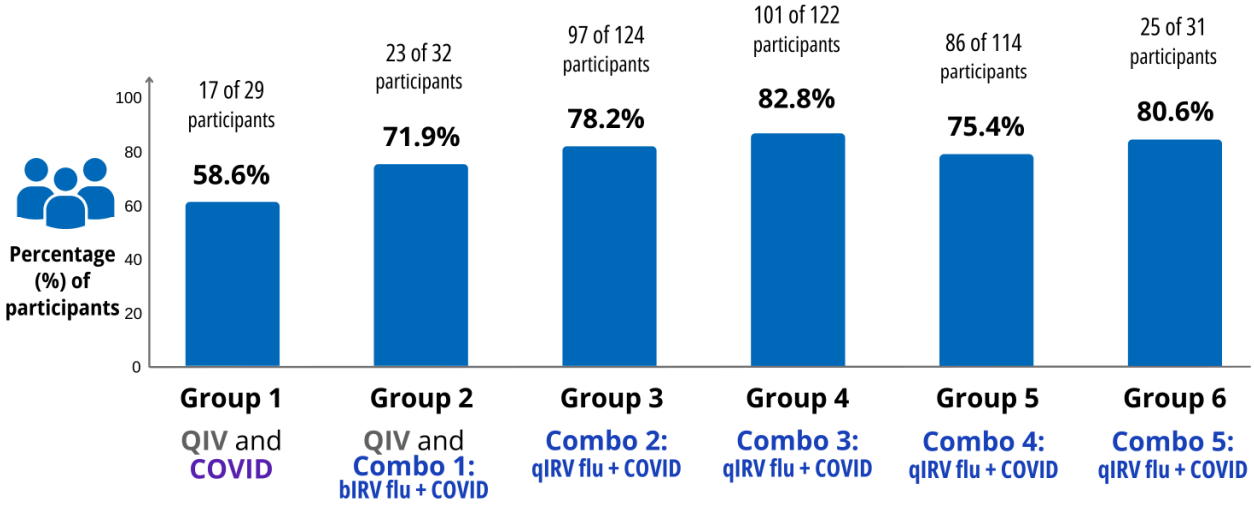
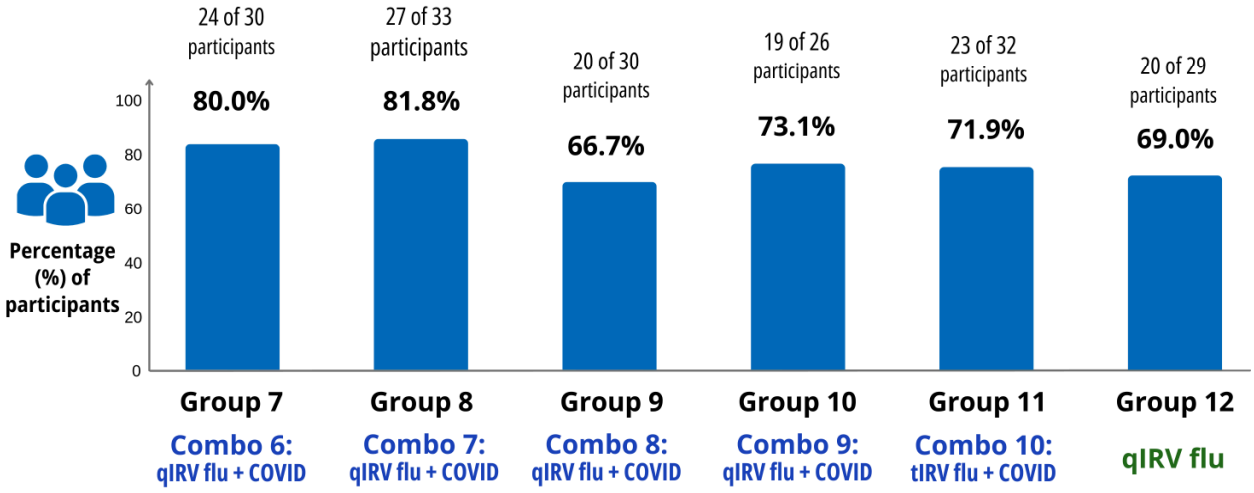


Chart B **Substudy B: 18 years through 64 years of age – Groups 7 to 12**



Among participants in Substudy B:

- Most local reactions were mild or moderate in severity.
- The most common local reaction within 7 days after vaccination was pain at the injection site.

How many participants had any systemic reactions (fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain) within 7 days after vaccination?

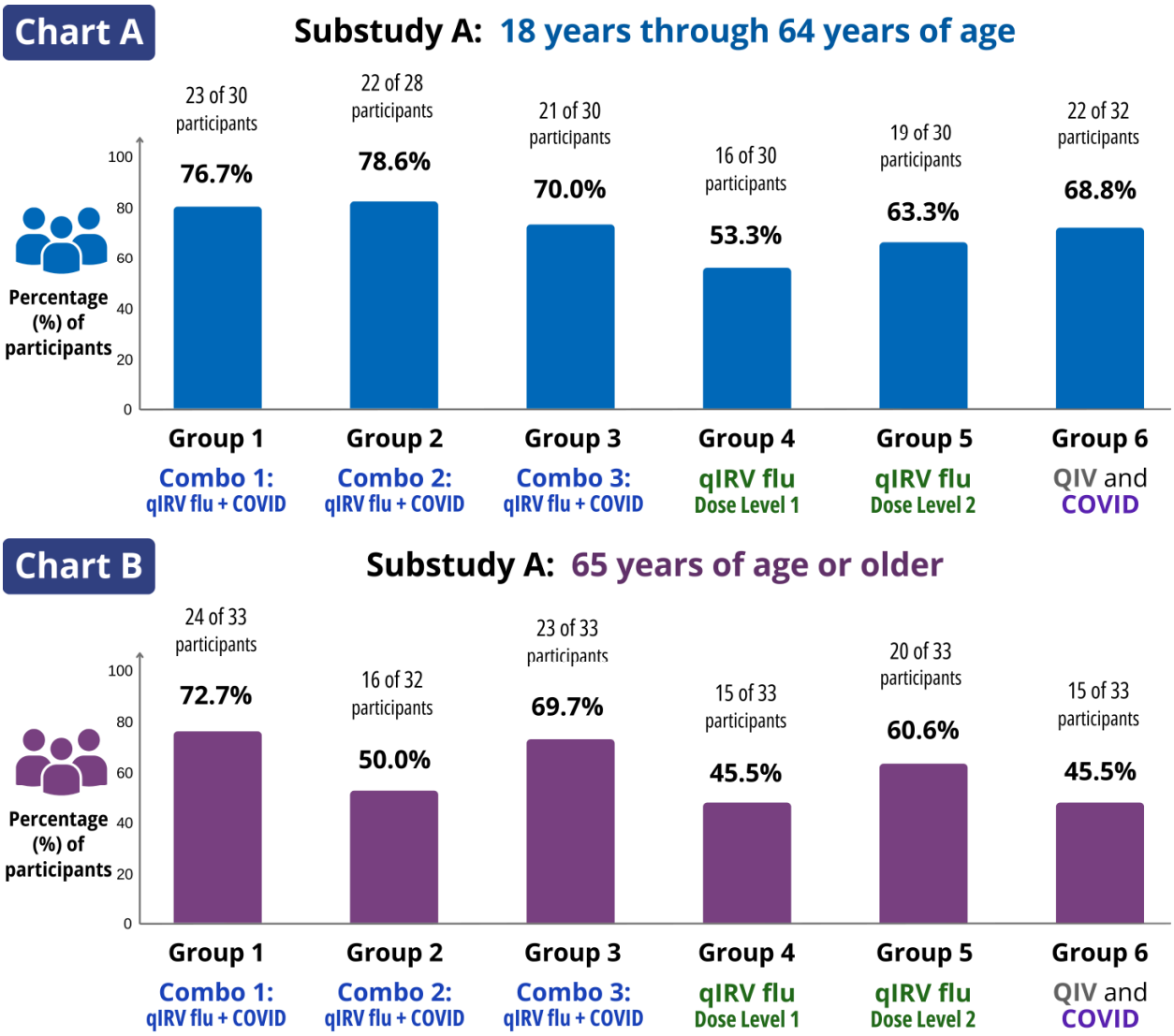
Researchers checked how many participants recorded on their electronic diary or app in their phone whether they had any **systemic reactions** (such as fever, tiredness, headache, chills, vomiting, diarrhea, new or worsened muscle pain, or new or worsened joint pain) within 7 days after vaccination. Then, researchers calculated the percentage of participants with systemic reactions.

Substudy A:

The charts in Figure 6 below show how many participants in each age group had any systemic reactions within 7 days after vaccination in Substudy A.

- **18 years through 64 years of age:** **Chart A** shows that **53.3%** to **78.6%** of participants across the 6 groups had any systemic reactions within 7 days after vaccination.
- **65 years of age and older:** **Chart B** shows that **45.5%** to **72.7%** of participants across the 6 groups had any systemic reactions within 7 days after vaccination.

Figure 6. How many participants had any systemic reactions within 7 days after vaccination in Substudy A?



In both age groups of Substudy A:

- Most systemic reactions were mild or moderate in severity.
- The most common systemic reactions within 7 days after vaccination were tiredness, headache, and chills.

Substudy B:

The charts in Figure 7 below show how many participants had any systemic reactions within 7 days after vaccination in Substudy B.

- **Chart A** (Groups 1 to 6) and **Chart B** (Groups 7 to 12) show that **48.3%** to **80.6%** of participants across the 12 groups had any systemic reactions within 7 days after vaccination.

Figure 7. How many participants had any systemic reactions within 7 days after vaccination in Substudy B?

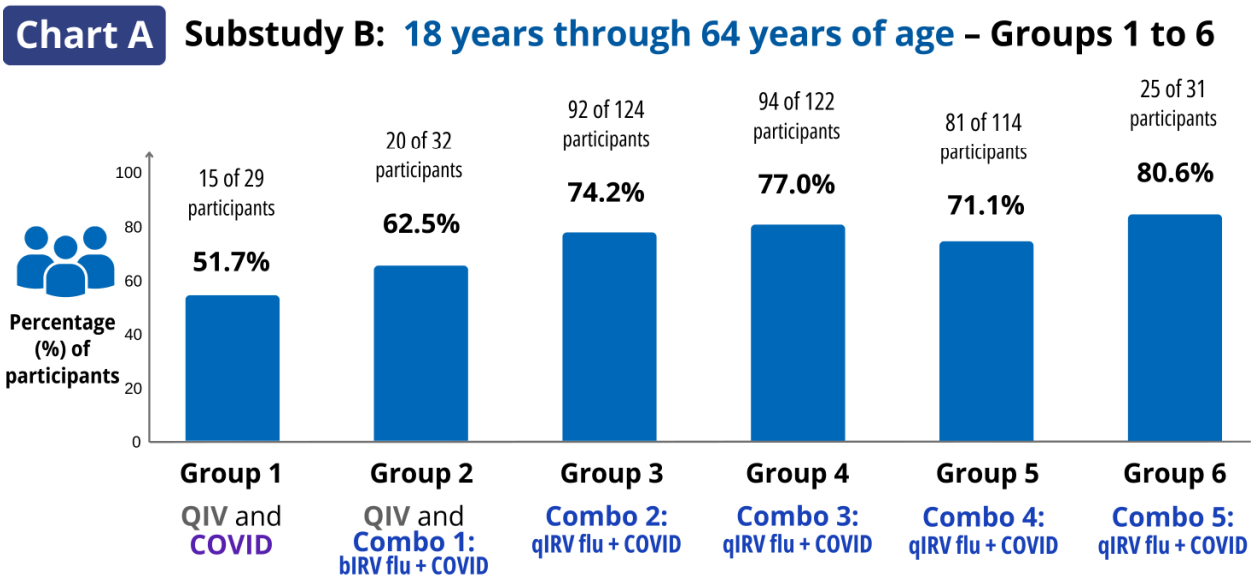
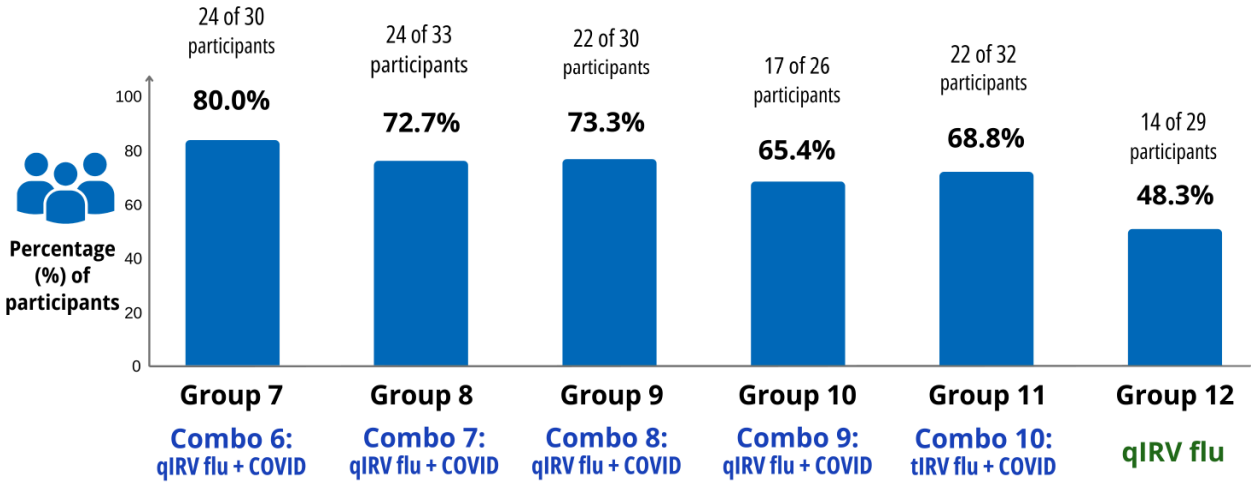


Chart B **Substudy B: 18 years through 64 years of age – Groups 7 to 12**



Among participants in Substudy B:

- Most systemic reactions were mild or moderate in severity.
- The most common systemic reactions within 7 days after vaccination were tiredness, headache, and chills.

How many participants had high troponin I levels within 7 days after vaccination?

Participants had blood tests to measure troponin I levels before and after vaccination.

At 1 week after vaccination, out of all participants across Substudies A and B, 1 participant had an abnormal troponin I result that was judged to be of no medical importance. This participant was from **Substudy A** (18 years through 64 years of age) **Group 1** who got qIRV flu plus COVID combo vaccine. Researchers found that this participant did not have myocarditis or pericarditis.

How many participants had new abnormal ECG findings within 7 days after vaccination?

Participants had ECG tests to measure the electrical activity of the heart before and after vaccination.

Researchers looked at the results of participants who had at least 1 ECG result after vaccination in the study.

Within 7 days of vaccination, none of the participants in Substudy A or B had new abnormal ECG findings that suggested myocarditis or pericarditis. None of the new abnormal ECG findings after vaccination in Substudy A or B were judged to be of medical importance.

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 unknown underlying disease or by chance). Or, medical problems could also have been caused by a study vaccine or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many vaccine groups in many studies, doctors try to understand what effects a study vaccine might have on a participant.

Results of Substudy A and Substudy B showed that vaccination with **flu plus COVID combo vaccine** at the tested dose levels was safe and well tolerated by participants 18 years through 64 years of age and participants 65 years of age and older.

How many participants had medical problems within 1 month after vaccination?

Substudy A:

The charts in Figure 8 below show how many participants in each age group had any medical problems within 1 month after vaccination in Substudy A.

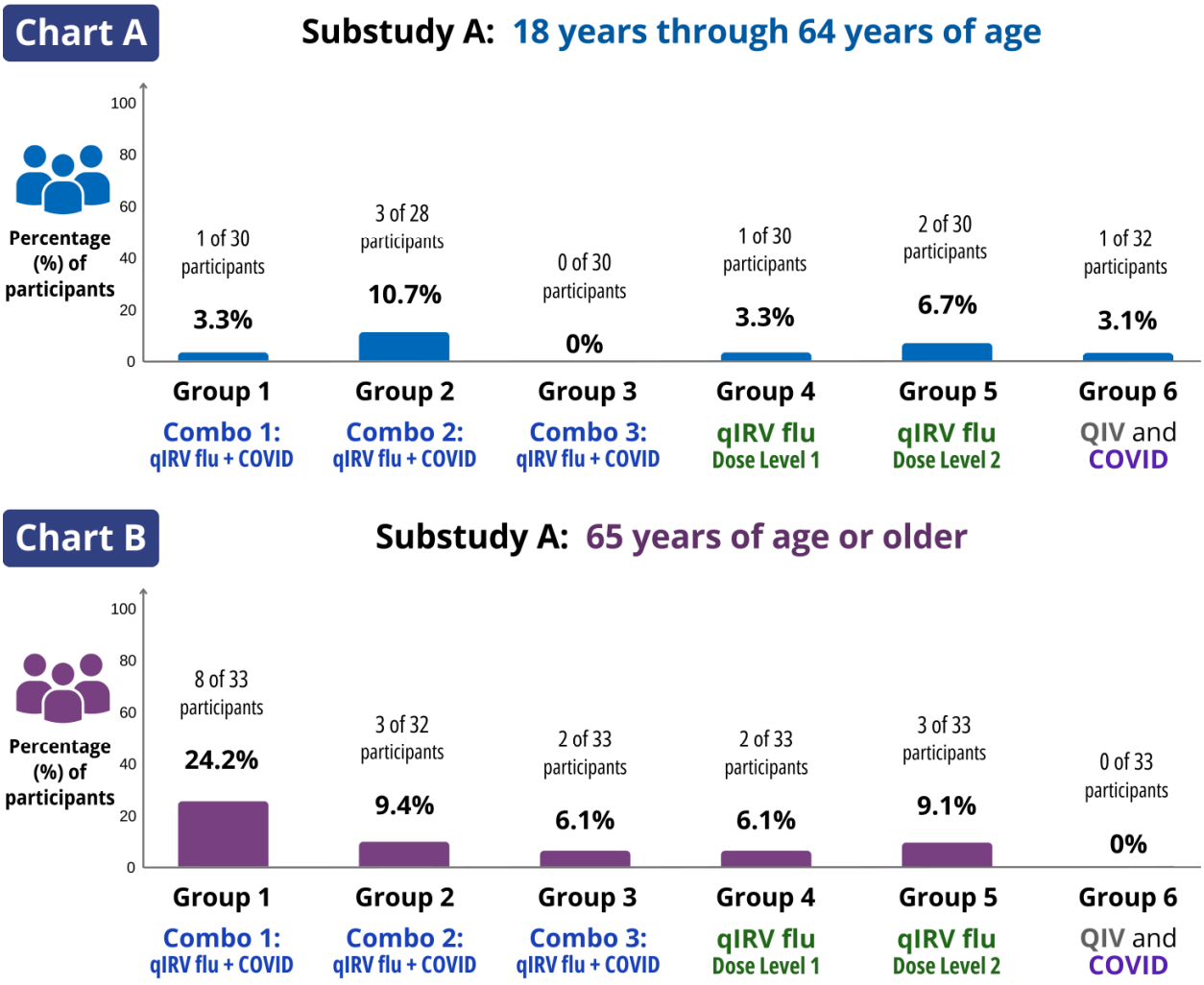
18 years through 64 years of age:

- **Chart A** shows that **0%** to **10.7%** of participants across the 6 groups had medical problems within 1 month after vaccination.
- None of the individual medical problems were reported by more than 1 participant.

65 years of age and older:

- **Chart B** shows that **24.2%** of participants in **Group 1** and **0%** to **9.4%** of participants across **Groups 2 to 6** had medical problems within 1 month after vaccination.
- The most common medical problem within 1 month after vaccination – reported by at least 2 participants in any vaccine groups – was **high blood pressure**. This was reported by 2 out of 33 participants (**6.1%**) in Group 1. Researchers thought this medical problem of the 2 participants was not caused by the study vaccine.

Figure 8. How many participants had medical problems within 1 month after vaccination in Substudy A?



Throughout Substudy A, no participant left the study because of medical problems.

Substudy B:

The charts in Figure 9 below show how many participants had any medical problems within 1 month after vaccination in Substudy B.

- **Chart A** (Groups 1 to 6) and **Chart B** (Groups 7 to 12) show that **0%** to **9.7%** of participants across the 12 groups had medical problems within 1 month after vaccination.
- None of the individual medical problems were reported by more than 1 participant.

Figure 9. How many participants had medical problems within 1 month after vaccination in Substudy B?

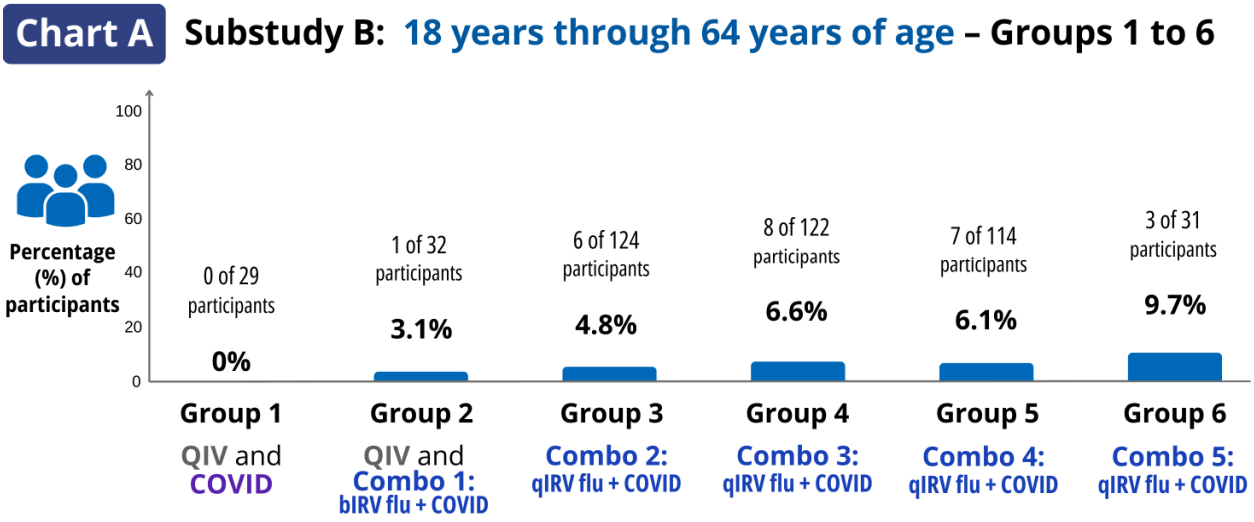
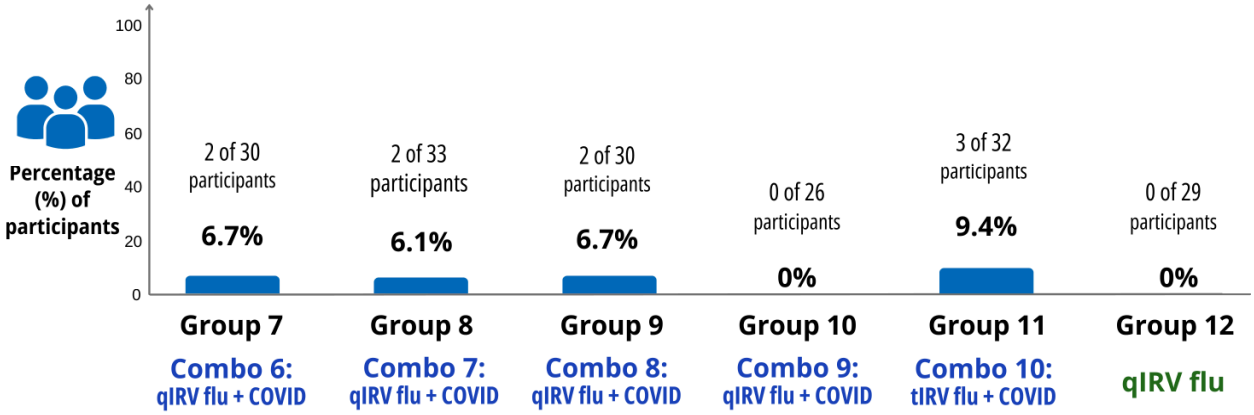


Chart B **Substudy B: 18 years through 64 years of age – Groups 7 to 12**



Throughout Substudy B, no participant left the study because of medical problems.

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.

How many participants had serious medical problems within 6 months after vaccination?

Substudy A:

The list below shows how many participants in each age group had any serious medical problems within 6 months after vaccination in Substudy A.

18 years through 64 years of age:

- 1 participant in **Group 2** who got qIRV flu plus COVID combo vaccine had stomach ulcer.
- 1 participant in **Group 6** who got QIV and COVID vaccines had a narrowing of the space around the spine due to an injury.

Researchers thought that these 2 serious medical problems were not caused by the study vaccine.

65 years of age and older:

- 1 participant in **Group 4** who got qIRV flu vaccine (Dose Level 1) had gallbladder infection.
- 1 participant in **Group 4** who got qIRV flu vaccine (Dose Level 1) had a spinal fracture due to an injury.

Researchers thought that these 2 serious medical problems were not caused by the study vaccine.

No participant in either age group of Substudy A died during the study.

Substudy B:

The list below shows how many participants had any serious medical problems within 6 months after vaccination in Substudy B.

- 1 participant in **Group 6** who got qIRV flu plus COVID combo vaccine had appendicitis.

Researchers thought that this serious medical problem was not caused by the study vaccine.

No participant in Substudy B died during the study.

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 **C5261001**

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

www.clinicaltrials.gov	Use the study identifier **NCT05596734**

Please remember that researchers look at the results of many studies to find out which vaccines 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!