

Plain Language Clinical Study Summary

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: Comirnaty® (also known as PF-07302048 or BNT162b2)

Protocol Number: C4591054 (Substudy A)

Dates of Study: 10 August 2023 to 28 February 2024

Title of this Study: A Study to Learn About New COVID-19 RNA Vaccine Candidates for New Variants in Healthy Individuals (Substudy A)

[A Phase 2/3 Protocol to Investigate the Safety, Tolerability, and Immunogenicity of BNT162b2 RNA-Based Vaccine Candidates for SARS-CoV-2 New Variants in Healthy Individuals]

Date of this Report: 06 August 2025

– Thank You –

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



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

Why was this study done?

What is COVID-19?

Coronavirus disease 2019 (or COVID-19) is caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 spreads easily from person to person and can cause mild to severe illness. People with COVID-19 can have symptoms such as fever, chills, cough, loss of taste or smell, muscle pain, sore throat, vomiting, diarrhea, or trouble breathing.

All viruses, including the COVID-19 virus, are expected to change over time. These changes or mutations from the original virus are called different “variants” (or strains). One of the strains of SARS-CoV-2 is **Omicron** (also called **Omi**).

Compared to the original COVID-19 virus, the Omi strain spreads more easily between people.

Over the past few years, there have been many different versions of the Omi strain. These Omi strains are being closely watched to see which may cause more severe illness for people and if they are being targeted by current vaccines.

Health authorities continue to track new COVID-19 strains and recommend that scientists update the COVID-19 vaccines depending on the currently circulating strains.

Health authorities recommend people to stay up to date with COVID-19 vaccinations, especially before the fall and winter months when COVID-19 infections are expected to rise. Vaccination can help protect people from illnesses caused by new COVID-19 virus strains.

What are BNT162b2 and BNT162b2 (Omi XBB.1.5) vaccines?

These injectable vaccines may help the body's immune system to defend against COVID-19.

BNT162b2 is the original monovalent COVID-19 vaccine designed to target the original strain of the COVID-19 virus. A monovalent COVID-19 vaccine can target 1 strain of the COVID-19 virus.

- It does not contain a whole virus or any part of the virus that can cause COVID-19.
- It is made up of a part of the virus's genetic code, surrounded by fatty particles called lipids. It uses the body's own cells to produce a spike protein, which may help the body produce antibodies to fight against COVID-19.

In 2021, health agencies approved BNT162b2 (original formulation) for use in people 16 years of age and older.

In this study, participants got an updated version of BNT162b2 called **BNT162b2 (Omi XBB.1.5)**. BNT162b2 (Omi XBB.1.5) was designed to help protect against the **Omi XBB.1.5** strain. Omi XBB.1.5 strain was the most widespread COVID-19 virus strain worldwide at the start of this study.

During this study, in 2023, health agencies in the United States (US) and other countries authorized or approved BNT162b2 (Omi XBB.1.5) for use in people 6 months of age and older.

Comirnaty® is the brand name for the BNT162b2 COVID-19 vaccine, including both the original formulation and updated versions such as BNT162b2 (Omi XBB.1.5).



What was the purpose of this study?

The study was divided into 3 substudies: Substudy A, Substudy B, and Substudy C, each with their own group of participants. This report only includes what happened in **Substudy A**. Results of Substudy B and Substudy C are discussed in separate reports.

The main purpose of Substudy A was to learn if BNT162b2 (Omi XBB.1.5) given to healthy people is safe and may produce immune responses against the COVID-19 strains circulating at the time of this study.



When a person first gets a vaccine, a protective **immune response** is triggered in the body. This means that the body's immune system is activated to make **antibodies**.

- **Antibodies** are proteins that can fight off infections and help prevent disease.
- An **immune response** is the body's ability to find and fight off germs that cause disease.

Researchers wanted to know:

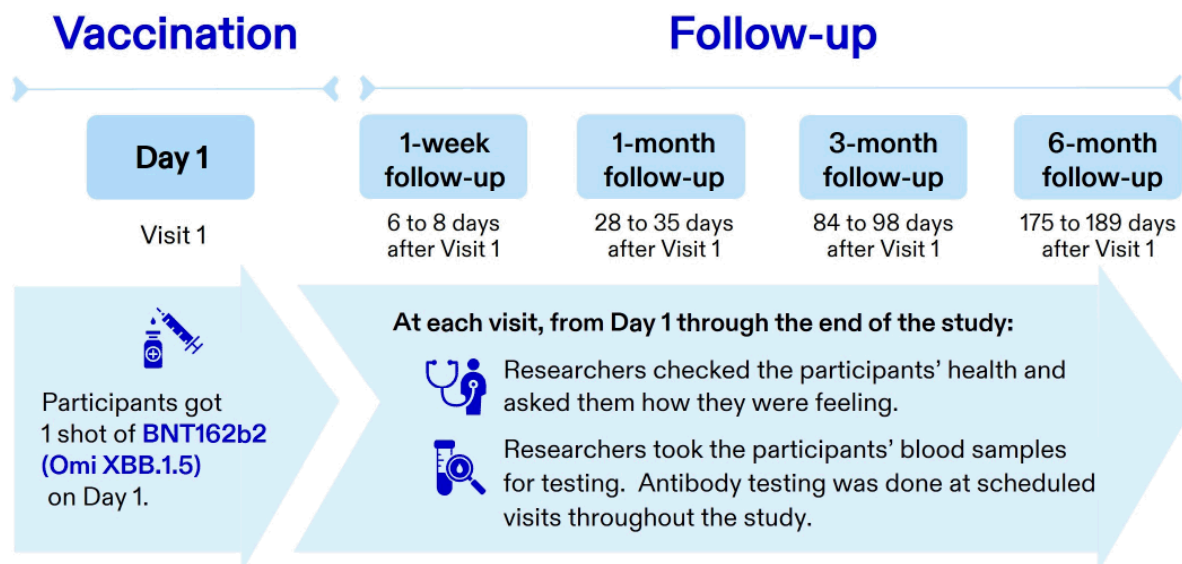
- Can BNT162b2 (Omi XBB.1.5) vaccine produce immune responses to help protect against COVID-19 virus in participants who have previously gotten COVID-19 vaccines?
 - What medical problems did participants have during the study?
-

What happened during the study?

How was the study done?

Participants got 1 shot of BNT162b2 (Omi XBB.1.5) 30 micrograms (mcg) in this study. Figure 1 shows how the study was done.

Figure 1. Study plan



This study was “open-label”, which means that the participants, their parents/guardians (for participants 12 to 17 years of age), and researchers knew that all participants got BNT162b2 (Omi XBB.1.5) in this study.

Where did this study take place?

The Sponsor ran this study in the US.

When did this study take place?

Substudy A began on 10 August 2023 and ended on 28 February 2024.

Who participated in this study?

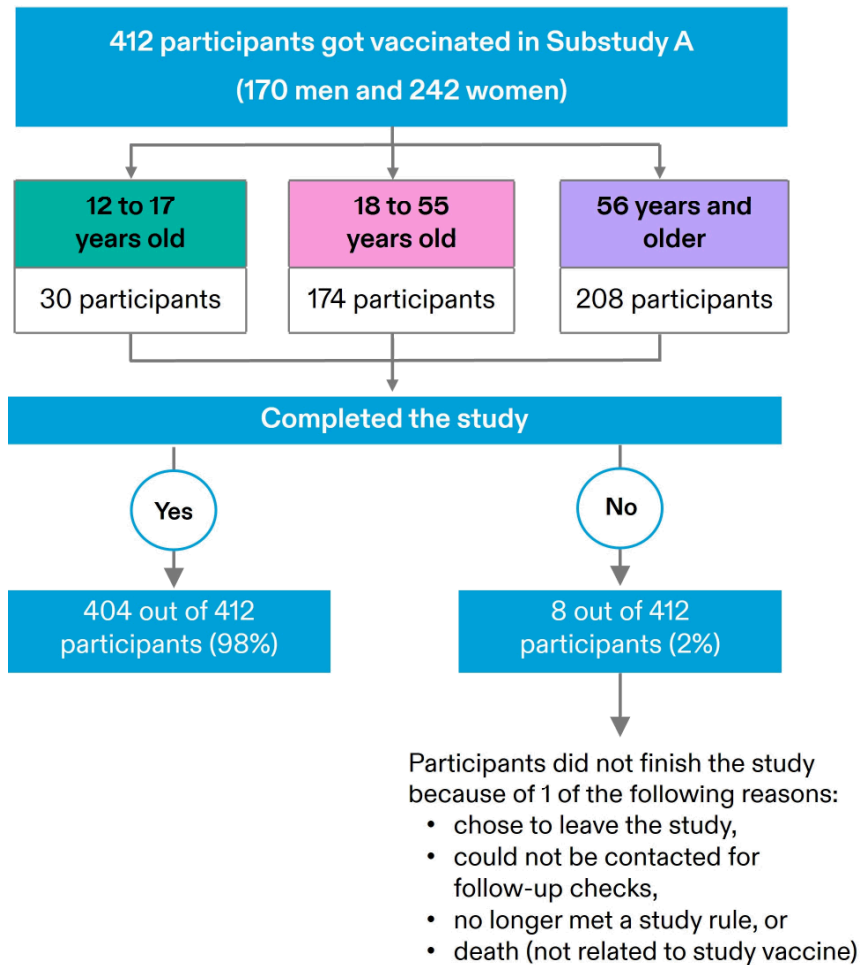
The study included participants at least 12 years old who were considered healthy by the researchers. They must have previously gotten at least 3 shots of US-authorized COVID-19 vaccines, with the last shot being **BNT162b2 (original/Omi BA.4/BA.5)** given at least 5 months before joining this study.

BNT162b2 (original/Omi BA.4/BA.5) is a bivalent form of the original BNT162b2 vaccine. A bivalent vaccine can target 2 strains of a virus.

In 2022, health agencies in the US and other countries authorized or approved BNT162b2 (original/Omi BA.4/BA.5) for use in people 6 months of age and older. BNT162b2 (original/Omi BA.4/BA.5) was designed to help protect against the **original** and **Omi BA.4/BA.5** strains, which were the circulating COVID-19 strains at that time.

Figure 2 shows how many participants joined the study.

Figure 2. How many participants joined Substudy A?



How long did the study last?

Substudy A participants were in the study for about 6 months. Substudy A took about 7 months to complete. It was completed as planned.

When Substudy A ended in February 2024, 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?

Can BNT162b2 (Omi XBB.1.5) vaccine produce immune responses to help protect against COVID-19 virus in participants who have previously gotten COVID-19 vaccines?

To answer the question:



Researchers measured the participants' **antibody levels** against Omi XBB.1.5 and Omi BA.4/BA.5 strains of the COVID-19 virus **before** and 1 month **after BNT162b2 (Omi XBB.1.5)** vaccination.



Researchers also checked how many participants had **strong immune responses** against Omi XBB.1.5 and Omi BA.4/BA.5. In this study, a strong immune response means the antibody levels were at least **4 times higher** at 1 month **after** vaccination compared to **before** vaccination.

Researchers then compared the results of participants from this study to the results of selected participants from another study (Study C4591044). Both studies included healthy participants at least 12 years of age.

In **Study C4591044**, participants got 3 shots of BNT162b2 30 mcg before joining the study and got **BNT162b2 (original/Omi BA.4/BA.5) 30 mcg** as the 4th shot during Study C4591044.

In Study C4591044, researchers tested BNT162b2 (original/Omi BA.4/BA.5), as well as new vaccine candidates. These vaccines were designed to target the COVID-19 virus strains circulating at the time of the study, which included the **original** and **Omi BA.4/BA.5** strains.

Antibody levels:

Researchers found that at 1 month after vaccination:

- Participants across all age groups in this study who got BNT162b2 (Omi XBB.1.5) showed **increased antibody levels** against the Omi XBB.1.5 and Omi BA.4/BA.5 strains of the COVID-19 virus.
- Participants in this study who got BNT162b2 (Omi XBB.1.5) had **higher antibody levels** against Omi XBB.1.5 and Omi BA.4/BA.5 strains than that of Study C4591044 participants who got BNT162b2 (original/Omi BA.4/BA.5).
- In terms of the **average increase in antibodies**, participants in this study who got BNT162b2 (Omi XBB.1.5) had **higher** average increase in antibodies against Omi XBB.1.5 strain and **lower** average rise in antibodies against Omi BA.4/BA.5 strain than that of Study C4591044 participants who got BNT162b2 (original/Omi BA.4/BA.5).

Average increase in antibodies means how much higher antibody levels are **after** vaccination compared to **before** vaccination.

Immune responses:

Researchers found that at 1 month after vaccination:

- The percentages of participants in this study who got BNT162b2 (Omi XBB.1.5) with **strong immune responses** against Omi XBB.1.5 and Omi BA.4/BA.5 strains were generally **similar** across all age groups.
- The percentage of participants in this study who got BNT162b2 (Omi XBB.1.5) with strong immune responses was **higher** against Omi XBB.1.5

strain and **lower** against BA.4/BA.5 strain than that of Study C4591044 participants who got BNT162b2 (original/Omi BA.4/BA.5).



Compared to the older version of the vaccine (BNT162b2 [original/Omi BA.4/BA.5]), study results showed that **BNT162b2 (Omi XBB.1.5)**, when given to healthy participants at least 12 years old who had previously gotten US-authorized COVID-19 vaccines, produced improved immune responses that may help protect against:

- Omi XBB.1.5 strain, the circulating strain at the time of the study, and
- Omi BA.4/BA.5 strain, the circulating strains before this study started.

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.

How many participants had any local reaction and systemic event within 7 days after vaccination?

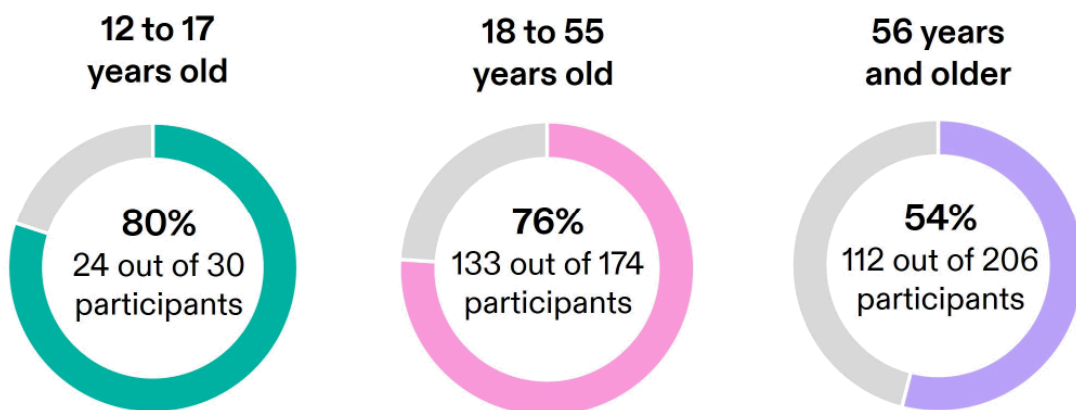
“**Local reactions**” include pain, redness, and swelling at the injection site (area on the arm where the vaccine was injected).

“**Systemic events**” are reactions that affect the whole body like fever, chills, diarrhea, vomiting, headache, tiredness, muscle pain, and joint pain.

To answer the question, researchers checked the electronic diary records of participants in this study.

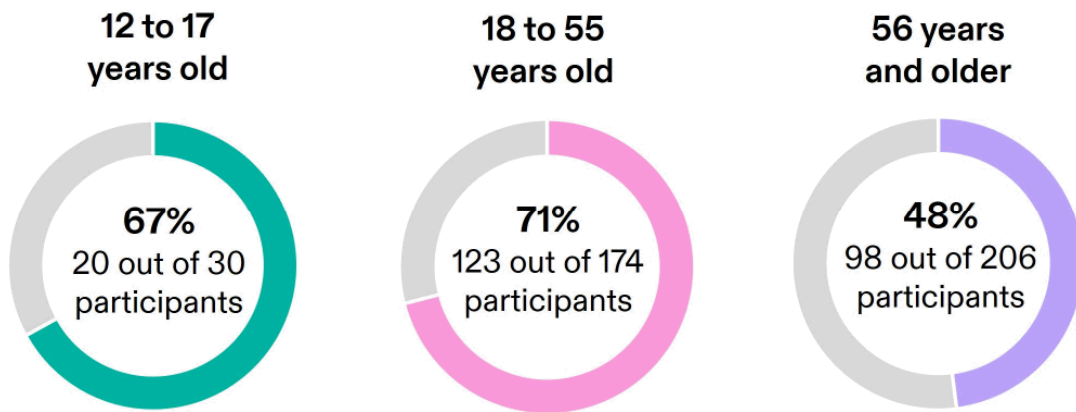
Figure 3 and Figure 4 show the answer to the question by age group.

Figure 3. Number of participants with any local reaction within 7 days after vaccination – by age group



The most common local reaction in all age groups was **pain at the injection site**. All local reactions were mild or moderate in severity and lasted for 1 to 3 days.

Figure 4. Number of participants with any systemic event within 7 days after vaccination

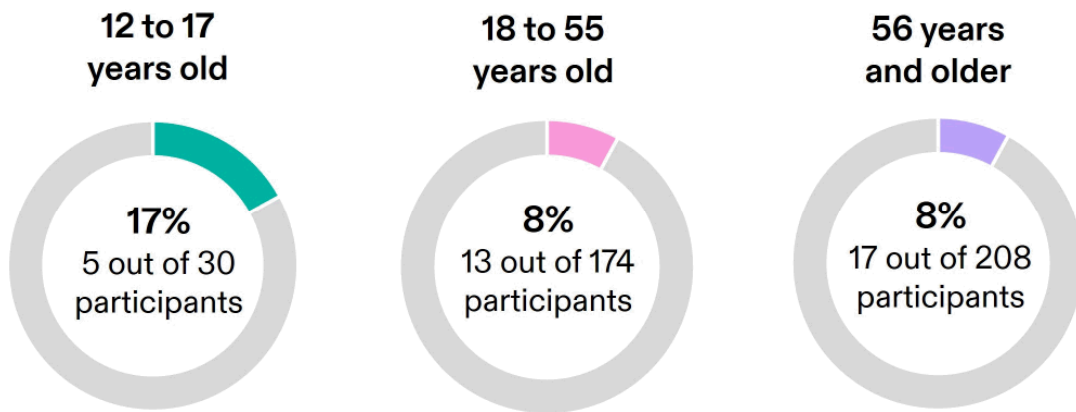


The most common systemic event in all age groups was **tiredness**. Most systemic events were mild or moderate in severity and lasted for 1 to 2 days.

How many participants had any medical problem within 1 month after vaccination?

Figure 5 shows that, across the 3 age groups, a total of 35 out of 412 participants (9%) had at least 1 medical problem within 1 month after vaccination.

Figure 5. Number of participants with any medical problem within 1 month after vaccination – by age group



Most of the medical problems within 1 month after vaccination were mild or moderate in severity. None of the medical problems reported within 1 month after vaccination happened in more than 2 participants.

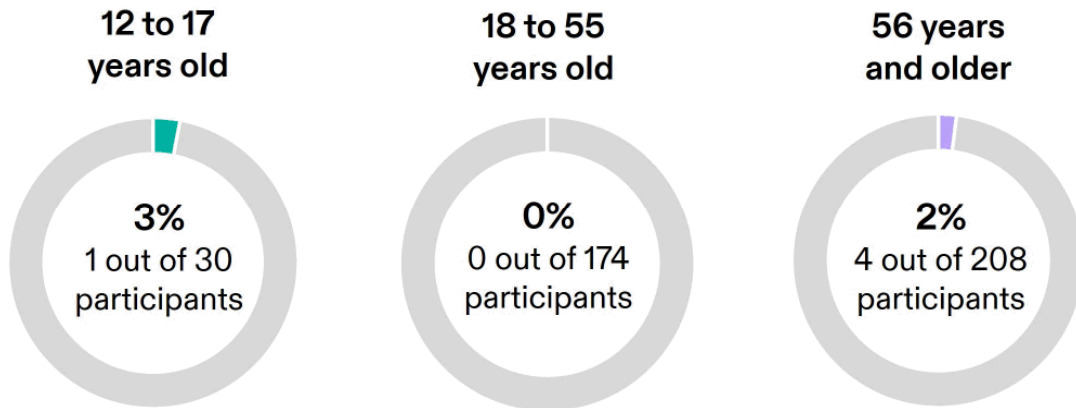
Did study participants have any serious medical problems?

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?

Figure 6 shows that, across the 3 age groups, a total of 5 out of 412 participants (1%) had serious medical problems within 6 months after vaccination.

Figure 6. Number of participants with any serious medical problems within 6 months after vaccination – by age group



These 5 participants had a total of 7 serious medical problems that researchers believe were not caused by BNT162b2 (Omi XBB.1.5).

During Substudy A, 1 participant in the 56 years and older age group died due to “**cardiac arrest**” 106 days (or 3 and a half months) after vaccination. Researchers believe that the cause of death was not due to BNT162b2 (Omi XBB.1.5). This participant was diagnosed with “high cholesterol” before joining this study.

- Cardiac arrest is a condition where a person’s heart stops beating.
- High cholesterol is a condition where there is too much fat-like substance in the blood. This can increase the risk of heart problems.

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](http://www.pfizer.com/research/research_clinical_trials/trial_results)

Use the protocol number
C4591054 (Substudy A)

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

www.clinicaltrials.gov

Use the study identifier **NCT05997290**

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 or your child 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!

