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 C)

Dates of Study: 10 May 2024 to 13 March 2025

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

[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: 05 September 2025

– Thank You –

Pfizer

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 **s**evere **a**cute **r**espiratory **s**yndrome **co**rona**v**irus **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, BNT162b2 (Omi JN.1), and BNT162b2 (Omi KP.2) 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, researchers tested 2 updated versions of BNT162b2 called **BNT162b2 (Omi JN.1)** and **BNT162b2 (Omi KP.2)**.

BNT162b2 (Omi JN.1) was designed to help protect against the **Omi JN.1** strain, while BNT162b2 (Omi KP.2) was designed to help protect against the **Omi KP.2** strain. The Omi JN.1 strain was the most widespread COVID-19 virus strain worldwide, and the Omi KP.2 strain was spreading quickly in the United States (US) at the start of this study.

During this study, in 2024, health agencies in the US and other countries authorized or approved BNT162b2 (Omi KP.2) for use in people 6 months of age and older. Also in 2024, health agencies in the European Union authorized BNT162b2 (Omi JN.1) for use in people 6 months of age and older.

> Comirnaty® is the brand name for the BNT162b2 COVID-19 vaccine, including the original formulation and updated versions such as BNT162b2 (Omi JN.1) and BNT162b2 (Omi KP.2).

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 C**. Results of Substudy A and Substudy B are discussed in separate reports.

The main purpose of Substudy C was to learn if BNT162b2 (Omi JN.1) and BNT162b2 (Omi KP.2), when given to healthy people, are safe and may produce immune responses against the COVID-19 strains circulating at the time of this study.

Researchers wanted to know:

- **Do BNT162b2 (Omi JN.1) and BNT162b2 (Omi KP.2) vaccines produce immune responses that may help protect against COVID-19 virus in healthy participants?**
- **What medical problems did participants have during the study?**

What happened during the study?

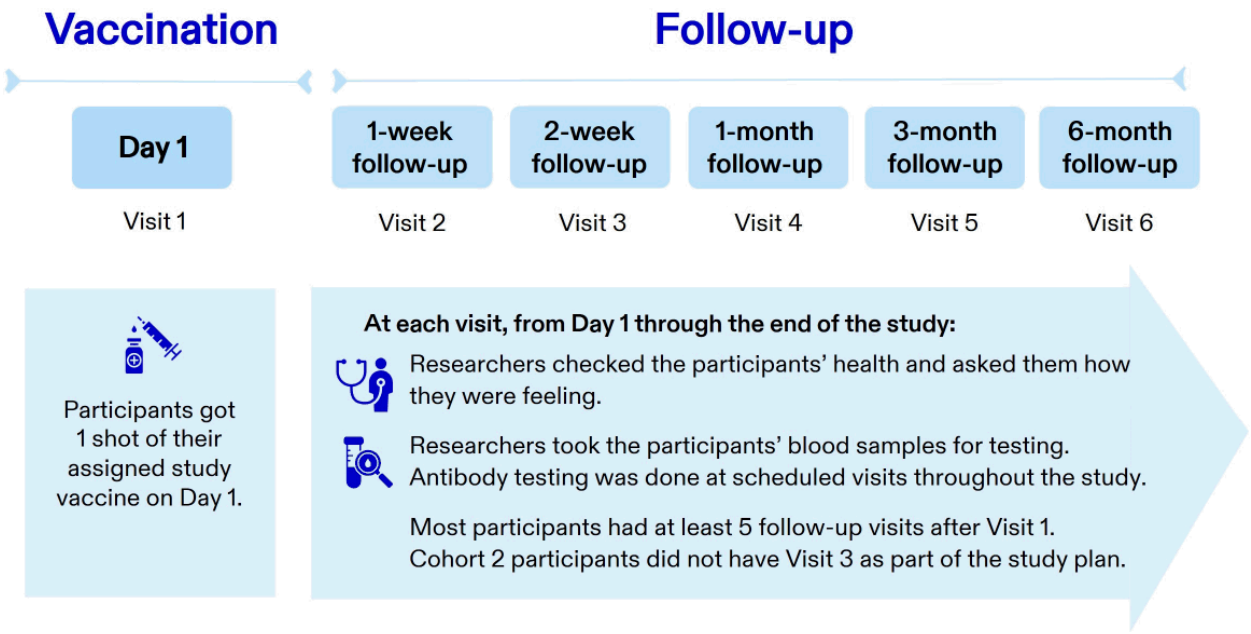
How was the study done?

Participants received 1 shot of the study vaccine (30 micrograms [mcg]).
Participants joined 1 of 3 cohorts (or groups of participants):

	Participant age	Vaccine given
Cohort 1	at least 18 years old	BNT162b2 (Omi JN.1)
Cohort 2	at least 12 years old	
Cohort 3	at least 18 years old	BNT162b2 (Omi KP.2)

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 JN.1 or Omi KP.2) in this study.

Where did this study take place?

The Sponsor ran this study in the US.

When did this study take place?

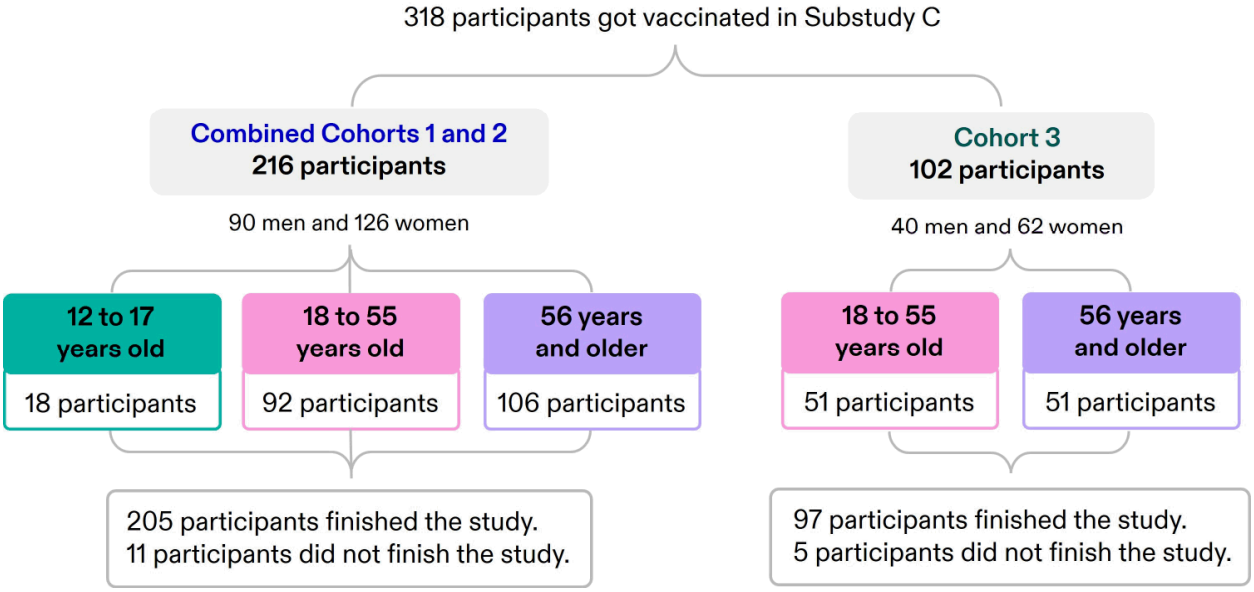
Substudy C began on 10 May 2024 and ended on 13 March 2025.

Who participated in this study?

The study included participants at least 12 years of age for Cohort 2 and at least 18 years of age for Cohorts 1 and 3. Participants must have been considered healthy by the researchers.

Figure 2 shows how many participants joined the study.

Figure 2. Number of participants in Substudy C



In the combined Cohorts 1 and 2, the most common reason why some participants did not finish the study was that they could not be contacted for follow-up checks.

In Cohort 3, the most common reason why some participants did not finish the study was that they no longer met a study rule.

How long did the study last?

Each participant in Substudy C was in the study for about 6 months. The entire Substudy C took about 10 months to complete. It was completed as planned.

When the study ended in March 2025, 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?

Do BNT162b2 (Omi JN.1) and BNT162b2 (Omi KP.2) vaccines produce immune responses that may help protect against COVID-19 virus in healthy participants?

To answer the question:

Researchers measured the participants' **antibody levels** against Omi JN.1, Omi KP.2, and Omi XBB.1.5 strains of the COVID-19 virus **before** and 1 month **after** getting the study vaccine.

This was done to see how the immune system responded to both the older strain and the new strain that the updated study vaccines were designed to protect against.

Researchers also checked how many participants had **strong immune responses** against Omi JN.1, Omi KP.2, and Omi XBB.1.5 strains. In this study, a strong immune response means the antibody levels were at least **4 times higher** 1 month **after** vaccination compared to **before** vaccination.

The sections below describe the results for each study vaccine.

Immune responses against Omi JN.1 and Omi XBB.1.5 strains after BNT162b2 (Omi JN.1) vaccination – Combined Cohorts 1 and 2

Researchers compared the results of the combined Cohorts 1 and 2 participants who got **BNT162b2 (Omi JN.1)** to the results of selected participants in Substudy A of this same study. Both groups included healthy participants at least 12 years of age.

Substudy A participants got **BNT162b2 (Omi XBB.1.5)** 30 mcg, which was designed to help protect against the **Omi XBB.1.5** strain.

Antibody levels:

Researchers found that at 1 month after vaccination (see Figure 3):

- Combined Cohorts 1 and 2 participants across all age groups who got BNT162b2 (Omi JN.1) showed **increased** antibody levels against both Omi JN.1 and Omi XBB.1.5 strains of the COVID-19 virus.
- Combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1) had **generally higher** antibody levels against Omi JN.1 strain and **generally lower** antibody levels against Omi XBB.1.5 than that of Substudy A participants who got BNT162b2 (Omi XBB.1.5).
- In terms of the **average increase in antibodies**, combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1) had **generally higher** average increase in antibodies against Omi JN.1 strain and **generally lower** average increase in antibodies against Omi XBB.1.5 strain than that of Substudy A participants who got BNT162b2 (Omi XBB.1.5).

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

Figure 3. Antibody levels against Omi JN.1 (Chart A) and Omi XBB.1.5 (Chart B) strains before and 1 month after vaccination

Chart A: Omi JN.1 strain

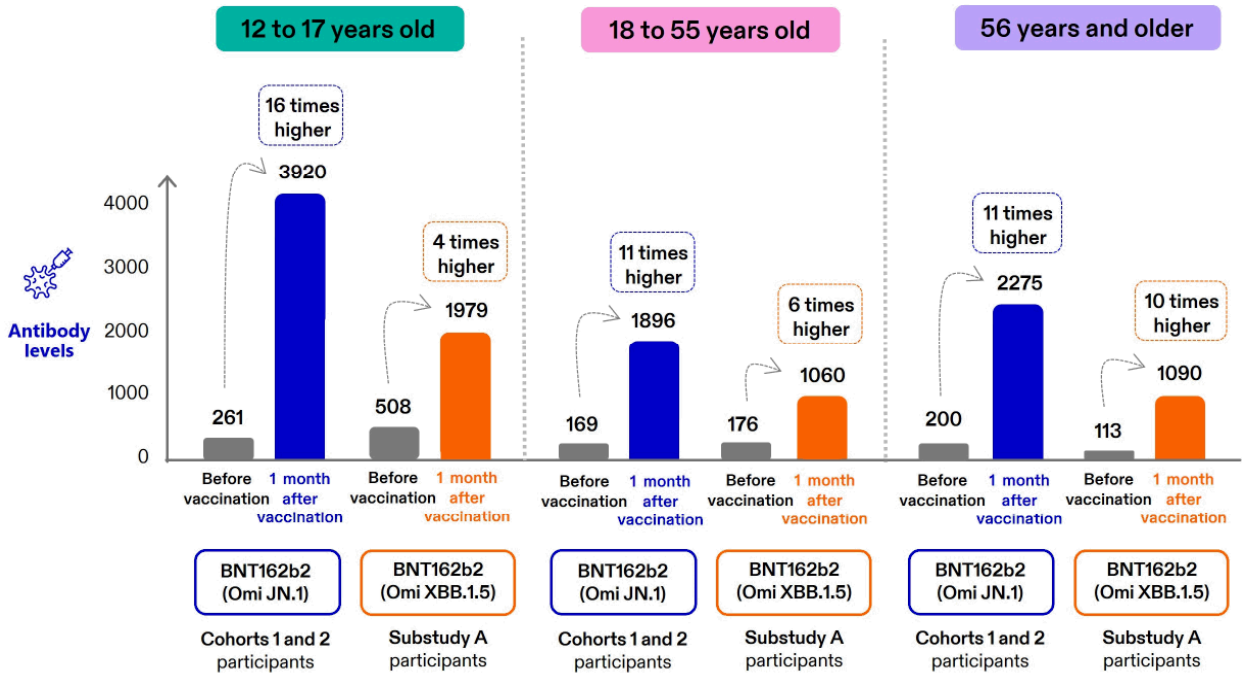
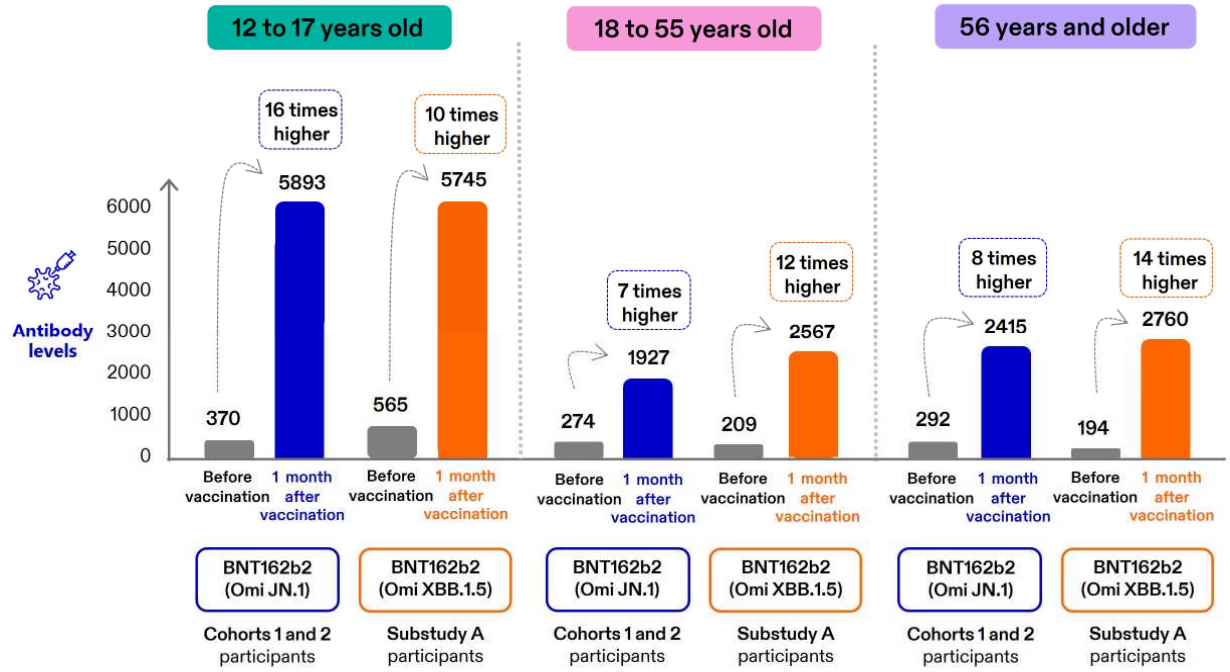


Chart B: **Omi XBB.1.5 strain**



Immune responses:

Researchers found that at 1 month after vaccination (see Figure 4):

- The percentages of combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1) with strong immune responses against Omi JN.1 and Omi XBB.1.5 strains were **generally similar** across all age groups.
- Compared to Substudy A participants who got BNT162b2 (Omi XBB.1.5), the percentages of combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1) with strong immune responses were:
  - **slightly higher** against Omi JN.1 strain
  - **generally lower** against Omi XBB.1.5 strain

Figure 4. Percentages of participants with strong immune responses against Omi JN.1 (Chart A) and Omi XBB.1.5 (Chart B) strains 1 month after vaccination

Chart A: Omi JN.1 strain

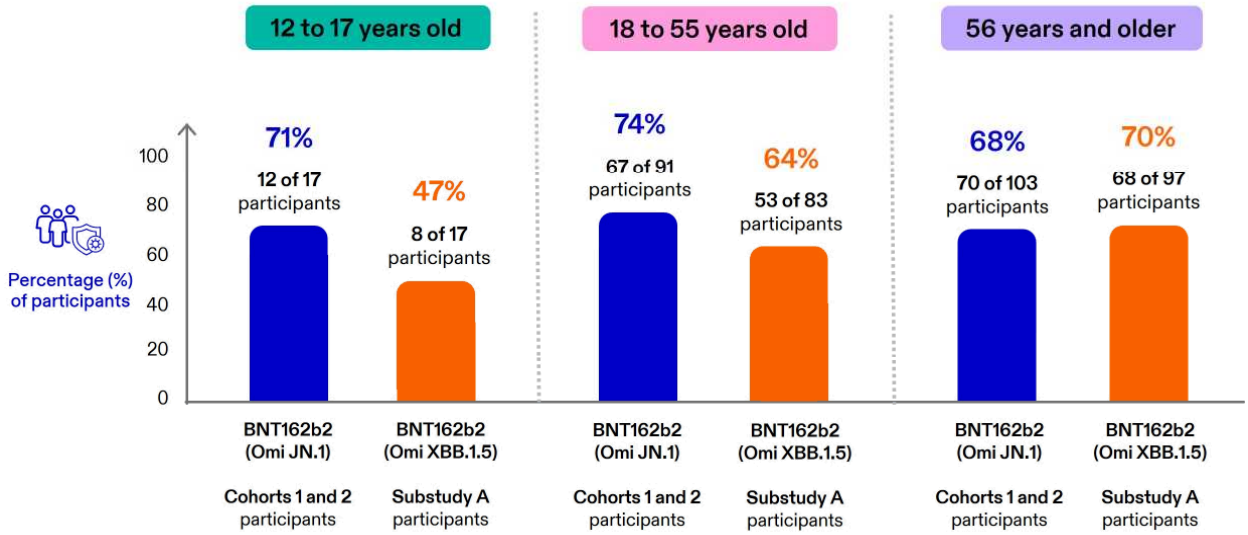
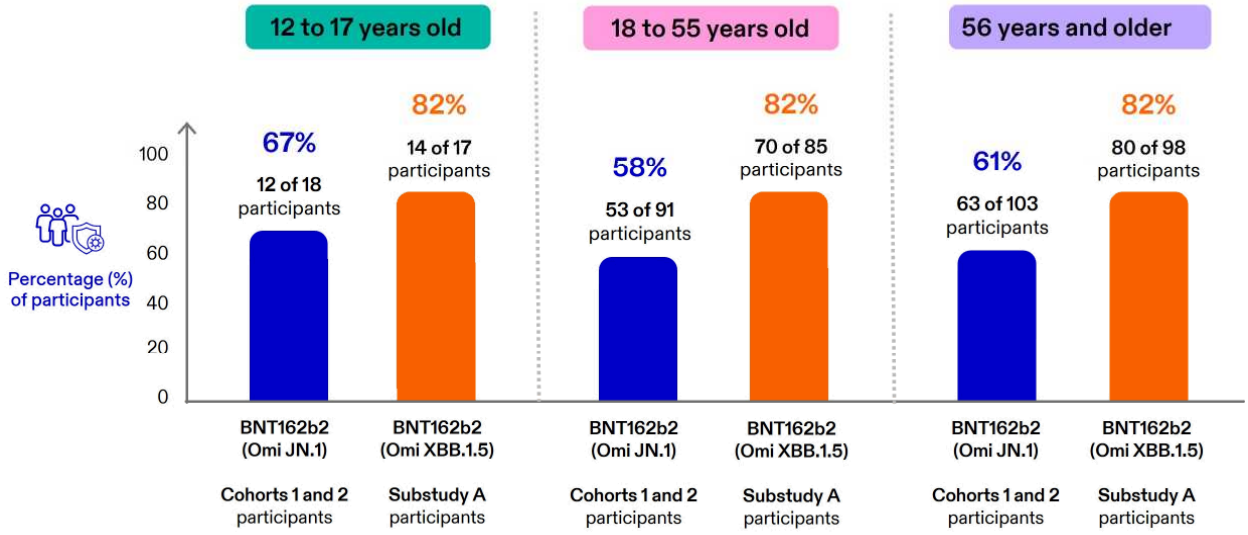


Chart B: Omi XBB.1.5 strain



Immune responses against Omi KP.2 and Omi JN.1 strains after BNT162b2 (Omi KP.2) vaccination – Cohort 3

Researchers compared the results of Cohort 3 participants who got **BNT162b2 (Omi KP.2)** to the results of the combined Cohorts 1 and 2 participants who got **BNT162b2 (Omi JN.1)**.

Antibody levels:

Researchers found that at 1 month after vaccination (see Figure 5):

- Cohort 3 participants across all age groups showed **increased** antibody levels against both Omi KP.2 and Omi JN.1 strains of the COVID-19 virus.
- Cohort 3 participants who got BNT162b2 (Omi KP.2) had **higher** antibody levels against Omi KP.2 and Omi JN.1 strains than that of the combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1).
- In terms of the **average increase in antibodies**, Cohort 3 participants who got BNT162b2 (Omi KP.2) had **generally similar** average increase in antibodies against Omi KP.2 strain and **generally lower** average rise in antibodies against Omi JN.1 strain than that of the combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1).

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Figure 5. Antibody levels against Omi KP.2 (Chart A) and Omi JN.1 (Chart B) strains before and 1 month after vaccination

Chart A: Omi KP.2 strain

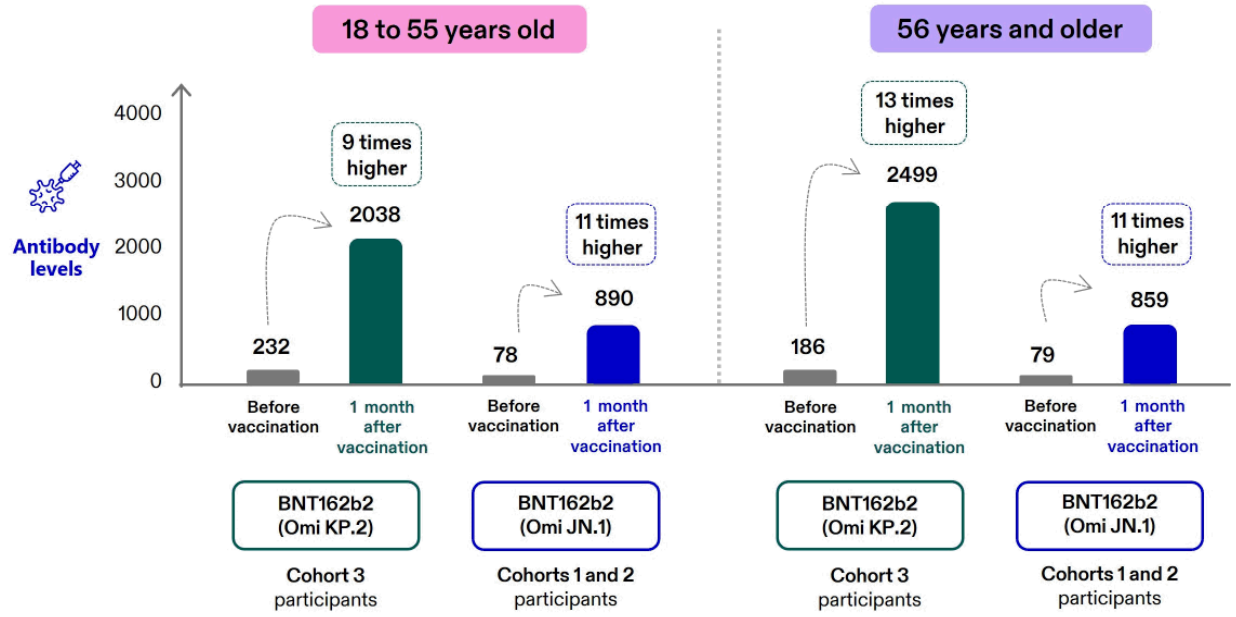
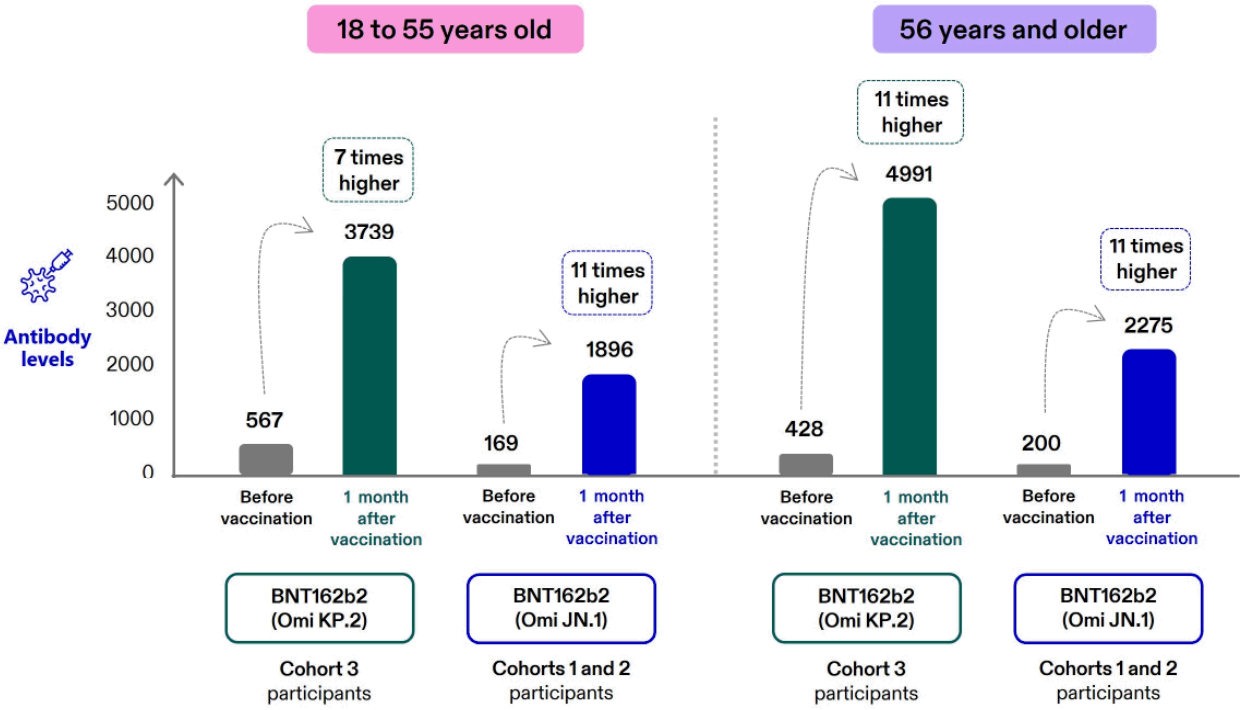


Chart B: Omi JN.1 strain



Immune responses:

Researchers found that at 1 month after vaccination (see Figure 6):

- The percentages of Cohort 3 participants who got BNT162b2 (Omi KP.2) with strong immune responses against Omi KP.2 and Omi JN.1 strains were **generally similar** across all age groups.
- Compared to the combined Cohorts 1 and 2 participants who got BNT162b2 (Omi JN.1), the percentages of Cohort 3 participants who got BNT162b2 (Omi KP.2) with strong immune responses were:
  - **generally higher** against Omi KP.2 strain
  - **generally lower** against Omi JN.1 strain

Figure 6. Percentages of participants with strong immune responses against Omi KP.2 (Chart A) and Omi JN.1 (Chart B) strains 1 month after vaccination

Chart A: **Omi KP.2 strain**

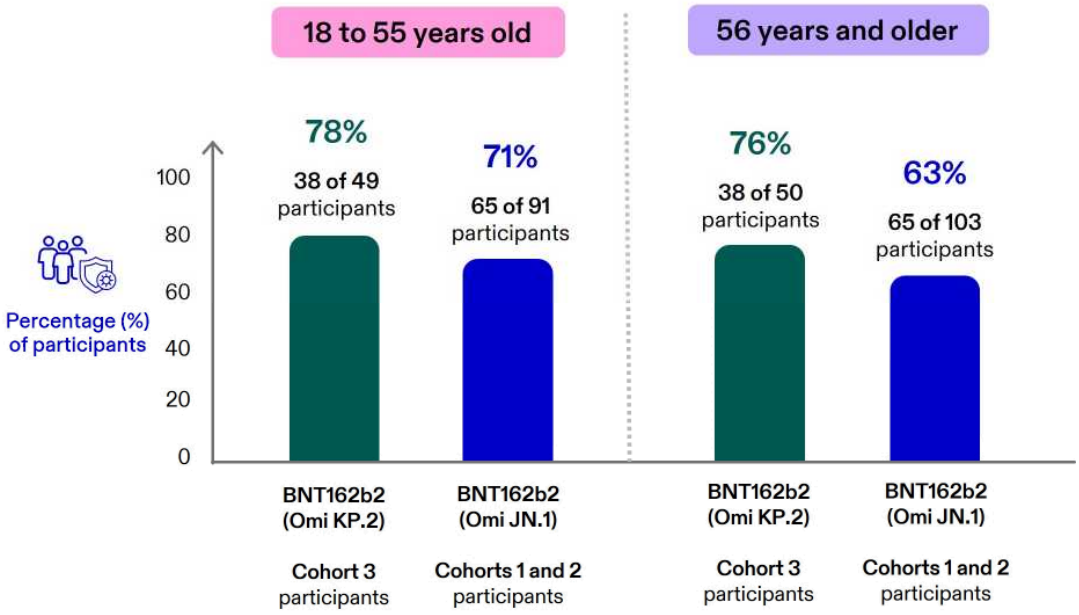
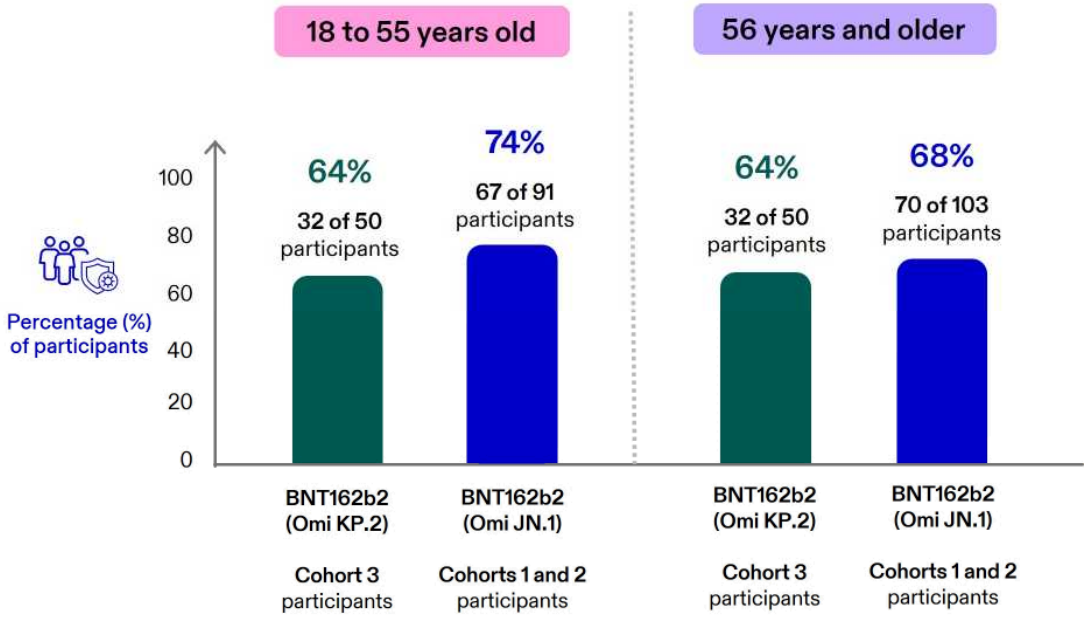


Chart B: **Omi JN.1 strain**



Overall, results showed that the updated versions of the BNT162b2 vaccine (Omi JN.1 and Omi KP.2) given to healthy participants produced immune responses that may help protect against the circulating strains of COVID-19 virus at the start of the study.

BNT162b2 (Omi JN.1) and BNT162b2 (Omi KP.2) produced higher immune responses against the specific Omi strain each was designed to target.

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 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).

Figure 7 (combined Cohorts 1 and 2) and Figure 8 (Cohort 3) show the answer to the question.

Figure 7. Number of participants by age group with any local reaction within 7 days after vaccination – combined Cohorts 1 and 2

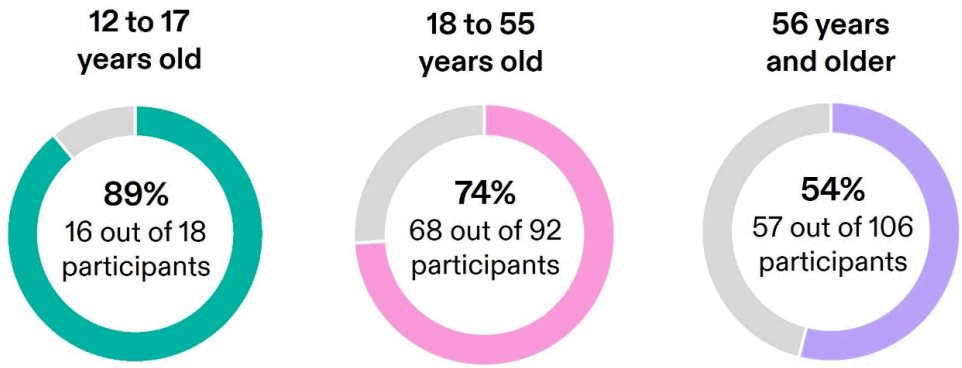


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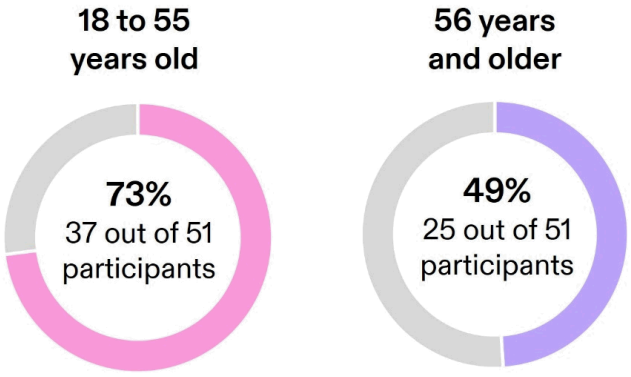
Figure 8. Number of participants by age group with any local reaction within 7 days after vaccination – Cohort 3



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

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

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

Figure 9 (combined Cohorts 1 and 2) and Figure 10 (Cohort 3) show the answer to the question.

Figure 9. Number of participants by age group with any systemic event within 7 days after vaccination – combined Cohorts 1 and 2

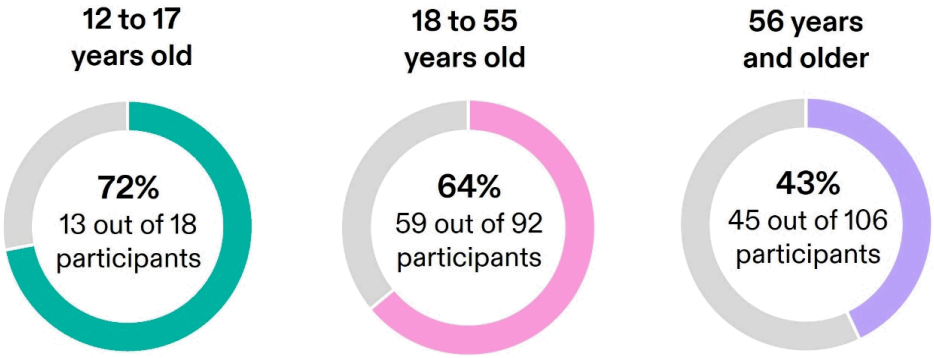
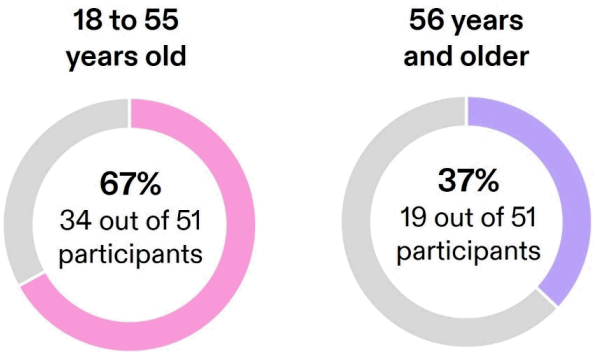


Figure 10. Number of participants by age group with any systemic event within 7 days after vaccination – Cohort 3



Across the 3 cohorts, the most common systemic event in all age groups was **tiredness**. Most of the systemic events were mild or moderate in severity and lasted for 1 to 5 days.

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

Figure 11 (combined Cohorts 1 and 2) and Figure 12 (Cohort 3) show the answer to the question.

Figure 11. Number of participants by age group with any medical problem within 1 month after vaccination – combined Cohorts 1 and 2

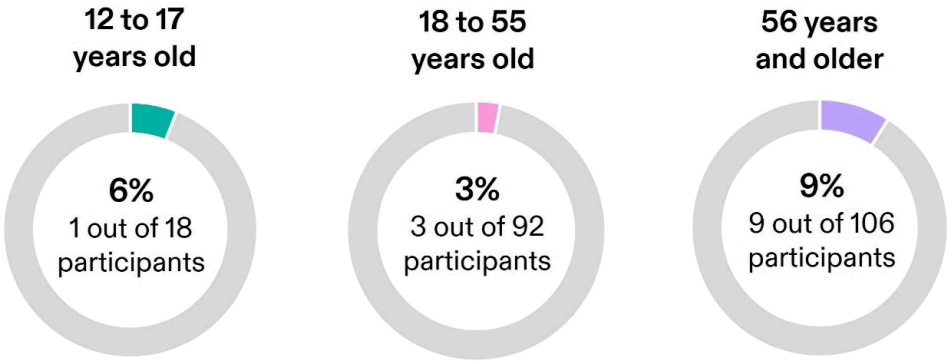
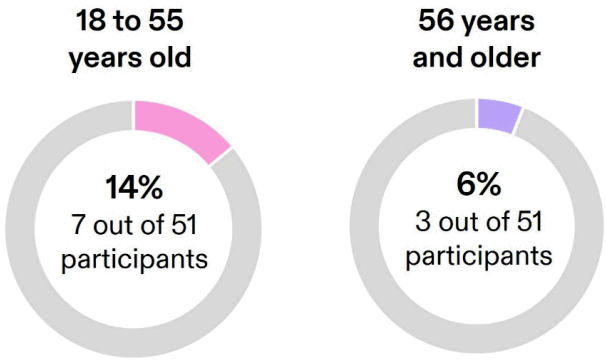


Figure 12. Number of participants by age group with any medical problem within 1 month after vaccination – Cohort 3



Across the 3 cohorts, most of the medical problems reported within 1 month after vaccination were mild or moderate in severity. Researchers believe that most of the medical problems were not caused by the study vaccine.

The most common medical problems – reported by more than 1 participant – were:

- **Ear infection** in 2 out of 102 participants (2%) in Cohort 3
- **Sinusitis** (or swelling of the sinuses) in 2 out of 102 participants (2%) in Cohort 3

None of the participants left the study because of a medical problem.

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 13 (combined Cohorts 1 and 2) and Figure 14 (Cohort 3) show the answer to the question.

Figure 13. Number of participants by age group with any serious medical problem within 6 months after vaccination – combined Cohorts 1 and 2

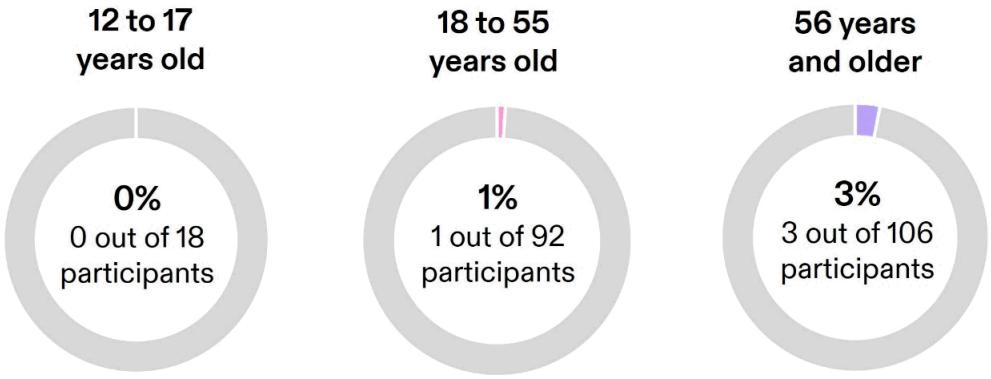
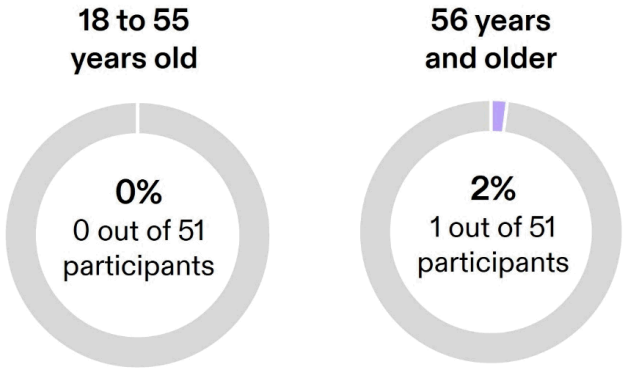


Figure 14. Number of participants by age group with any serious medical problem within 6 months after vaccination – Cohort 3



Across the 3 cohorts, none of the serious medical problems reported within 6 months after vaccination happened in more than 2 participants. Researchers believe that all serious medical problems were not caused by the study vaccine.

During the study, 1 participant died due to "**respiratory failure**" (or the inability of the lungs to work properly). The participant was in the combined Cohorts 1 and 2, 56 years and older age group. Researchers believe that the cause of death was not due to BNT162b2 (Omi JN.1).

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 **C4591054 (Substudy C)**

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!

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