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:	Comirnaty® (BNT162b2)
Protocol Number:	C4591044
Dates of Study:	26 July 2022 to 26 March 2024
Title of this Study:	A Study to Learn About New COVID-19 RNA Vaccine Candidates in COVID-19 Vaccine-Experienced Individuals [An Interventional, Randomized, Active-Controlled, Phase 1/2/3 Study to Investigate the Safety, Tolerability, and Immunogenicity of BNT162b RNA-Based Vaccine Candidates in COVID-19 Vaccine–Experienced Healthy Individuals]
Date of this Report:	24 September 2024

– 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. If you or your child 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 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**). Compared to the original COVID-19 virus, the **Omicron** strain spreads more easily between people.

At the time of this summary, the Omicron strain (also called **OMI**) has become the most widespread COVID-19 virus strain worldwide and has caused the most illnesses. Over the past few years, there have been many different versions of the Omicron strain. These Omicron 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 is BNT162b2?

BNT162b2 (also known as Comirnaty®) is an injectable mRNA vaccine that may help the body's immune system to defend against COVID-19.

- 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.

BNT162b2 is the original monovalent COVID-19 vaccine. A **monovalent** vaccine is designed to protect against 1 strain of a virus. BNT162b2 was designed to protect against the **original strain** of the COVID-19 virus. The original strain was also called **wild-type (WT)** before.

In 2021, researchers started looking into whether the vaccines should target more than just the original strain since the Omicron strain was causing a lot of illnesses despite vaccinations. Like all variants, this Omicron strain has mutations in the spike protein of the COVID-19 virus that make it different from the original strain. To protect against new strains of the COVID-19 virus, vaccines have been created or updated to target the strains that were spreading (circulating).

During this study, in 2022, health agencies in the United States (US) and other countries authorized or approved **Bivalent BNT162b2** for use in people 6 months of age and older. A **bivalent** vaccine is designed to protect against 2 strains of a virus. The approved version of **Bivalent BNT162b2** was designed to target 2 different COVID-19 strains that were circulating at the time of this study. In the US, these were the **original** and **Omicron BA.4/BA.5** strains.

What was the purpose of this study?

The main purpose of this study was to find out if the BNT162b vaccines used in this study can help produce immune responses against different strains of the COVID-19 virus and are safe for people.

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.

A person's immune protection from their first dose or doses of a vaccine can fade over time. An additional shot of a vaccine (previously called a "booster") can help the immune system maintain or boost the level of protection against a disease.

This study was done to see if BNT162b2 COVID-19 vaccine can be improved in 2 ways:

- Adapting (or updating) the current vaccine to target one of the new Omicron strains
- Modifying (or changing) the current vaccine in different ways to create a new COVID-19 vaccine

Researchers wanted to see if the vaccines used in this study remained safe for people. Researchers also wanted to find out if these vaccines could produce a better immune response, especially against the current Omicron strains. Producing a better immune response may help to offer more protection against COVID-19.

In this study, researchers tested **Bivalent BNT162b2**, the Omicron strain-updated vaccine authorized in the US since 2022.

- **BNT162b2 Bivalent (original/OMI BA.4/BA.5)** is designed to protect against both the **original** and the **Omicron BA.4/BA.5** strains.

  The above vaccine was compared against the **Original BNT162b2** and **BNT162b2 Bivalent (original/OMI BA.1)**, which were given to participants in another study.

In this study, researchers also tested new **BNT162b** vaccine candidates.

These new vaccine candidates are called **BNT162b5**, **BNT162b6**, and **BNT162b7**. They are similar to how **BNT162b2** is made but they have been modified to contain different versions of the spike protein. Researchers wanted to know if these new vaccines can better protect against new COVID-19 strains.

As described below, the vaccine candidates are designed to protect against the **original** and/or different **Omicron** strains of the COVID-19 virus.

The new vaccine below was compared against **BNT162b2 Bivalent (original/OMI BA.1)**, which was also given in this study.

- **BNT162b5 Bivalent (original/OMI BA.2)** is designed to protect against both the **original** and the **Omicron BA.2** strains.

The new vaccines below were compared against **BNT162b2 Bivalent (original/OMI BA.4/BA.5)**, which was also given in this study.

- **BNT162b5 Bivalent (original/OMI BA.4/BA.5)**, **BNT162b6 Bivalent (original/OMI BA.4/BA.5)**, and **BNT162b7 Bivalent (original/OMI BA.4/BA.5)** are designed to protect against both the **original** and the **Omicron BA.4/BA.5** strains.
- **BNT162b7 Monovalent (OMI BA.4/BA.5)** is designed to protect against the **Omicron BA.4/BA.5** strain.

In this summary:

- **BNT162b2 Monovalent (original)** is called **"Original BNT-2"**. Earlier reports may have called this vaccine as "Original BNT", "BNT162b2", or "BNT".
- **BNT162b2 Bivalent (original/OMI BA.1)** is called **"Bivalent BNT-2 (original/OMI BA.1)"**.
- **BNT162b2 Bivalent (original/OMI BA.4/BA.5)** is called **"Bivalent BNT-2 (original/OMI BA.4/BA.5)"**.
- **BNT162b5 Bivalent (original/OMI BA.2)** is called **"Bivalent BNT-5 (original/OMI BA.2)"**.
- **BNT162b5 Bivalent (original/OMI BA.4/BA.5)** is called **"Bivalent BNT-5 (original/OMI BA.4/BA.5)"**.
- **BNT162b6 Bivalent (original/OMI BA.4/BA.5)** is called **"Bivalent BNT-6 (original/OMI BA.4/BA.5)"**.
- **BNT162b7 Bivalent (original/OMI BA.4/BA.5)** is called **"Bivalent BNT-7 (original/OMI BA.4/BA.5)"**.
- **BNT162b7 Monovalent (OMI BA.4/BA.5)** is called **"Monovalent BNT-7 (OMI BA.4/BA.5)"**.

Researchers wanted to know:

- **What were the participants' immune responses 1 month after vaccination in this study?**
- **How many participants had redness, swelling, or pain at the injection site within 7 days after vaccination?**
- **How many participants had fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain within 7 days after vaccination?**
- **What medical problems did participants have during the study?**

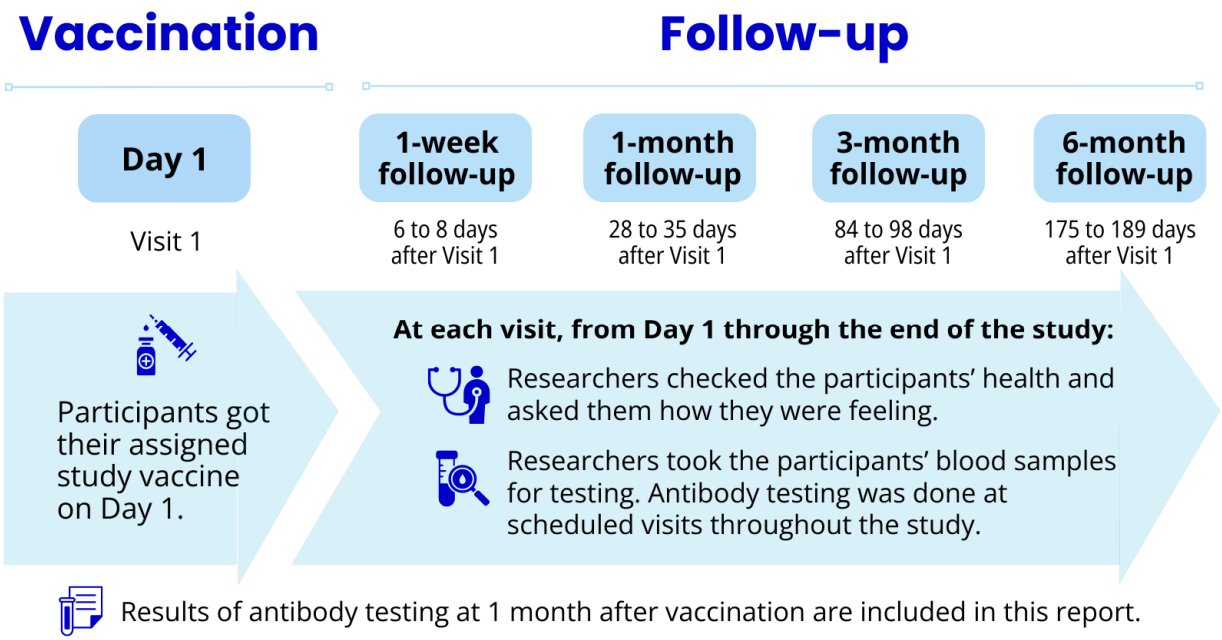
For each of the questions above, researchers wanted to know the answers for each of the vaccines used in this study, compared to the original vaccine and/or another updated vaccine that had been tested in another study.

What happened during the study?

How was the study done?

Participants received their assigned vaccine on Day 1 of the study. Then, they had check-ups at the study site at scheduled visits through 6 months after vaccination. At planned timepoints during the study, researchers took blood samples from participants for testing. Throughout the study, researchers also checked the participants' health and asked them how they were feeling. Figure 1 below shows how the study was done.

Figure 1. Schedule of activities in the study



In this study, researchers tested different vaccines on participants across 4 large groups called **cohorts**. Each cohort was made up of smaller groups. All participants in each cohort must have been COVID-19 vaccine-experienced.

People who have previously received a COVID-19 vaccine (1 dose or more) before joining this study are also called **COVID-19 vaccine-experienced**.

Observer-blinded study:

The study was observer-blinded in the groups listed below. In an observer-blinded study, only the person at the study site who gave the injection knew which vaccine (or dose level of the vaccine) each participant got. The participants (and the children's parents/guardians) and researchers did not know which vaccine (or dose level of the vaccine) the participants got during the study.

Cohort 1:	Cohort 2:	Cohort 4:
Groups 1 and 2	Groups 2 to 5	Groups 1 to 5

Open-label study:

The study was open-label in the groups listed below. In an open-label study, participants (and the children's parents/guardians), researchers, and study staff knew which vaccine (and dose level of the vaccine) the participants got.

Cohort 2:	Cohort 3:
Group 1	Groups 1 and 2

Study of new adapted COVID-19 vaccines – Cohorts 2 and 3

In **Cohorts 2** and **3**, researchers tested **Bivalent BNT-2** (original/OMI BA.4/BA.5), a new bivalent form of the **Original BNT-2** vaccine, in healthy participants. The **Original BNT-2** was updated to **Bivalent BNT-2**, which was designed to target Omicron BA.4/BA.5, the COVID-19 virus strain circulating at the time, and the original strain. **Bivalent BNT-2** was the vaccine that was approved for use in the US in 2022.

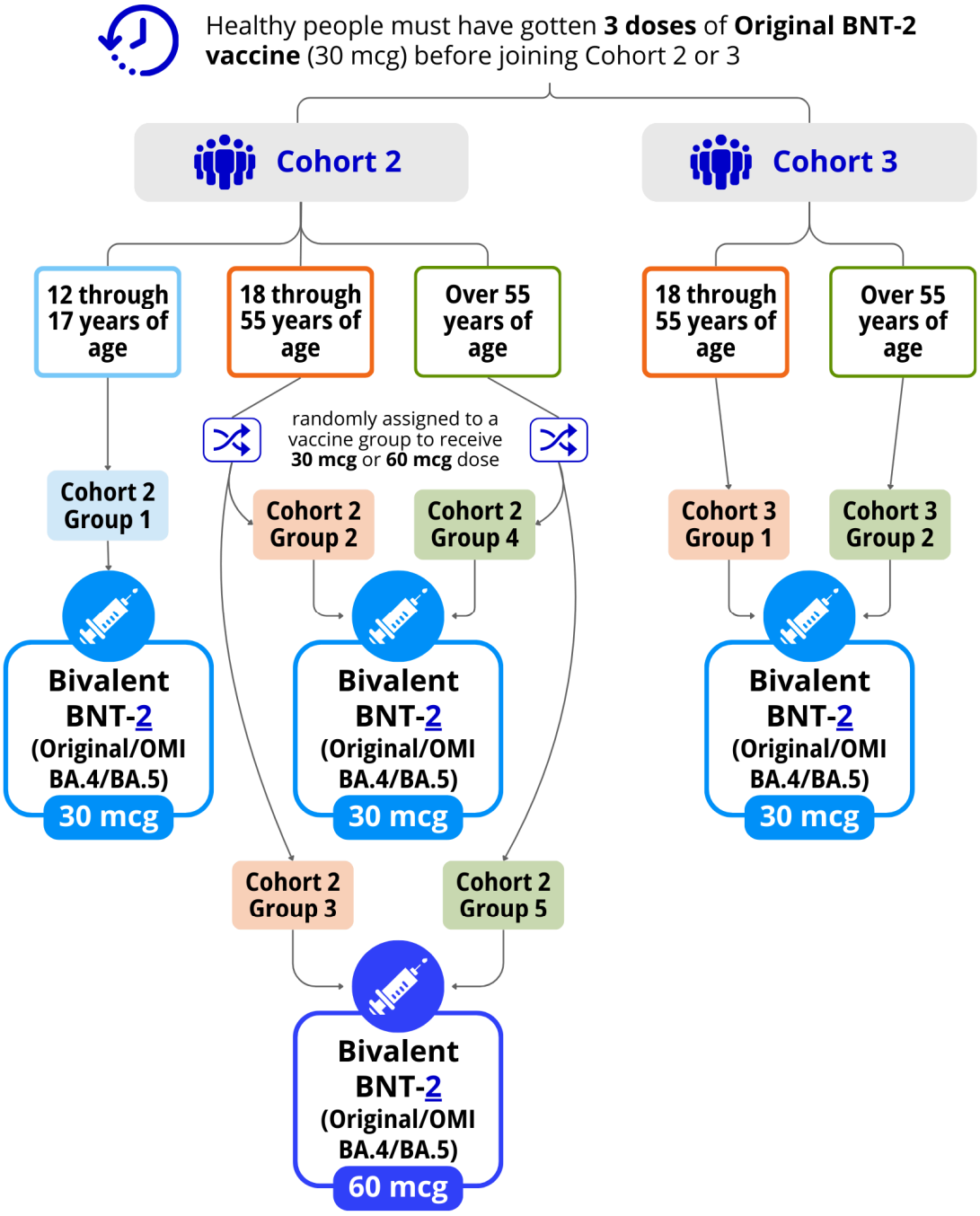
In **Cohort 2**, researchers tested 2 dose levels of **Bivalent BNT-2 (original/OMI BA.4/BA.5)** across 3 age groups. This was done to find out if the 2 dose levels of the study vaccine are safe and can help produce immune responses against the COVID-19 virus.

- All participants **12 through 17 years of age** were assigned to receive **30 micrograms (mcg)** of Bivalent BNT-2 (original/OMI BA.4/BA.5).
- Among participants in the 2 older age groups (**18 through 55 years of age** and **over 55 years of age**), researchers used a computer program to randomly assign participants to receive either **30 mcg** or **60 mcg** of Bivalent BNT-2 (original/OMI BA.4/BA.5).

In **Cohort 3**, researchers tested 1 dose level (30 mcg) of **Bivalent BNT-2 (original/OMI BA.4/BA.5)** in 2 age groups: **18 through 55 years of age** and **over 55 years of age**. This was done to find out if the study vaccine is safe and can help produce immune responses against the COVID-19 virus.

The study vaccine assignments in Cohorts 2 and 3 are shown in Figure 2 below.

Figure 2. Study vaccines given in Cohorts 2 and 3



Study of new COVID-19 vaccine candidates − Cohorts 1 and 4

In **Cohorts 1** and **4**, researchers tested new vaccine candidates (**BNT-5**, **BNT-6**, and **BNT-7**) in healthy participants 18 through 55 years of age. These new vaccine candidates are similar to how the **Original BNT-2** is made but have been modified to contain different versions of the spike protein. The vaccine candidates were designed to target the COVID-19 virus strains that were circulating at the time.

Researchers wanted to compare the **new vaccine candidates (BNT-5**, **BNT-6**, and **BNT-7)** against **Bivalent BNT-2** with regards to safety and the immune responses produced against the COVID-19 virus.

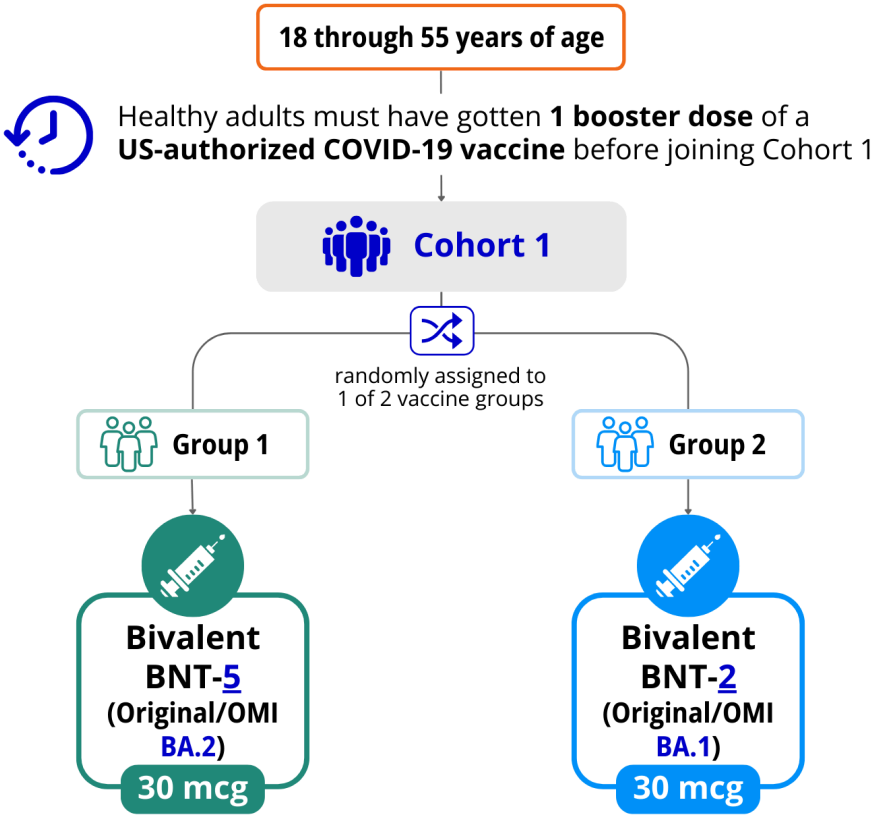
For each of the 2 cohorts, researchers used a computer program to randomly assign participants to one of the groups.

Cohort 1 started in July 2022 when the OMI BA.2 strain was becoming more common than OMI BA.1. As shown in Figure 3 below, participants in Cohort 1 had an equal chance of being assigned to 1 of 2 groups.

- **Group 1:** Bivalent BNT-**5** (original/OMI BA.2)
- **Group 2:** Bivalent BNT-**2** (original/OMI BA.1)

Results of participants in **Group 1** given **Bivalent BNT-5** (original/OMI BA.2) were compared to results of those in **Group 2** given **Bivalent BNT-2** (original/OMI BA.1).

Figure 3. Study vaccines given in Cohort 1



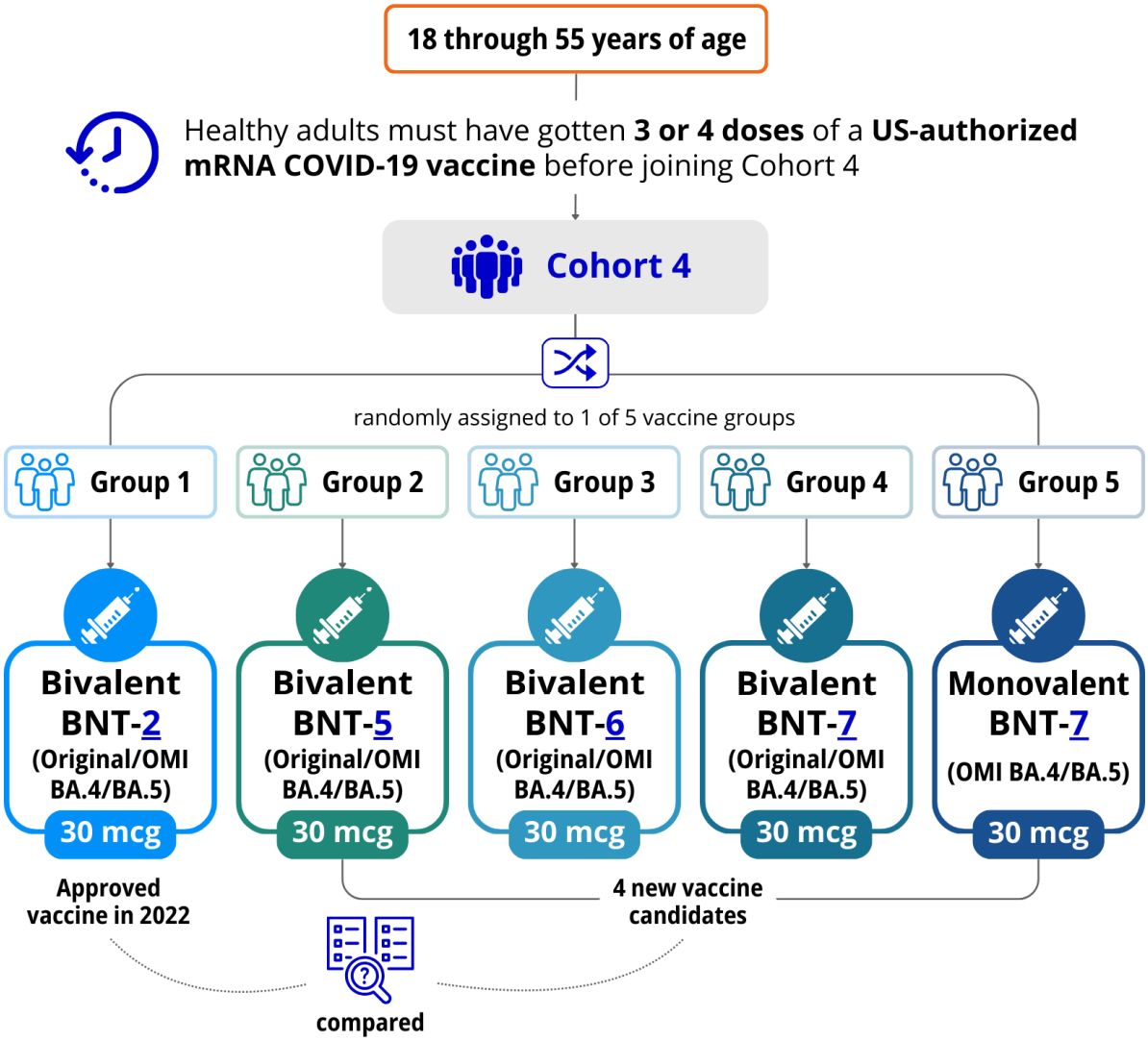
Cohort 4 started in September 2023 after the bivalent COVID-19 vaccines targeting OMI BA.4/BA.5 strain were authorized for use in people.

As shown in Figure 4 below, participants in **Cohort 4** had an equal chance of being assigned to 1 of 5 groups.

- **Group 1:** Bivalent BNT-2 (original/OMI BA.4/BA.5) 30 mcg
- **Group 2:** Bivalent BNT-5 (original/OMI BA.4/BA.5) 30 mcg
- **Group 3:** Bivalent BNT-6 (original/OMI BA.4/BA.5) 30 mcg
- **Group 4:** Bivalent BNT-7 (original/OMI BA.4/BA.5) 30 mcg
- **Group 5:** Monovalent BNT-7 (OMI BA.4/BA.5) 30 mcg

Bivalent BNT-2 (original/OMI BA.4/BA.5) 30 mcg given to participants in **Group 1** was the approved vaccine for adults in the US at the time of the study. Results of participants in **Groups 2 to 5** given one of the new **vaccine candidates** were compared to the results of those in **Group 1** given **Bivalent BNT-2**.

Figure 4. Study vaccines given in Cohort 4



Where did this study take place?

The 4 cohorts of this study ran at 31 locations in the US.

When did this study take place?

The study began on 26 July 2022 and ended on 26 March 2024.

Who participated in this study?

The study included people 12 years of age and older whom the study doctors have assessed as healthy and were COVID-19 vaccine-experienced.

- **Cohort 1:** Participants 18 through 55 years of age must have received 1 booster dose of a US-authorized COVID-19 vaccine, with the last dose received 3 months or more before Visit 1 (Day 1).
- **Cohort 2:** Participants 12 years of age or older must have received 3 doses of Original BNT-2 vaccine (30 mcg), with the last dose received 5 months to 1 year before Visit 1 (Day 1).
- **Cohort 3:** Participants 18 years of age or older must have received 3 doses of Original BNT-2 vaccine (30 mcg), with the last dose received 5 months to 1 year before Visit 1 (Day 1).
- **Cohort 4:** Participants 18 through 55 years of age must have received 3 or 4 doses of a US-authorized mRNA COVID-19 vaccine, and the last dose received must have been Bivalent BNT-2 (original/OMI BA.4/BA.5) at least 5 months before Visit 1 (Day 1).

The table below shows how many participants in each cohort took part in this study.

Table 1. Number of participants in each cohort

	Cohort 1	Cohorts 2 and 3	Cohort 4
Started the study	206 participants	940 participants	307 participants
Finished the study	198 of 206 participants (96.1%)	908 of 940 participants (96.6%)	288 of 307 participants (93.8%)
Did not finish the study	8 of 206 participants (3.9%)	31 of 940 participants (3.3%)	19 of 307 participants (6.2%)

All participants across the 4 cohorts that started the study got their assigned vaccination except for 1 participant. This participant that did not get vaccinated in the study was part of Cohort 2.

Among those who did not finish the study (Table 1), the most common reason was that participants (or the children's parent/guardian) chose for them to leave the study before it was over.

Cohort 1

- A total of 96 men (46.6%) and 110 women (53.4%) participated.
- All participants were between the ages of 18 and 55 years.

Cohorts 2 and 3 (combined)

- A total of 404 boys/men (43.1%) and 534 girls/women (56.9%) participated.
- All participants were between the ages of 12 and 87 years.

Cohort 4

- A total of 122 men (39.7%) and 185 women (60.3%) participated.
- All participants were between the ages of 18 and 55 years.

How long did the study last?

Each participant was in the study for about 6 months. The entire study took 1 year and 8 months to complete.

The Sponsor Agent began reviewing the information collected while the study was ongoing. The Sponsor Agent created reports of the results after each review. When the study ended in March 2024, the Sponsor Agent reviewed the information collected that was not reported before. The Sponsor Agent then created a report of the results. This is a summary of the reports.

What were the results of the study?

What were the participants' immune responses 1 month after vaccination in this study?

Researchers wanted to find out if participants across the 4 cohorts had immune responses 1 month after getting 1 shot of the study vaccine.

To answer the question:

Researchers measured the participants' **antibody levels** against the COVID-19 virus strains that were being targeted by the study vaccines. Antibody levels were measured **before** and 1 month **after** getting the study vaccine.

Researchers also checked how many participants had **strong immune responses** against the COVID-19 virus strains that were being targeted by the study vaccines. This was done at 1 month after participants got vaccinated in the study.

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.

The sections below describe the results for each cohort.

Immune responses to new adapted COVID-19 vaccines − Cohorts 2 and 3

How did the immune responses compare across the different age groups at 1 month after vaccination with Bivalent BNT-2 (original/OMI BA.4/BA.5) or Bivalent BNT-2 (original/OMI BA.1)?

Researchers wanted to compare 2 different Omicron-updated BNT-2 vaccines, **Bivalent BNT-2 (original/OMI BA.4/BA.5)** and the earlier **Bivalent BNT-2 (original/OMI BA.1)**, based on the amount of antibodies against **OMI BA.4/BA.5**, **OMI BA.1**, and **original** strains of the COVID-19 virus at 1 month after vaccination.

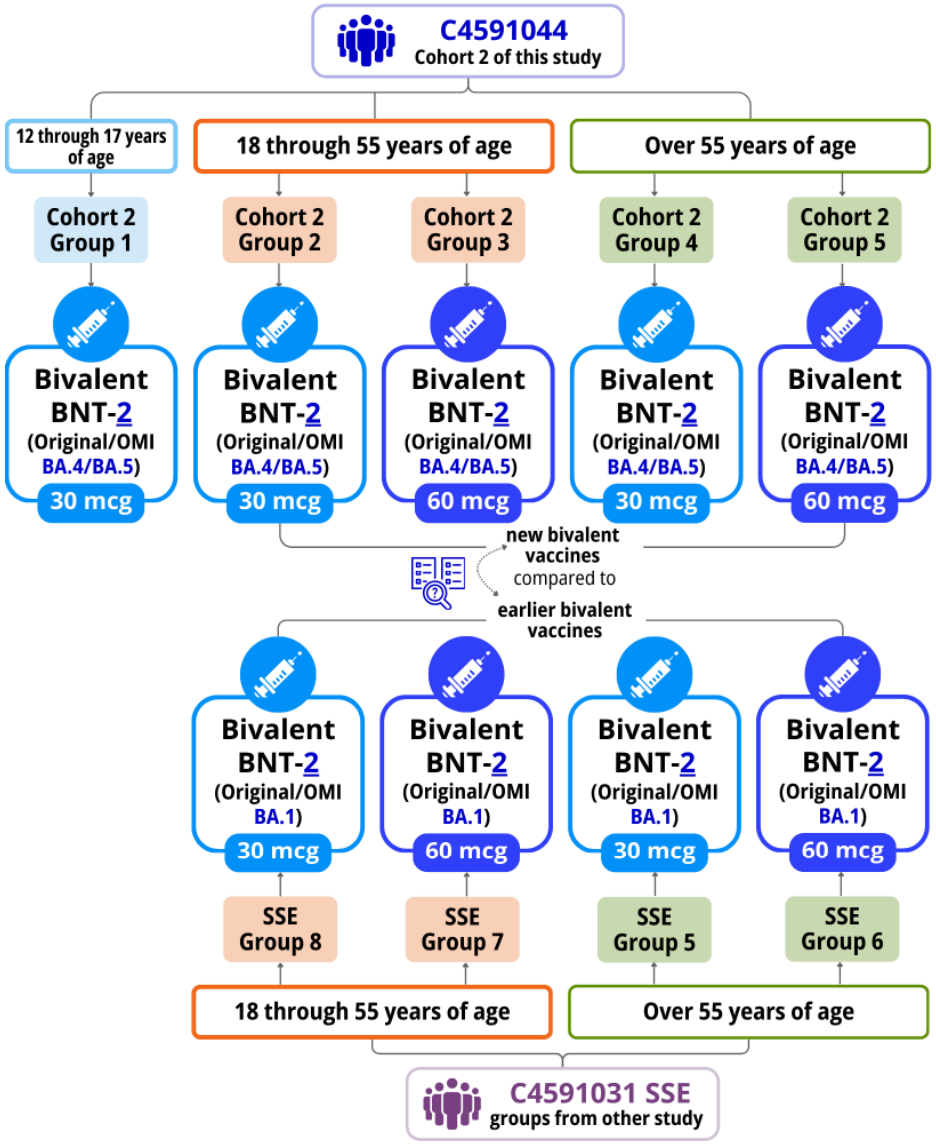
Researchers checked the antibody levels of **Cohort 2** participants across the 3 age groups.

Researchers compared the results of participants **18 through 55 years of age** and those **over 55 years of age** from **Cohort 2** in this study with the results of participants of the same age groups from an earlier study called **C4591031 Substudy E (SSE)** based on the dose levels they received.

> This was done to find out how 2 dose levels of **Bivalent BNT-2 (original/OMI BA.4/BA.5)** given to **Cohort 2** compared to the same dose levels of **Bivalent BNT-2 (original/OMI BA.1)** given to **C4591031 SSE** groups in producing immune responses when given to participants 18 years of age and older.

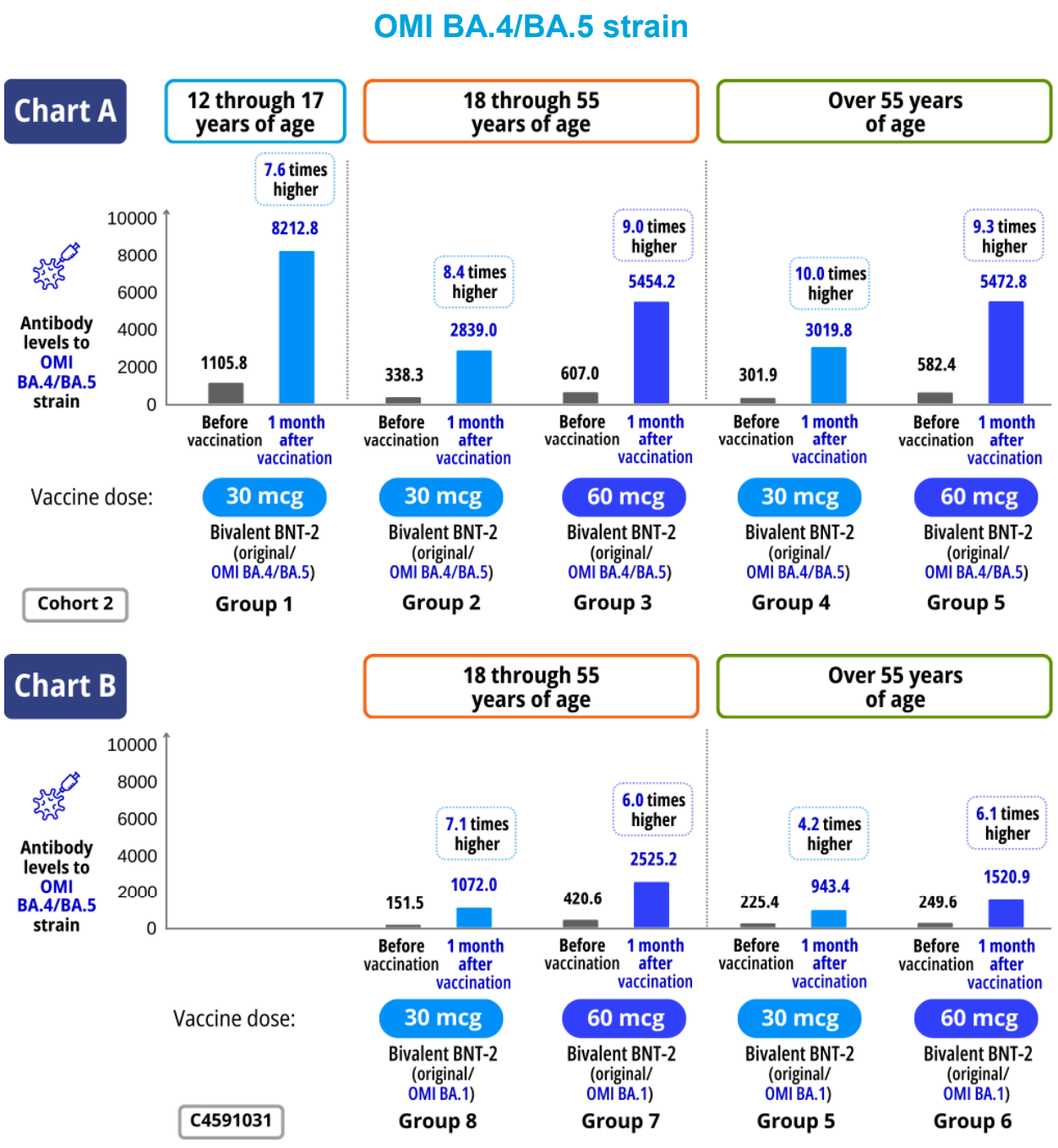
The groups in each study are shown in Figure 5 below.

Figure 5. Cohort 2 groups and the C4591031 SSE groups

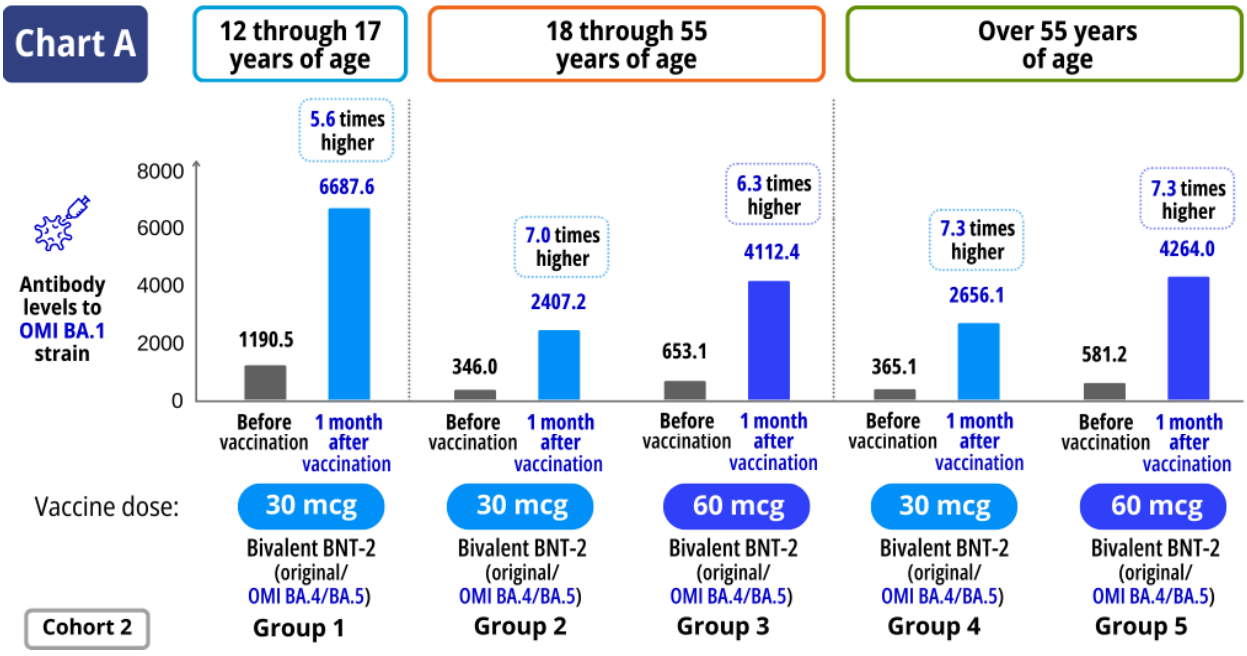


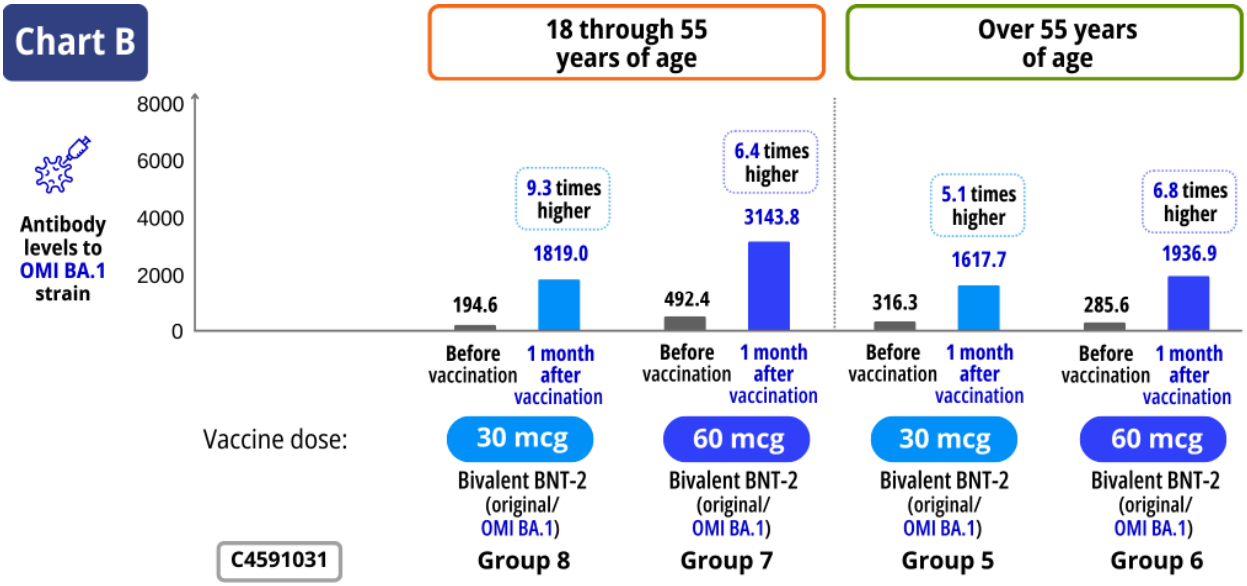
The charts in Figure 6 below show the participants' **antibody levels** against **OMI BA.4/BA.5**, **OMI BA.1**, and **original** strains of the COVID-19 virus **before** and 1 month **after** vaccination of participants in **Cohort 2** (**Chart A**) and those in **C4591031 SSE** (**Chart B**). The charts also show the average rise in antibodies from before to after vaccination.

Figure 6. Antibody levels against OMI BA.4/BA.5, OMI BA.1, and original strains of the COVID-19 virus before and after vaccination – Cohort 2 and C4591031 SSE

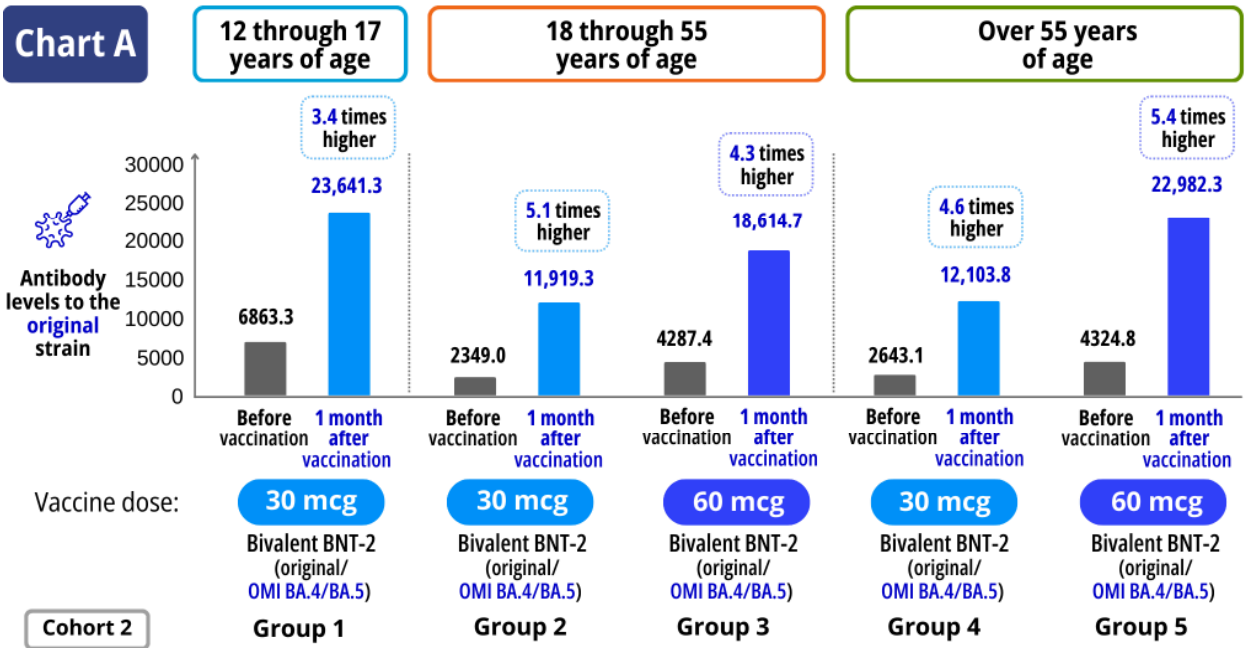


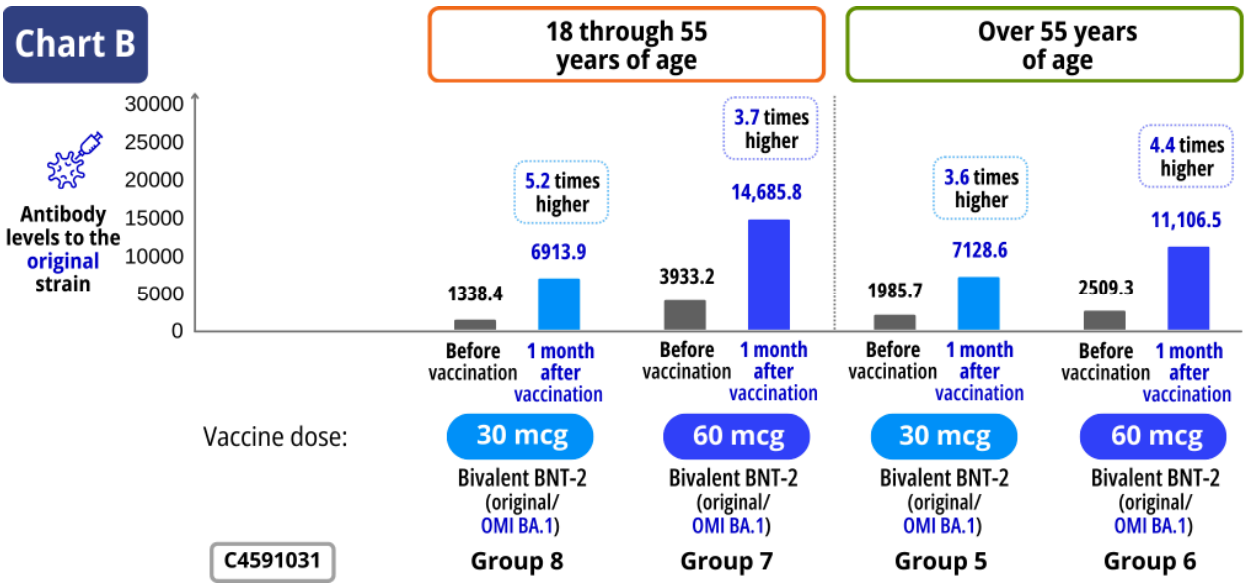
OMI BA.1 strain





Original strain





The charts in Figure 6 above show that at 1 month after vaccination:

Among the 3 age groups in **Cohort 2**, the younger age group (**12 through 17 years of age**) had higher **antibody levels** against OMI BA.4/BA.5, OMI BA.1, and original strains of the COVID-19 virus compared to the antibody levels of the older age groups (**18 through 55 years of age** and **over 55 years of age**).

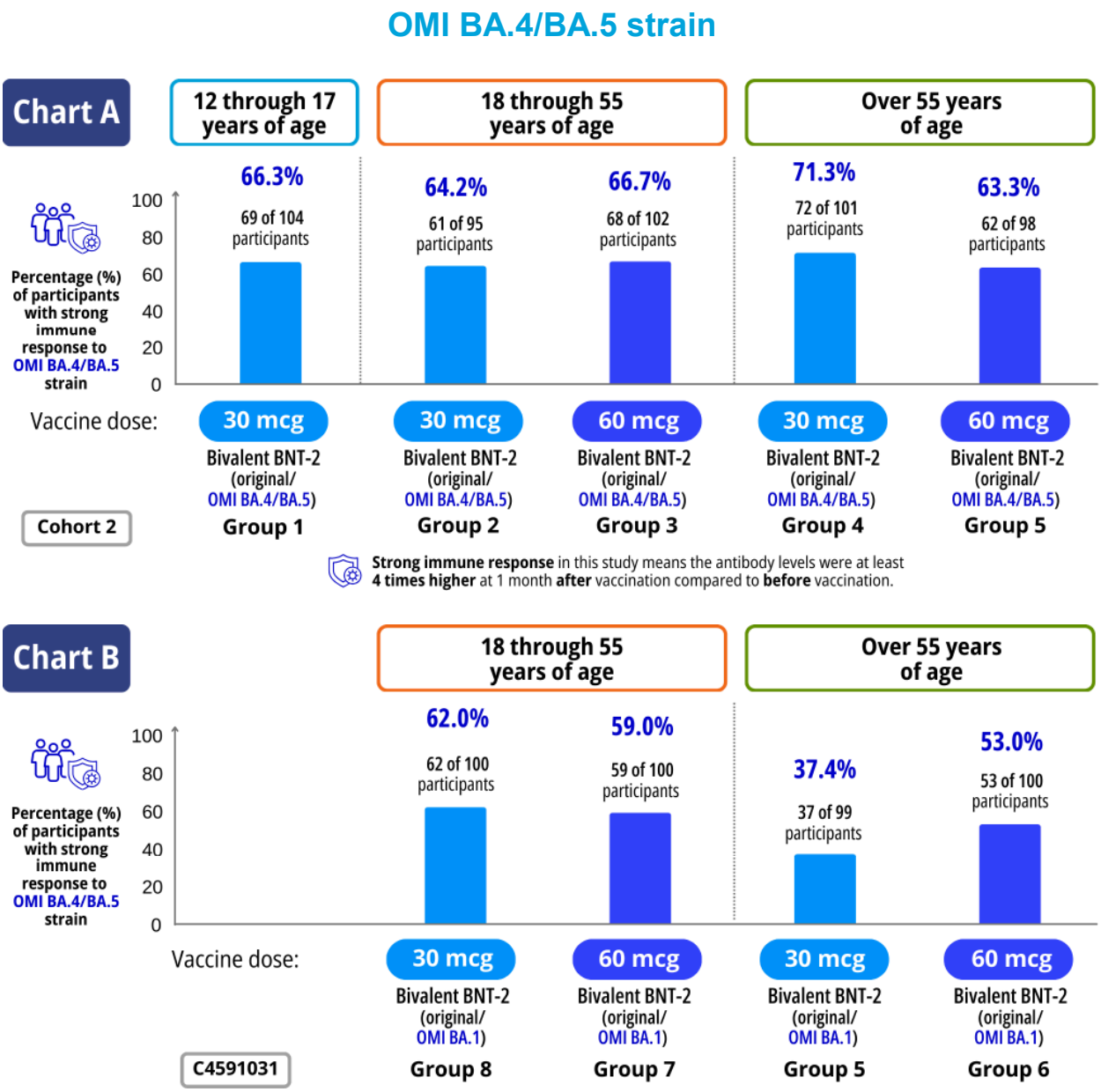
Among the 2 older age groups, **18 through 55 years of age** and those **over 55 years of age:**

- Participants in **Cohort 2** who got either dose level of the study vaccine had **antibody levels** against **OMI BA.4/BA.5** strain of the COVID-19 virus that were higher than the antibody levels of participants in the matching **C4591031 SSE** groups. The average rise in antibodies of participants in **Cohort 2** was higher than that of participants in the matching **C4591031 SSE** groups.
- Participants in **Cohort 2** who got either dose level of the study vaccine had **antibody levels** against **OMI BA.1** and **original** strains of the COVID-19 virus that were **at least similar to** the antibody levels of participants in the matching **C4591031 SSE** groups. The average rise in antibodies of participants in **Cohort 2** was at least similar to that of participants in the matching **C4591031 SSE** groups.
- Participants who got the **60-mcg** dose had higher antibody levels than those who got the **30-mcg** dose.

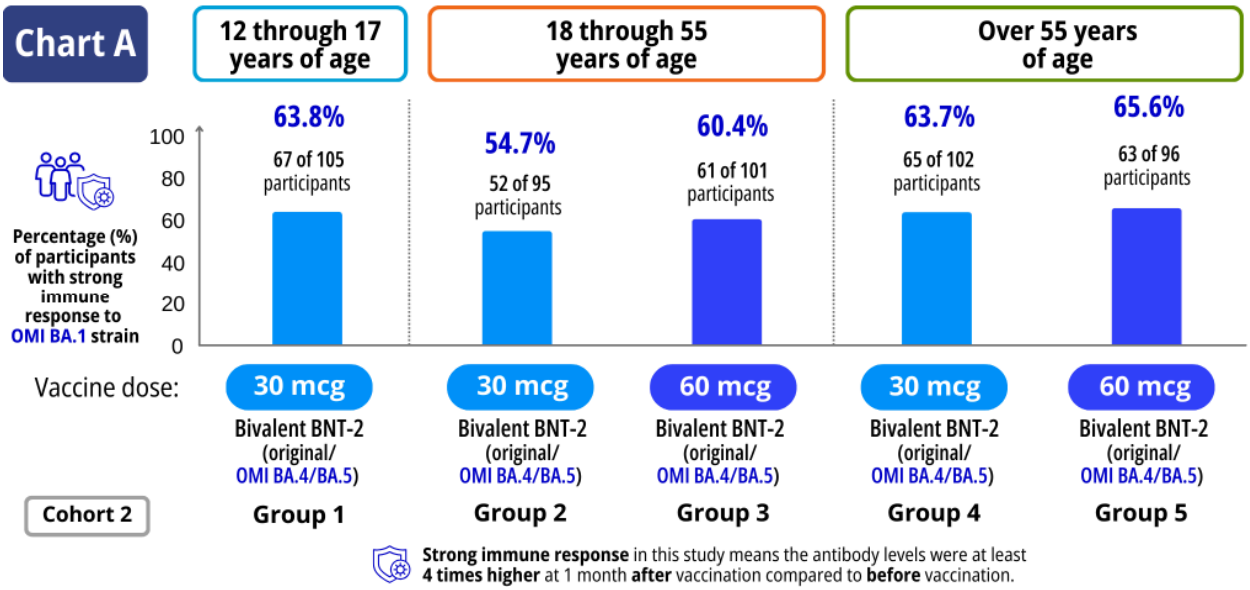
Researchers also wanted to know if **Bivalent BNT-2 (original/OMI BA.4/BA.5)**, an Omicron-updated vaccine, works as good as the earlier Omicron-updated vaccine, **Bivalent BNT-2 (original/OMI BA.1)**, based on how many participants had strong immune responses against the **OMI BA.4/BA.5**, **OMI BA.1**, and **original** strains of the COVID-19 virus at 1 month after vaccination.

The charts in Figure 7 below show these results of groups in **Cohort 2** (**Chart A**) and groups in **C4591031 SSE** (**Chart B**).

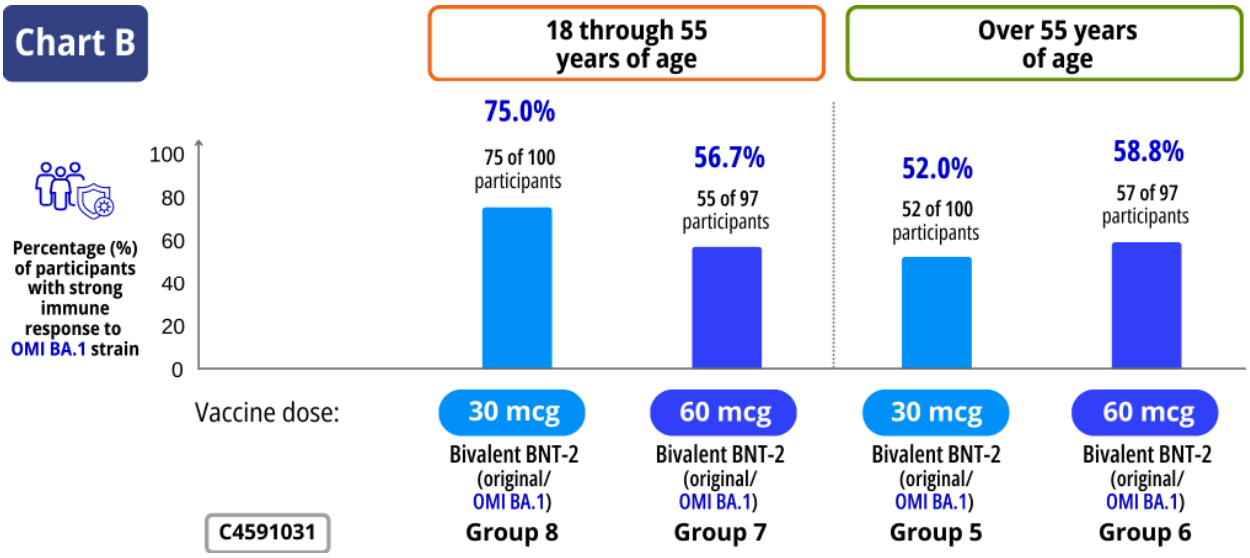
Figure 7. Percentage of participants with strong immune responses against OMI BA.4/BA.5, OMI BA.1, and original strains of the COVID-19 virus at 1 month after vaccination – Cohort 2 and C4591031 SSE



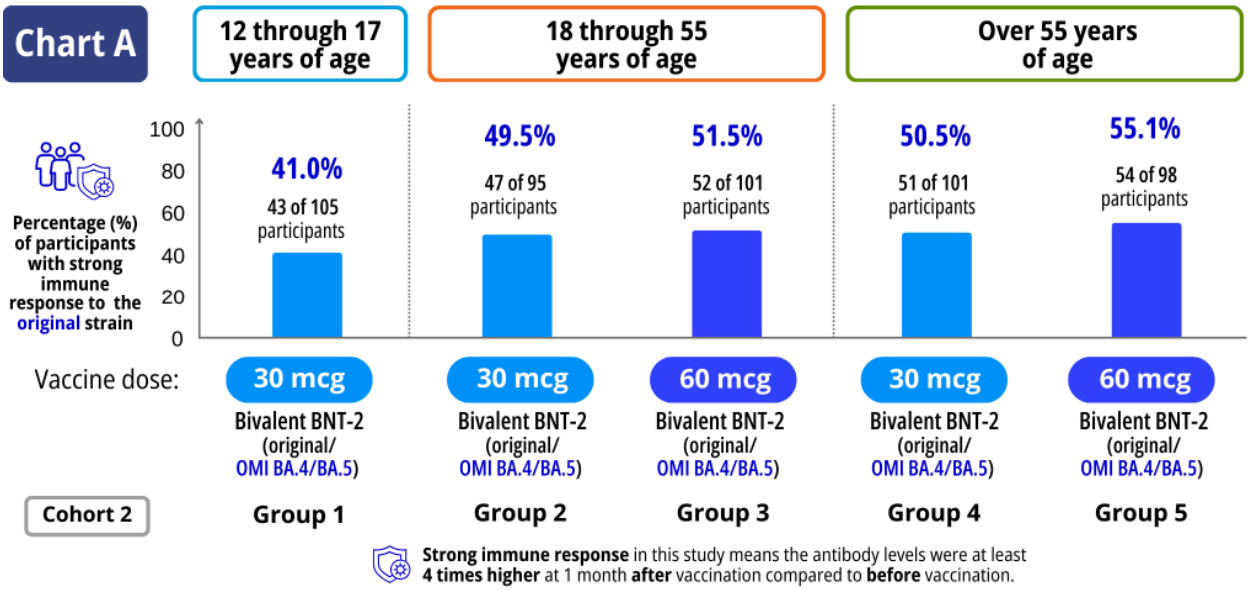
OMI BA.1 strain

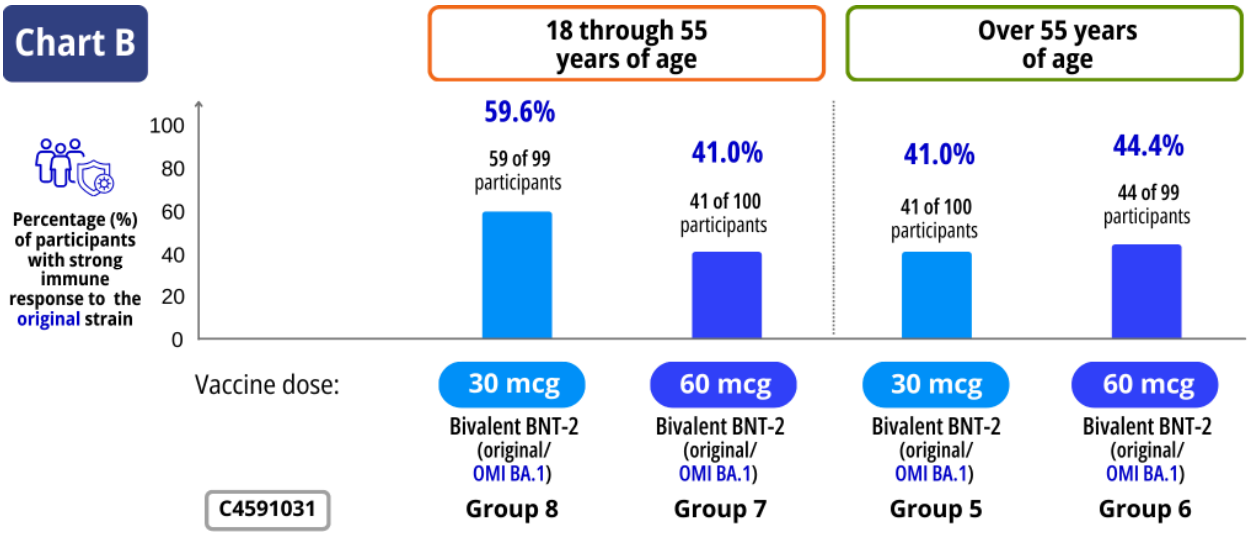


Strong immune response in this study means the antibody levels were at least **4 times higher** at 1 month **after** vaccination compared to **before** vaccination.



Original strain





The charts in Figure 7 above show that at 1 month after vaccination:

- Across the 5 groups in **Cohort 2**, the percentages of participants with **strong immune responses** against OMI BA.4/BA.5, OMI BA.1, and original strains of the COVID-19 virus were similar.
- The percentages of participants in the 2 older age groups in **Cohort 2** with **strong immune responses** against OMI BA.4/BA.5, OMI BA.1, and original strains of the COVID-19 virus were generally higher than those of participants in the matching **C4591031 SSE** groups.

Overall, study results of **Cohort 2** showed that **Bivalent BNT-2 (original/OMI BA.4/BA.5)** given as the 4th dose to healthy children 12 through 17 years of age (30 mcg) and healthy adults 18 years of age and older (either 30 mcg or 60 mcg) may help to protect them against COVID-19 infection caused by OMI BA.4/BA.5, OMI BA.1, and original strains.

Bivalent BNT-2 (original/OMI BA.4/BA.5) in **Cohort 2** may protect against **OMI BA.1** and **original** strains similar to the protection from **Bivalent BNT-2 (original/OMI BA.1)**, the vaccine given in C4591031 SSE. **Bivalent BNT-2 (original/OMI BA.4/BA.5)** in **Cohort 2** may protect against **OMI BA.4/BA.5** strain better than **Bivalent BNT-2 (original/OMI BA.1)**, the vaccine given in C4591031 SSE.

Results also showed a better immune response in the younger age group (**12 through 17 years of age**) and with the higher dose of the study vaccine in the older age groups (**at least 18 years of age**).

Does Bivalent BNT-2 (original/OMI BA.4/BA.5) produce better immune responses than Original BNT-2?

Researchers wanted to know if **Bivalent BNT-2 (original/OMI BA.4/BA.5)**, an Omicron-updated vaccine, works better than the **Original BNT-2** based on the amount of antibodies against **OMI BA.4/BA.5** strain of the COVID-19 virus at 1 month after vaccination.

Researchers combined a group in **Cohort 2** with a group in **Cohort 3**. Both groups were over 55 years of age. Combining the participants into a larger group allowed researchers to do additional tests and compare the results to a group from **C4591031 SSE**. This was done to find out which of the 2 vaccines listed below can produce better immune responses against the OMI BA.4/BA.5 strain of the COVID-19 virus.

- **Bivalent BNT-2** (original/OMI BA.4/BA.5) 30 mcg given to participants in the combined **Cohort 2 (Group 4)** and **Cohort 3 (Group 2)** in this study
- **Original BNT-2** 30 mcg given to a group of participants in **C4591031 SSE**

The combined Cohorts 2 and 3 group in this study and the group in C4591031 SSE are shown in Figure 8 below.

Figure 8. The combined group from Cohorts 2 and 3 of this study and the C4591031 SSE group – Participants over 55 years of age

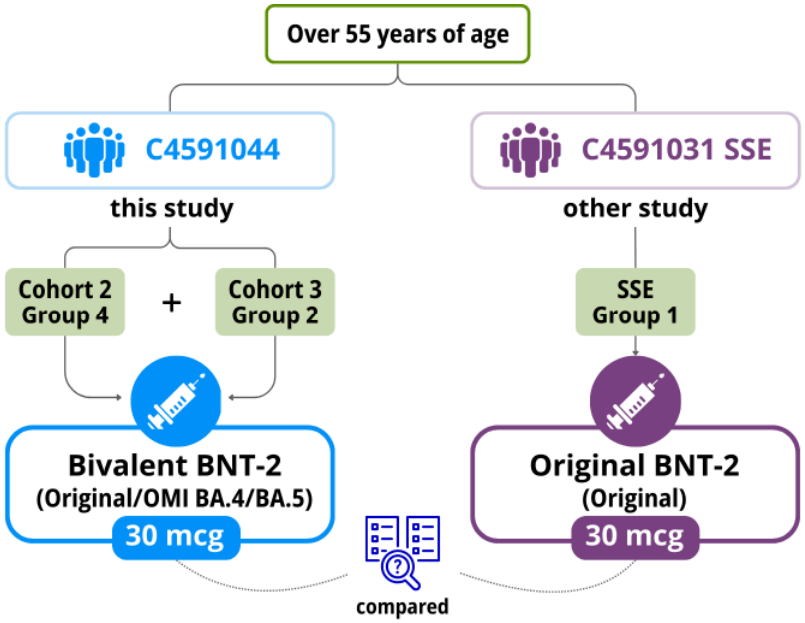
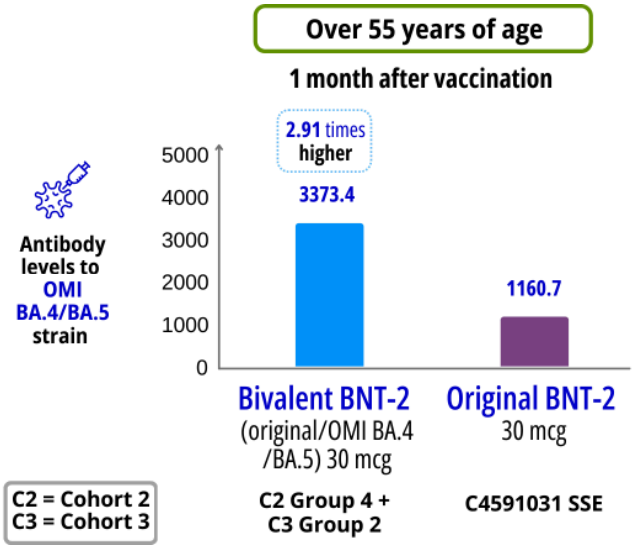


Figure 9 below shows the **antibody levels** against the **OMI BA.4/BA.5** strain of the COVID-19 virus between the 2 groups of participants over 55 years of age at 1 month **after** vaccination.

Figure 9. Antibody levels against OMI BA.4/BA.5 strain of the COVID-19 virus at 1 month after vaccination – Cohort 2 (Group 4) plus Cohort 3 (Group 2) and C4591031 SSE group



As shown in Figure 9 above among participants over 55 years of age at 1 month after vaccination:

- Participants who got **Bivalent BNT-2 (original/OMI BA.4/BA.5)** had **antibody levels** against OMI BA.4/BA.5 strain of the COVID-19 virus that were about **3 times (or 2.91 times) higher** than the antibody levels of those who got **Original BNT-2**.

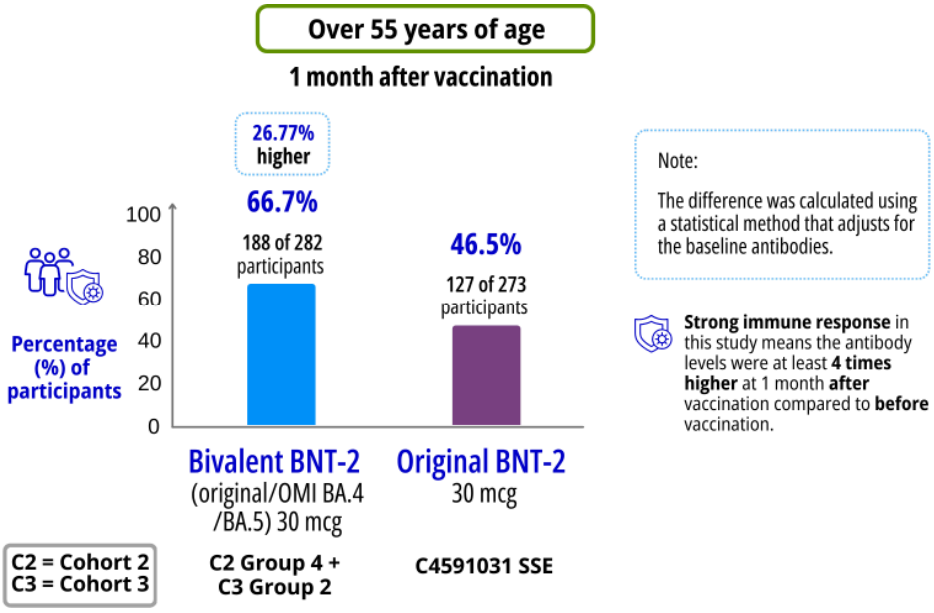
These study results mean that, among healthy adults **over 55 years of age** who have gotten 3 doses of **Original BNT-2** before, **Bivalent BNT-2 (original/OMI BA.4/BA.5)** 30 mcg may produce **antibodies** to help protect against **OMI BA.4/BA.5** strain of the COVID-19 virus **better than** the **Original BNT-2** 30 mcg.

Researchers also wanted to know if **Bivalent BNT-2 (original/OMI BA.4/BA.5)**, an Omicron-updated vaccine, works as good as the **Original BNT-2** based on how many participants had strong immune responses against the **OMI BA.4/BA.5** strain of the COVID-19 virus at 1 month after vaccination.

Figure 10 below shows these results at 1 month **after** vaccination between the 2 groups of participants over 55 years of age who got different vaccines.

- **Bivalent BNT-2** (original/OMI BA.4/BA.5) 30 mcg given to participants in the combined **Cohort 2 (Group 4)** and **Cohort 3 (Group 2)** in this study
- **Original BNT-2** 30 mcg given to a group of participants in **C4591031 SSE**

Figure 10. Percentage of participants with strong immune responses against OMI BA.4/BA.5 strain of the COVID-19 virus at 1 month after vaccination – Cohort 2 (Group 4) plus Cohort 3 (Group 2) and C4591031 SSE



As shown in Figure 10 above among participants over 55 years of age at 1 month after vaccination:

- The percentage of participants who got **Bivalent BNT-2 (original/OMI BA.4/BA.5)** with **strong immune responses** against OMI BA.4/BA.5 strain of the COVID-19 virus was about **27% (or 26.77%) higher** than that of participants who got **Original BNT-2**.

These study results mean that, among healthy adults **over 55 years of age** who have gotten 3 doses of **Original BNT-2** before, **Bivalent BNT-2 (original/OMI BA.4/BA.5)** 30 mcg may produce **strong immune responses** to help protect healthy adults over 55 years of age against OMI BA.4/BA.5 strain of the COVID-19 virus **as good as** the **Original BNT-2** 30 mcg.

Are the immune responses of participants 18 through 55 years of age similar to those over 55 years of age at 1 month after vaccination with Bivalent BNT-2 (original/OMI BA.4/BA.5)?

Researchers wanted to know if participants **18 through 55 years of age** and participants **over 55 years of age** had similar immune responses based on the amount of antibodies against the **OMI BA.4/BA.5** strain of the COVID-19 virus at 1 month after vaccination with **Bivalent BNT-2 (original/OMI BA.4/BA.5)**.

Researchers combined the groups in **Cohorts 2 and 3** who got **30 mcg** of Bivalent BNT-2 (original/OMI BA.4/BA.5) into 2 age groups. Combining the participants into 2 larger age groups allowed researchers to do additional tests to find out if participants in each age group can produce similar immune responses against the COVID-19 virus.

These groups are shown in Figure 11 below.

- **18 through 55 years of age:** Participants from **Cohort 2 (Group 2) plus Cohort 3 (Group 1)**
- **Over 55 years of age:** Participants from **Cohort 2 (Group 4) plus Cohort 3 (Group 2)**

Figure 11. Participants 18 through 55 years of age and those over 55 years of age who all got Bivalent BNT-2 (original/OMI BA.4/BA.5) – Cohorts 2 and 3 groups

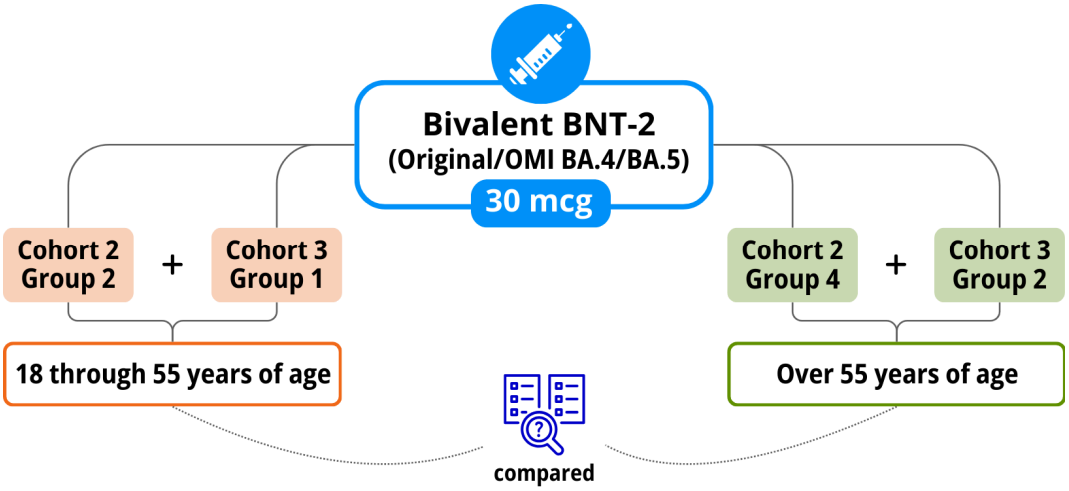
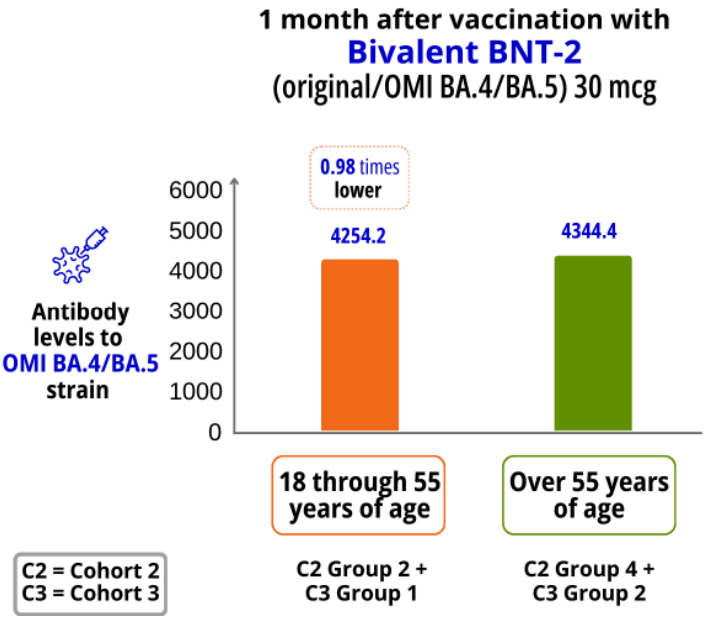


Figure 12 below shows the participants' **antibody levels** against **OMI BA.4/BA.5** strain of the COVID-19 virus at 1 month **after** getting **Bivalent BNT-2 (original/OMI BA.4/BA.5)**. The results are shown for the 2 age groups.

Figure 12. Antibody levels against OMI BA.4/BA.5 strain of the COVID-19 virus at 1 month after vaccination with Bivalent BNT-2 (original/OMI BA.4/BA.5) – 2 age groups Cohort 2 (Group 2) plus Cohort 3 (Group 1) and Cohort 2 (Group 4) plus Cohort 3 (Group 2)



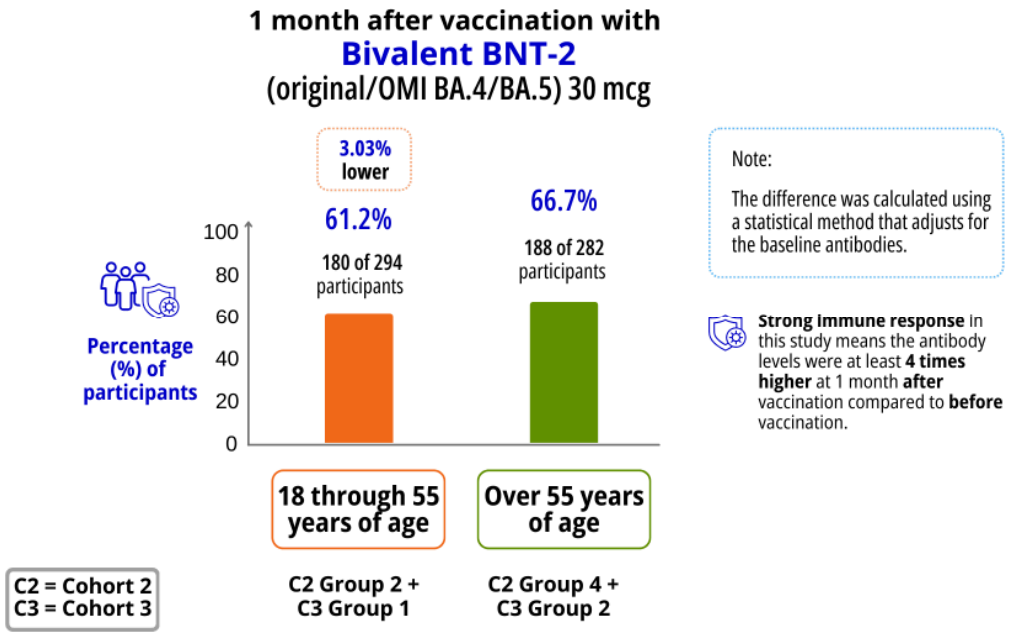
As shown in Figure 12 above, at 1 month after getting **Bivalent BNT-2 (original/OMI BA.4/BA.5)**:

- Participants **18 through 55 years of age** had **antibody levels** against OMI BA.4/BA.5 strain of the COVID-19 virus that were **0.98 times lower** than the antibody levels of participants **over 55 years of age**.

Researchers also wanted to know if participants **18 through 55 years of age** and participants **over 55 years of age** had similar immune responses based on how many participants had strong immune responses against the **OMI BA.4/BA.5** strain of the COVID-19 virus at 1 month after vaccination with **Bivalent BNT-2 (original/OMI BA.4/BA.5)**.

Figure 13 below shows these results between the 2 age groups.

Figure 13. Percentage of participants with strong immune responses against OMI BA.4/BA.5 strain of the COVID-19 virus at 1 month after vaccination with Bivalent BNT-2 (original/OMI BA.4/BA.5) – 2 age groups Cohort 2 (Group 2) plus Cohort 3 (Group 1) and Cohort 2 (Group 4) plus Cohort 3 (Group 2)



As shown in Figure 13 above, at 1 month after getting **Bivalent BNT-2 (original/OMI BA.4/BA.5)**:

The percentage of participants **18 through 55 years of age** with **strong immune responses** against OMI BA.4/BA.5 strain of the COVID-19 virus was about **3%** (or 3.03%) **lower** than that of participants **over 55 years of age**.

These study results mean that, among healthy adults who have gotten 3 doses of **Original BNT-2** before, **Bivalent BNT-2 (original/OMI BA.4/BA.5)** 30 mcg given as the 4th dose produces similar immune responses between the 2 age groups: **18 through 55 years of age** and **over 55 years of age**.

As the results were similar between the 2 age groups, this means that participants **18 through 55 years of age** would also have similar results with the participants **over 55 years of age** in the other analysis that compared **Bivalent BNT-2 (original/OMI BA.4/BA.5)** to the **Original BNT-2** given to participants in **C4591031 SSE**.

Overall, the study results suggest that, compared to Original BNT-2, **Bivalent BNT-2 (original/OMI BA.4/BA.5)** given to the combined groups from Cohorts 2 and 3 may offer more protection against new COVID-19 virus strains.

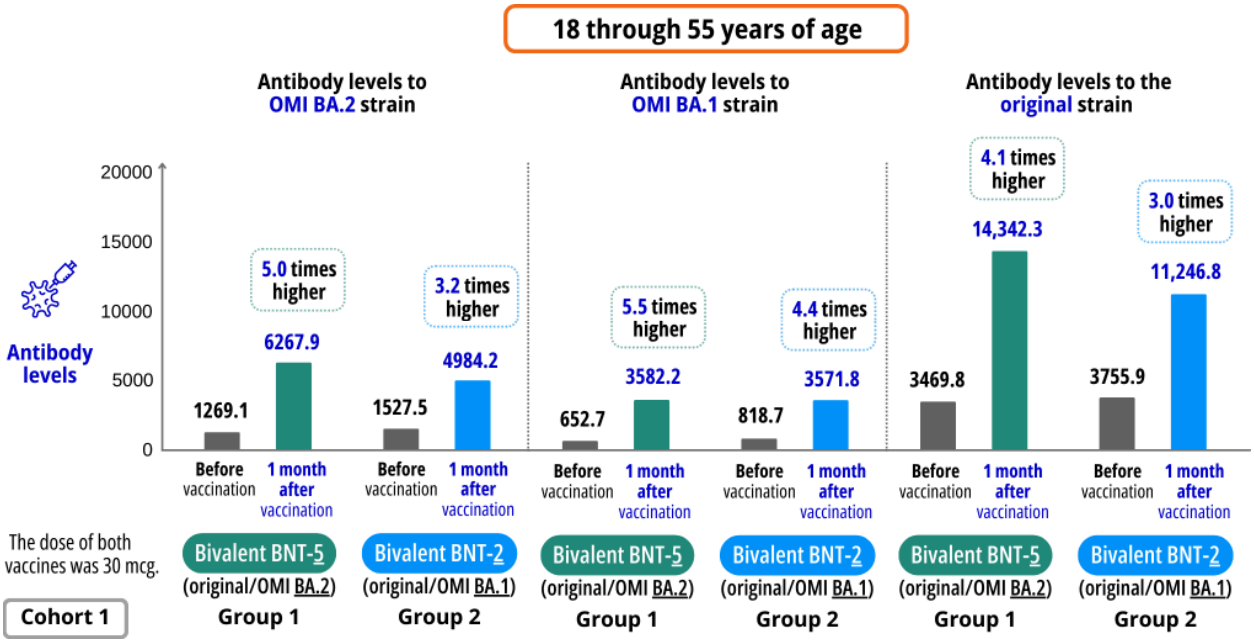
Immune responses to new COVID-19 vaccine candidates – Cohorts 1 and 4

Did participants have immune responses at 1 month after vaccination with Bivalent BNT-5 (original/OMI BA.2) or Bivalent BNT-2 (original/OMI BA.1)?

Researchers wanted to know how **Bivalent BNT-5 (original/OMI BA.2)**, a new modified vaccine, would compare with **Bivalent BNT-2 (original/OMI BA.1)** based on the amount of antibodies against the 3 strains of the COVID-19 virus that they are designed to target: **original**, **OMI BA.1**, and **OMI BA.2**.

Figure 14 below shows the participants' **antibody levels** against **OMI BA.2**, **OMI BA.1**, and **original** strains of the COVID-19 virus **before** and 1 month **after** vaccination in **Cohort 1**. It also shows the average rise in antibodies from before to after vaccination.

Figure 14. Antibody levels against OMI BA.2, OMI BA.1, and original strains of the COVID-19 virus before and after vaccination – Cohort 1



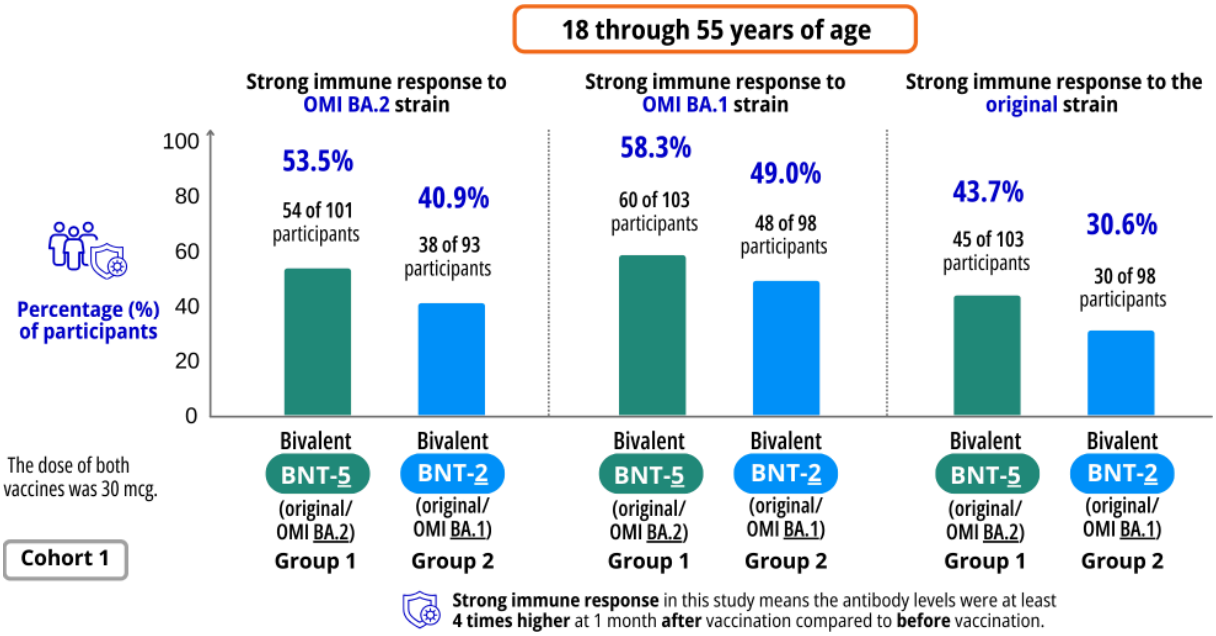
As shown in Figure 14 above, at 1 month after vaccination in **Cohort 1**:

- Participants in **Group 1** had **antibody levels** against **OMI BA.2** and **original** strains of the COVID-19 virus that were higher than the antibody levels of **Group 2**. Participants in **Group 1** had **antibody levels** against **OMI BA.1** strain of the COVID-19 virus that were similar to the antibody levels of **Group 2**.
- For the **OMI BA.2** strain, the average rise in antibodies of **Group 1** was higher than that of Group 2. For the **OMI BA.1** and **original** strains, the average rise in antibodies of **Group 1** was similar to that of **Group 2**.

Researchers also wanted to know how **Bivalent BNT-5 (original/OMI BA.2)**, a new modified vaccine, would compare with **Bivalent BNT-2 (original/OMI BA.1)** based on how many participants had strong immune responses against the **OMI BA.2**, **OMI BA.1**, and **original** strains of the COVID-19 virus at 1 month after vaccination.

Figure 15 below shows these results.

Figure 15. Percentage of participants with strong immune responses against OMI BA.2, OMI BA.1, and original strains of the COVID-19 virus at 1 month after vaccination – Cohort 1



As shown in Figure 15 above, at 1 month after vaccination in **Cohort 1**:

- The percentage of participants in **Group 1** with **strong immune responses** against **OMI BA.2**, **OMI BA.1**, and **original** strains of the COVID-19 virus was higher than that of participants in **Group 2**.

Overall, study results of **Cohort 1** showed that, among healthy adults **18 through 55 years of age** who have gotten 1 booster dose of US-authorized COVID-19 vaccine before:

Bivalent BNT-5 (original/OMI BA.2) or **Bivalent BNT-2 (original/OMI BA.1)** given as a booster dose may help to protect against COVID-19 infection caused by OMI BA.2, OMI BA.1, and original strains.

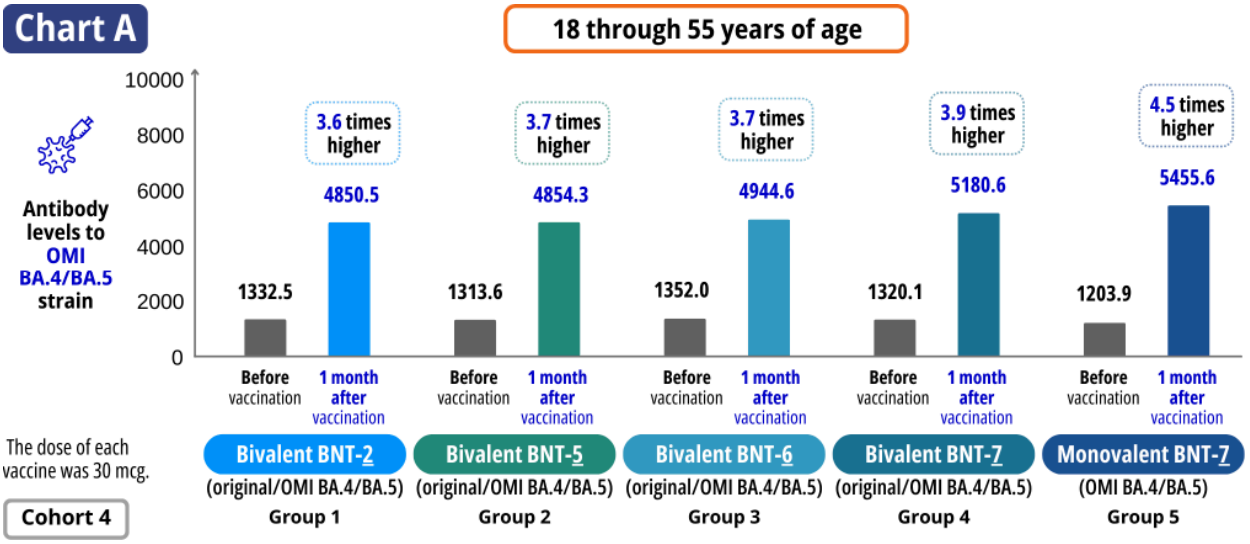
While these results in **Cohort 1** mean that participants in both vaccine groups showed strong immune responses, there was no significant difference in immune responses between the **Bivalent BNT-5** and the **Bivalent BNT-2** groups.

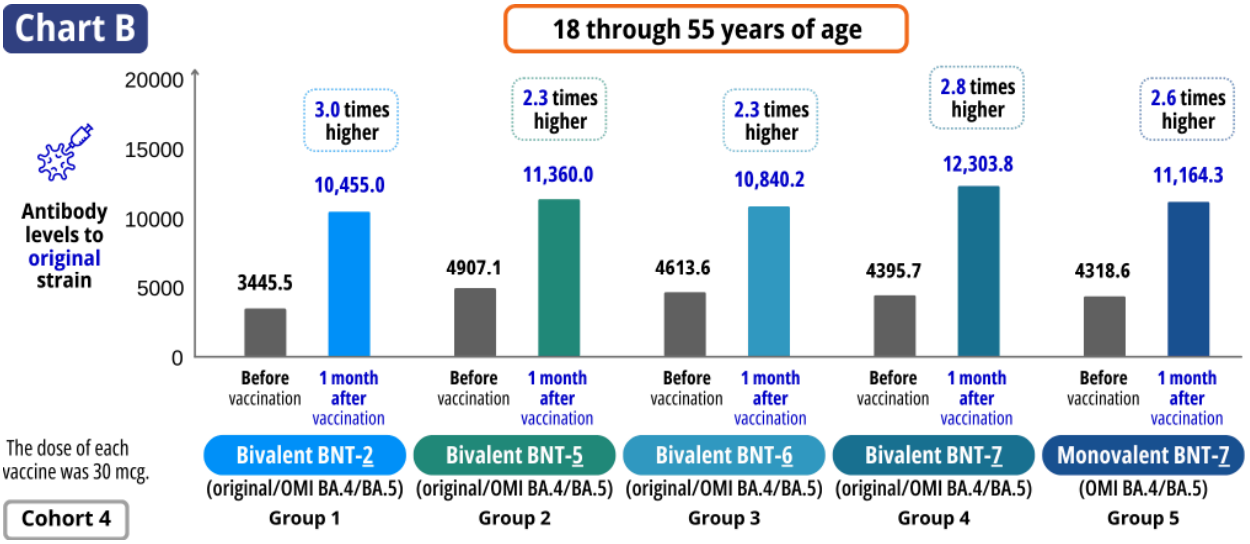
Did participants have immune responses at 1 month after vaccination with the BNT-5, BNT-6, or BNT-7 vaccine candidates?

Researchers wanted to know how the new vaccine candidates (**Bivalent BNT-5**, **BNT-6**, and **BNT-7 [original/OMI BA.4/OMI BA.5]** and **Monovalent BNT-7 [OMI BA.4/OMI BA.5]**) would compare with **Bivalent BNT-2 (original/OMI BA.4/BA.5)** based on the amount of antibodies against the 2 strains of the COVID-19 virus that the vaccines were modified to target: **OMI BA.4/BA.5** and **original** strains.

The charts in Figure 16 below show **Cohort 4** participants' **antibody levels** against the **OMI BA.4/BA.5** strain **(Chart A)** and **original** strain **(Chart B)** of the COVID-19 virus **before** and 1 month **after** vaccination. The charts also show the average rise in antibodies from before to after vaccination.

Figure 16. Antibody levels against OMI BA.4/BA.5 and original strains of the COVID-19 virus before and after vaccination – Cohort 4





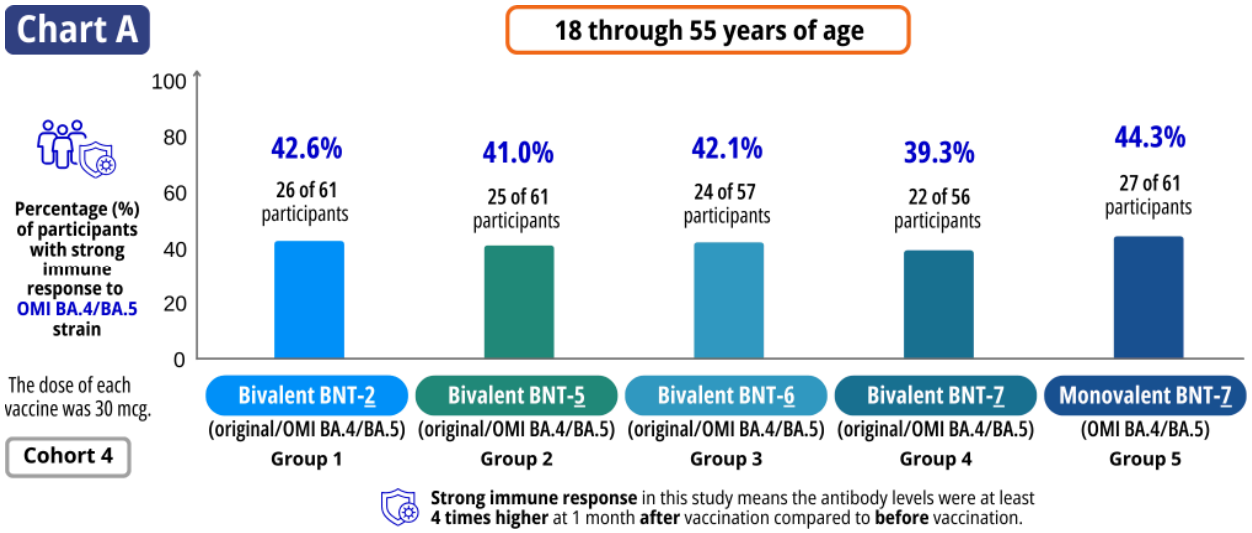
The charts in Figure 16 above show that at 1 month **after** vaccination in **Cohort 4**:

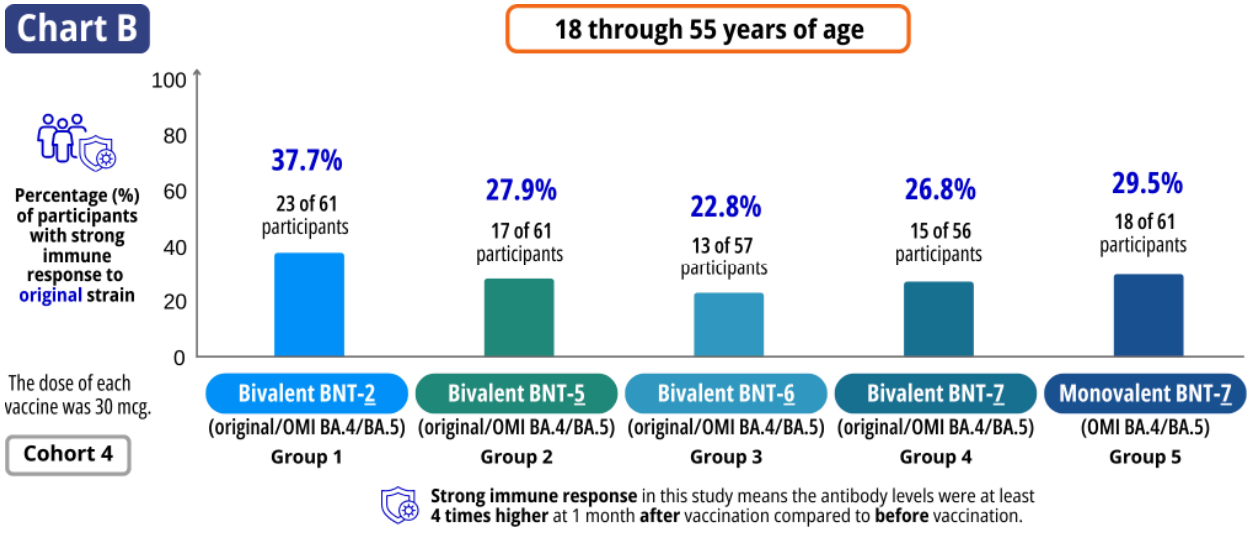
- Participants across the 5 groups had high **antibody levels** against OMI BA.4/BA.5 and original strains of the COVID-19 virus. The average rise in antibodies was similar across the 5 groups.

Researchers also wanted to know how the new vaccine candidates (**Bivalent BNT-5**, **BNT-6**, and **BNT-7 [original/OMI BA.4/OMI BA.5]** and **Monovalent BNT-7 [OMI BA.4/OMI BA.5]**) would compare with **Bivalent BNT-2 (original/OMI BA.4/BA.5)** based on how many participants had strong immune responses against the **OMI BA.4/BA.5** and **original** strains of the COVID-19 virus at 1 month after vaccination.

The charts in Figure 17 below show how many participants in **Cohort 4** had strong immune responses against **OMI BA.4/BA.5** strain (**Chart A**) and **original** strain (**Chart B**) of the COVID-19 virus at 1 month after vaccination.

Figure 17. Percentage of participants with strong immune responses against OMI BA.4/BA.5 and original strains of the COVID-19 virus at 1 month after vaccination – Cohort 4





The charts in Figure 17 above show that, at 1 month after vaccination in **Cohort 4**:

- The percentage of participants with **strong immune responses** against OMI BA.4/BA.5 and original strains of the COVID-19 virus was generally similar across the 5 groups.

Overall, study results of **Cohort 4** showed that, among healthy adults 18 through 55 years of age who had gotten 3 or 4 doses of a US-authorized mRNA COVID-19 vaccine before, the vaccines listed below (given as the 4th or 5th dose) may help to protect them against COVID-19 infection caused by OMI BA.4/BA.5 and original strains.

- **Bivalent BNT-2** (original/OMI BA.4/BA.5)
- **Bivalent BNT-5** (original/OMI BA.4/BA.5)
- **Bivalent BNT-6** (original/OMI BA.4/BA.5)
- **Bivalent BNT-7** (original/OMI BA.4/BA.5)
- **Monovalent BNT-7** (OMI BA.4/BA.5)

While these results in **Cohort 4** mean that participants across the 5 vaccine groups all showed strong immune responses, there was no significant difference in immune responses between the new vaccine candidates (**BNT-5**, **BNT-6**, or **BNT-7**) compared to **Bivalent BNT-2**.

How many participants had redness, swelling, or pain at the injection site within 7 days after vaccination?

Pain, redness, and swelling at the injection site (area on the arm where the vaccine was injected) are also called **local reactions**.

Researchers checked the electronic diary records of participants to find out if they had any local reactions within 7 days after vaccination.

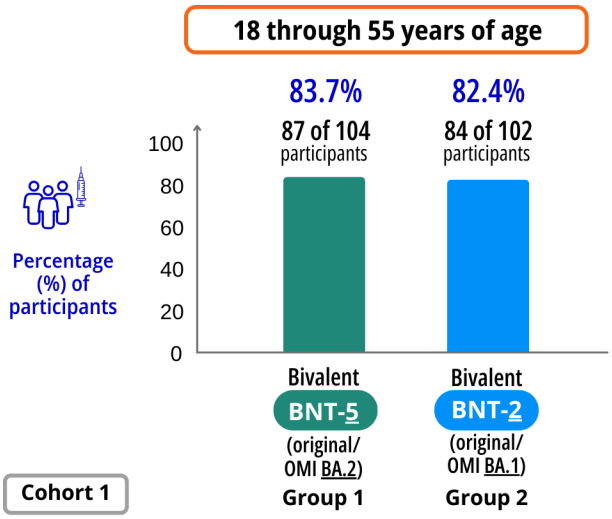
Figure 18 to Figure 21 below show how many participants across the 4 cohorts had local reactions within 7 days after vaccination in this study.

Overall, across the 4 cohorts:

- Most of the **local reactions** were mild or moderate in severity and lasted about 1 to 4 days.
- **Injection site pain** was the most common local reaction.

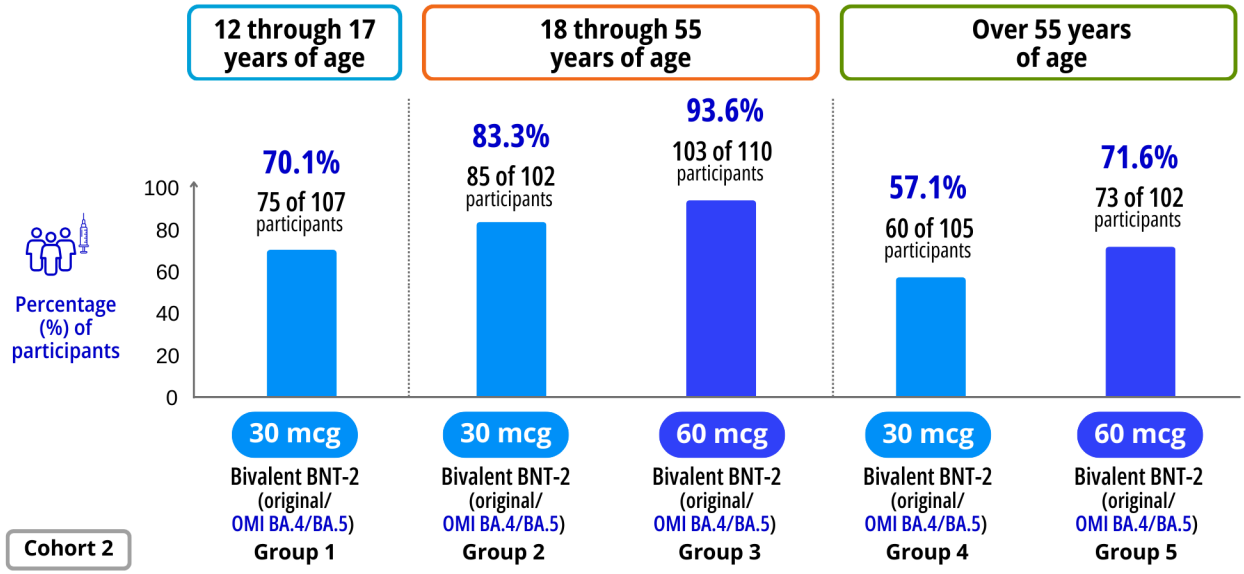
Cohort 1:

Figure 18. Percentage of participants who had any local reactions within 7 days after vaccination – Cohort 1



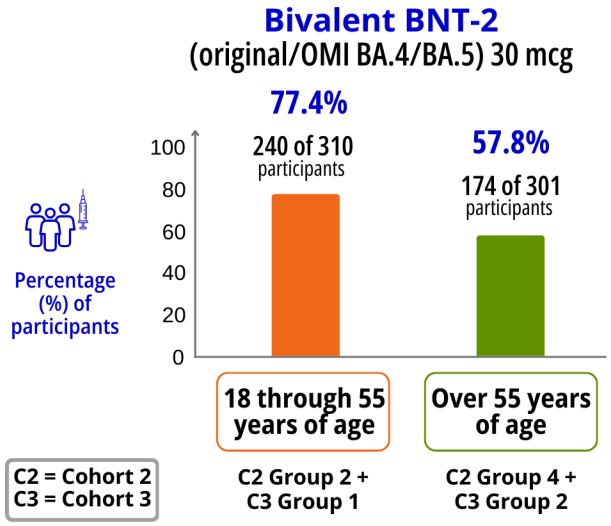
Cohort 2:

Figure 19. Percentage of participants who had any local reactions within 7 days after vaccination – Cohort 2



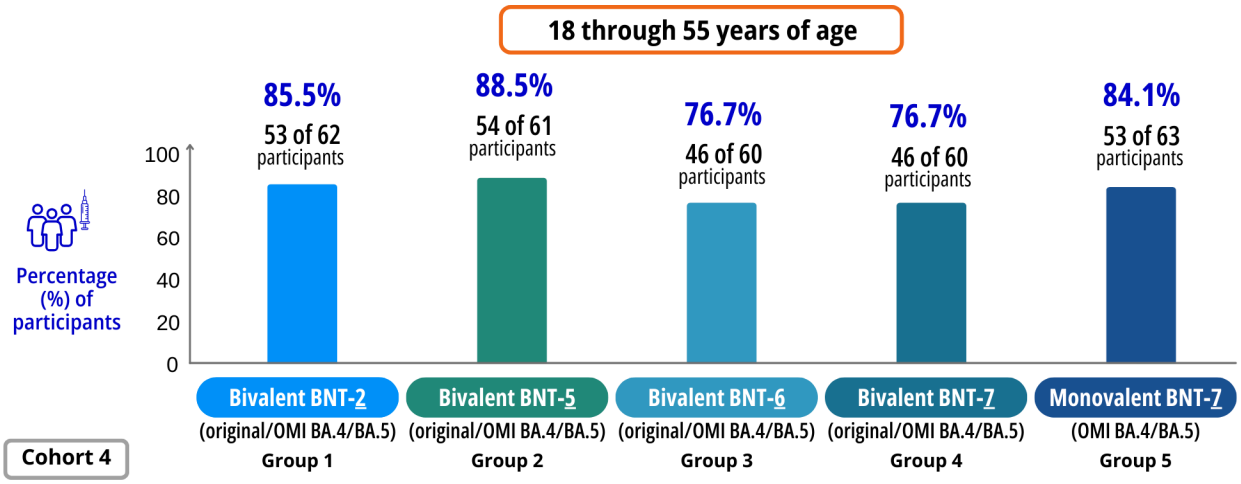
Combined Cohort 2 and Cohort 3:

Figure 20. Percentage of participants who had any local reactions within 7 days after vaccination − Combined groups in Cohorts 2 and 3



Cohort 4:

Figure 21. Percentage of participants who had any local reactions within 7 days after vaccination − Cohort 4



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

Fever, tiredness, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain are also called **systemic symptoms**. "Systemic" means it can affect the whole body.

Researchers checked the electronic diary records of participants to find out if they had any systemic symptoms within 7 days after vaccination.

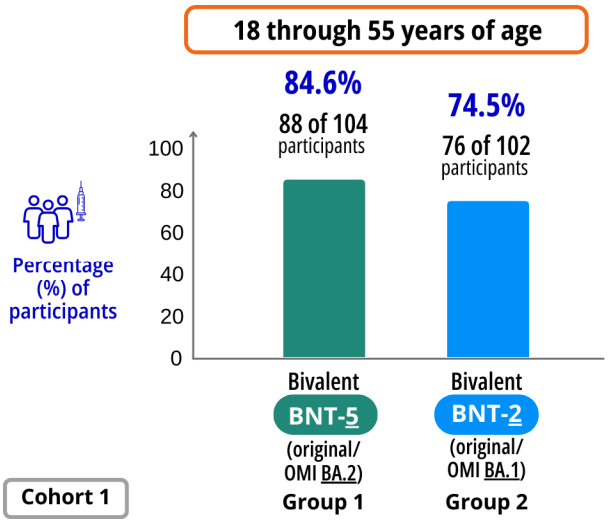
Figure 22 to Figure 25 below show how many participants across the 4 cohorts had systemic symptoms within 7 days after vaccination in this study.

Overall, across the 4 cohorts:

- Most of the **systemic symptoms** were mild or moderate in severity and lasted about 1 to 3 days.
- **Tiredness** was the most common systemic symptom.

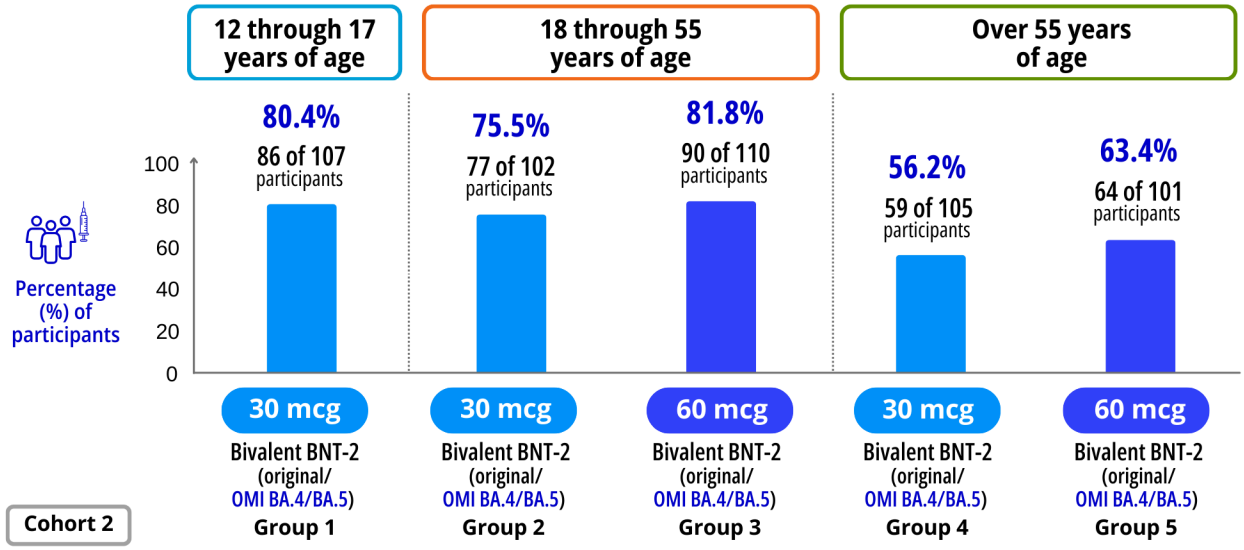
Cohort 1:

Figure 22. Percentage of participants who had any systemic symptoms within 7 days after vaccination – Cohort 1



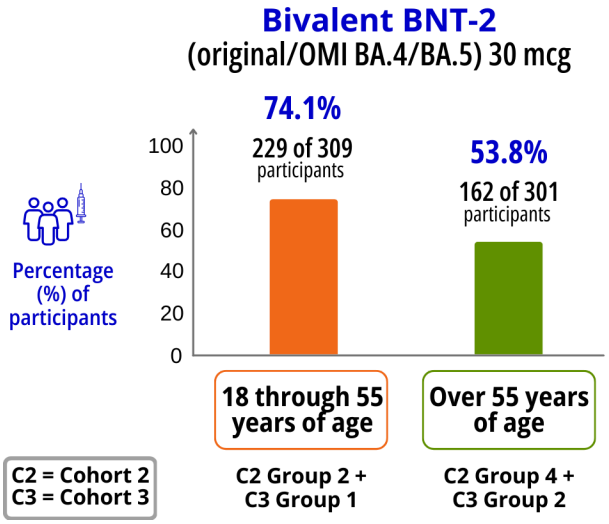
Cohort 2:

Figure 23. Percentage of participants who had any systemic symptoms within 7 days after vaccination – Cohort 2



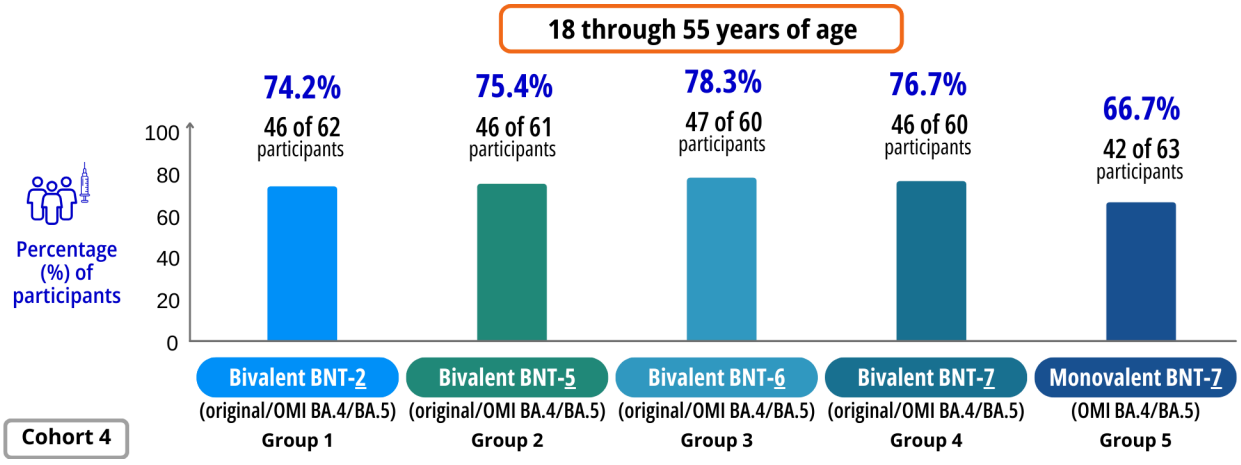
Combined Cohorts 2 and 3:

Figure 24. Percentage of participants who had any systemic symptoms within 7 days after vaccination – Combined groups in Cohorts 2 and 3



Cohort 4:

Figure 25. Percentage of participants who had any systemic symptoms within 7 days after vaccination – Cohort 4



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?

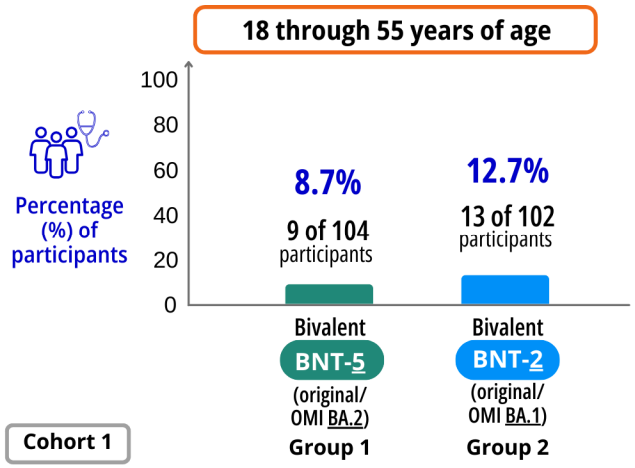
The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study vaccine or by 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 medical problems within 1 month after vaccination in this study?

Across the 4 cohorts, Figure 26 to Figure 29 below show that less than 15% of participants in each vaccine group had medical problems within 1 month after vaccination in this study.

Cohort 1:

Figure 26. Percentage of participants who had medical problems within 1 month after vaccination – Cohort 1



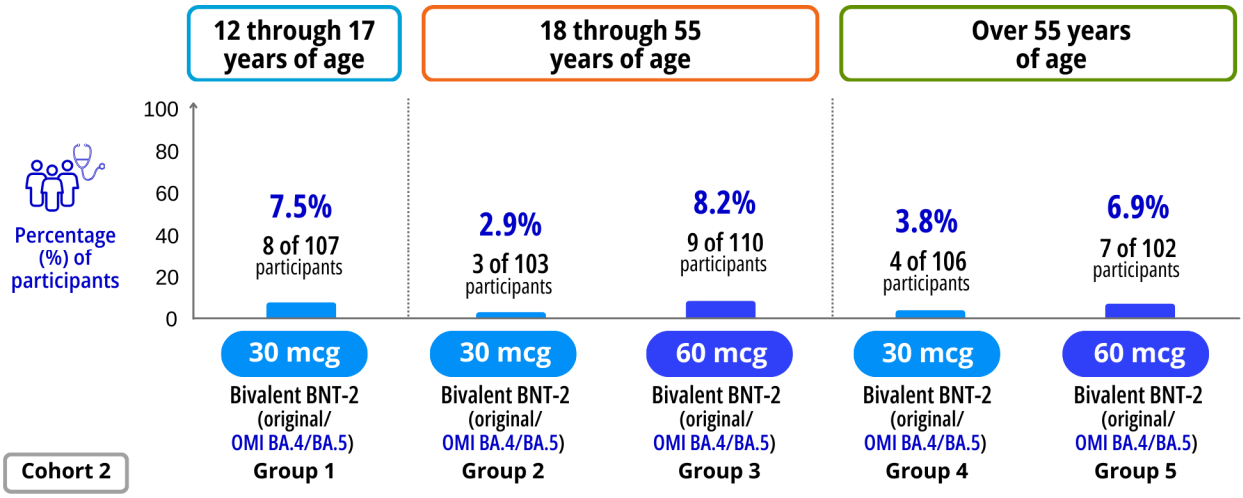
The most common medical problems in Cohort 1 – those reported by at least 2 participants in the total group – within 1 month after vaccination in this study are listed below.

- **COVID-19** was reported by 3 out of 104 participants (2.9%) who got **Bivalent BNT-5** (original/OMI BA.2) and 4 out of 102 participants (3.9%) who got **Bivalent BNT-2** (original/OMI BA.1).
- **Lymph node swelling** was reported by 1 out of 104 participants (1.0%) who got **Bivalent BNT-5** (original/OMI BA.2) and 1 out of 102 participants (1.0%) who got **Bivalent BNT-2** (original/OMI BA.1).

No participant in Cohort 1 left the study because of a medical problem within 1 month after vaccination or during the study.

Cohort 2:

Figure 27. Percentage of participants who had medical problems within 1 month after vaccination – Cohort 2



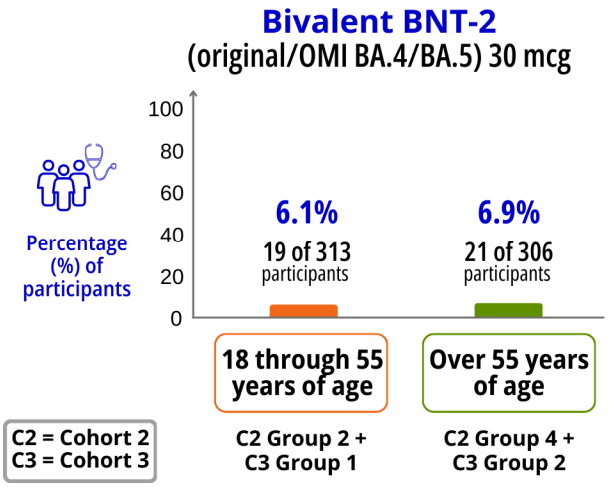
None of the individual medical problems in Cohort 2 were reported by 2 or more participants in any vaccine group within 1 month after vaccination in this study.

No participant in Cohort 2 left the study because of a medical problem within 1 month after vaccination.

Overall, 1 participant in the 12 through 17 years of age group in Cohort 2 left the study within 6 months after vaccination because of a medical problem. The participant reported having depression. Researchers believe that this medical problem was not related to the study vaccine.

Combined Cohort 2 and Cohort 3:

Figure 28. Percentage of participants who had medical problems within 1 month after vaccination – Combined groups in Cohorts 2 and 3



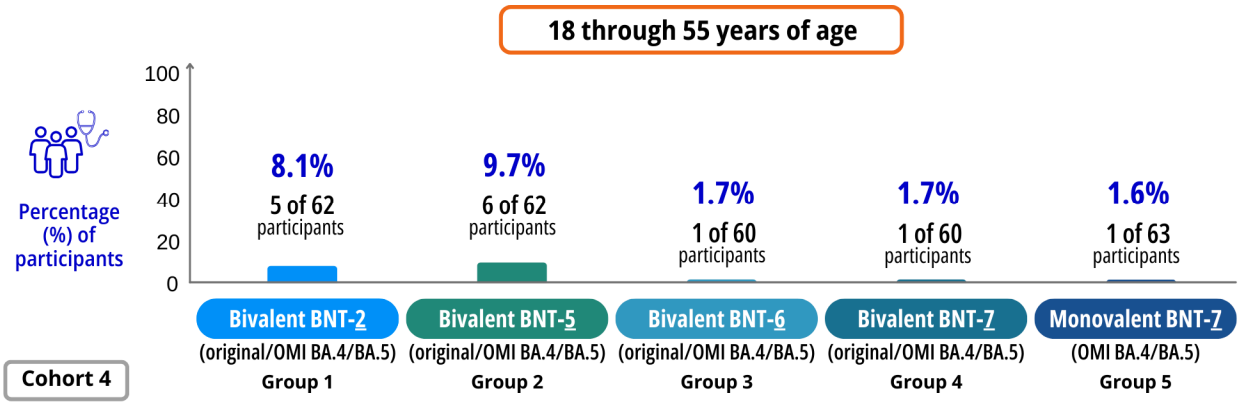
The most common medical problem – reported by at least 5 participants in either age group – within 1 month after vaccination in this study is listed below:

- **Lymph node swelling** was reported by 5 out of 313 participants (1.6%) in the **18 through 55 years of age** group and 1 out of 306 participants (0.3%) in the **over 55 years of age** group.

No participant in either age group of the combined groups in Cohorts 2 and 3 left the study because of a medical problem within 1 month after vaccination.

Cohort 4:

Figure 29. Percentage of participants who had medical problems within 1 month after vaccination – Cohort 4



None of the individual medical problems were reported by more than 1 participant in any of the 5 vaccine groups within 1 month after vaccination in Cohort 4 of this study.

No participant in Cohort 4 left the study because of a medical problem within 1 month after vaccination or during the study.

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 in this study?

Cohort 1:

A total of 3 participants in Cohort 1 had serious medical problems within 6 months after vaccination in this study. Of these 3 participants:

- 1 out of 104 participants (1.0%) who got **Bivalent BNT-5** (original/OMI BA.2) had the following serious medical problems: **stomach flu** (or gastroenteritis), **anemia** (fewer red blood cells than normal), and a sudden **kidney injury**.
- 2 out of 102 participants (2.0%) who got **Bivalent BNT-2** (original/OMI BA.1) had the following serious medical problems: 1 participant had a sudden **pancreatitis** (inflammation of the body organ called pancreas) and a **small intestinal obstruction** (blockage in the small intestine or gut). The other participant had **biliary colic** (pain in the abdomen area due to a gallbladder problem or gallstone).

Researchers believe that these serious medical problems reported in Cohort 1 were not related to the study vaccines.

No participant in Cohort 1 died during the study.

Cohort 2:

Overall, 6 participants in Cohort 2 who got Bivalent BNT-2 (original/OMI BA.4/BA.5) had serious medical problems within 6 months after vaccination in the study. The serious medical problems of these 6 participants are listed below by age group.

12 through 17 years of age:

- 1 out of 107 participants (0.9%) who got the **30-mcg** dose of the study vaccine had serious medical problems. The participant had **alcohol poisoning** and **thoughts of suicide**.

18 through 55 years of age:

- None of the participants in this age group who got the **30-mcg** dose of the study vaccine had a serious medical problem.
- 1 out of 110 participants (0.9%) in this age group who got the **60-mcg** dose of the study vaccine had a serious medical problem of **testicular cancer**.

Over 55 years of age:

- 4 out of 106 participants (3.8%) in this age group who got the **30-mcg dose** of the study vaccine had the following serious medical problems: 1 had **pancreatic cancer**, 1 had **prostate cancer**, 1 had **leukemia** (blood cancer), and 1 had heart rate or rhythm abnormality (**arrhythmia**) and **fainting**.
- None of the 102 participants who got the **60-mcg** dose of the study vaccine had serious medical problems.

Researchers believe that these serious medical problems reported in Cohort 2 were not related to the study vaccine.

No participant in Cohort 2 died during the study.

Cohort 3:

Overall, 8 participants in Cohort 3 who got Bivalent BNT-2 (original/OMI BA.4/BA.5) 30 mcg had serious medical problems within 6 months after vaccination in the study. The serious medical problems of these 8 participants are listed below by age group.

18 through 55 years of age:

- 2 participants in this age group had the following serious medical problems: 1 participant had **diverticulitis** (pouches called diverticula in the large intestine that became inflamed). The other participant had **low blood pressure**.

Over 55 years of age:

- 6 participants in this age group had the following serious medical problems: 1 had **low potassium levels in the blood** and **blockage in the urinary tract**, 1 had **low sugar levels in the blood**, 1 had **infection after surgery**, 1 had **type 2 diabetes mellitus**, 1 had **heart failure**, and 1 had **back pain**.

Researchers believe that these serious medical problems reported in Cohort 3 were not related to the study vaccine.

Overall, 1 participant who got Bivalent BNT-2 (original/OMI BA.4/BA.5) in Cohort 3 (over 55 years of age group) did not finish the study because of a serious medical problem. The participant had **heart failure** during surgery, which led to death. Researchers believe that this serious medical problem was not related to the study vaccine.

Cohort 4:

Overall, 1 participant in Cohort 4 had a serious medical problem within 6 months after vaccination in this study. The participant was 1 out of 62 participants (1.6%) who got Bivalent BNT-2 (original/OMI BA.4/BA.5), and they had **infectious enterocolitis** (inflammation of small and large intestines). Researchers believe that this serious medical problem was not related to the study vaccine.

No participant in Cohort 4 died during the study.

Where can I learn more about this study?

If you or your child 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 **C4591044**

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

www.clinicaltrials.gov	Use the study identifier **NCT05472038**
www.clinicaltrialsregister.eu	Use the study identifier **2022-002008-19**

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!