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® (Pfizer-BioNTech RNA-based COVID-19 Vaccine), also known as BNT162b2 or PF-07302048
Protocol Number:	C4591031 Substudy F
Dates of Study:	23 February 2022 to 30 October 2022
Title of this Study:	A Study of BNT162b2 COVID-19 Vaccine Given as a Booster Dose in Healthy Adults Aged 60 Years and Older in Israel who had Already Received BNT162b2 COVID-19 Vaccine Before [Substudy F Final Report: A Phase 3 Master Protocol to Evaluate Additional Dose(s) of BNT162b2 in Healthy Individuals Previously Vaccinated With BNT162b2]
Date of this Report:	23 October 2023

– Thank You –

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

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

Why was this study done?

What 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 fever, chills, cough, loss of taste or smell, 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 strains or **"variants"**. Compared to the original COVID-19 virus, the **Delta** and **Omicron** strains spread more easily between people.

What are BNT162b2 and BNT162b2 OMI COVID-19 vaccines?

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

BNT162b2 (also known as Comirnaty®) is called **BNT** in this summary. BNT is the original monovalent COVID-19 vaccine that was designed to target the original 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.

A **monovalent** COVID-19 vaccine can target 1 strain of the COVID-19 virus.

BNT162b2 OMI is called **BNT OMI** in this summary. BNT OMI is a modified form of the original BNT162b2 COVID-19 vaccine. BNT OMI is a monovalent vaccine that was designed to target the **Omicron BA.1** strain of the COVID-19 virus. 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.

BNT162b2 plus BNT162b2 OMI is a combination of the BNT162b2 and the BNT162b2 OMI COVID-19 vaccines. This combination is called the bivalent **BNT plus BNT OMI** in this summary. The bivalent **BNT plus BNT OMI** was designed to target both the original COVID-19 virus and the Omicron BA.1 strain of the COVID-19 virus.

A **bivalent** COVID-19 vaccine can target 2 strains of the COVID-19 virus.

At the time of this study, **BNT** had been widely approved around the world, and the bivalent **BNT plus BNT OMI** had not yet been approved. **BNT OMI** was not submitted to health agencies for approval.

What was the purpose of this study?

The main purpose of this study was:

> To learn if a booster shot of **BNT**, **BNT OMI**, and **bivalent BNT plus BNT OMI** COVID-19 vaccines at different strengths works well and is safe in healthy adults.

Participants were at least 60 years old who had already gotten 3 doses of the BNT COVID-19 vaccine before the start 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 to 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 a disease can fade over time.

- A **booster shot** is the extra dose of a vaccine after receiving the first dose or series of doses.
- A booster shot can help the immune system maintain or "**boost**" the level of protection against a disease.

Researchers wanted to know:

- **Did participants have immune responses to specific strains of the COVID-19 virus after they got a booster shot of COVID-19 vaccine?**
- **How many participants had redness, swelling, or pain at the injection site within 7 days after the booster shot?**
- **How many participants had fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain within 7 days after the booster shot?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

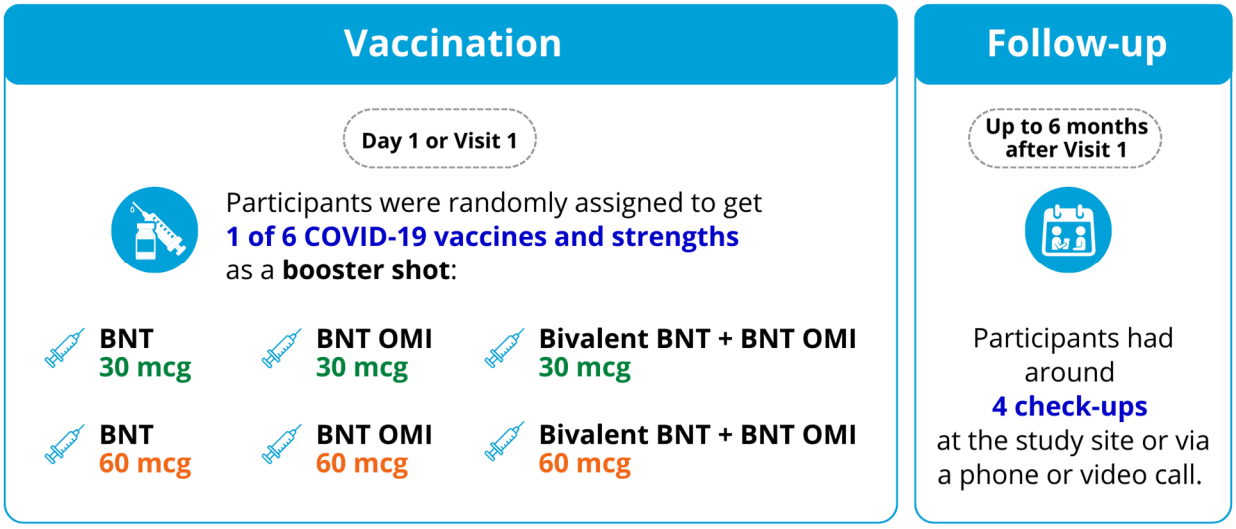
Participants were randomly assigned by chance to get **1 of 6 different COVID-19 vaccines and strengths**. These vaccines are listed in Figure 1 below. The vaccine strengths were measured in micrograms or mcg.

They got their assigned **BNT**, **BNT OMI**, or bivalent **BNT plus BNT OMI** COVID-19 vaccine in either **30 or 60 mcg** as **1 booster shot**.

Researchers then compared the results of participants in the 6 groups.

Figure 1 below shows what happened during the study.

Figure 1. What happened in this study?



Throughout the study, participants had blood samples taken and had health checks done.

Type of study:

At the start, the study was "open-label" to the Sponsor. This means that the healthcare staff who gave the injections and some of the researchers knew which booster shot the participants got. The participants did not know which booster shot they got.

> Based on the study plan, only 5 participants could enroll in each of the 6 groups at the start of the study. An independent group of experts and some of the researchers checked on the safety of these participants before letting more participants enroll.

Later on, when more participants were allowed to enroll, the study was "observer-blinded". This means that only the healthcare staff who gave the injections knew which booster shot the participants got. The study participants and researchers did not know which booster shot was given.

Where did this study take place?

This study ran at 1 location in Israel.

When did this study take place?

It began on 23 February 2022 and ended on 30 October 2022.

Who participated in this study?

The study included healthy adults at least 60 years old who had already gotten 3 doses of the BNT COVID-19 vaccine.

In total, 123 participants joined this study. One (1) participant did not get a study vaccine. Overall, 122 participants got a study vaccine:

- 61 men (50%) and 61 women (50%) participated.
- Participants were between the ages of 60 and 83 years old.

All 122 participants finished the study. No participant left the study before it was over.

How long did the study last?

Study participants were in the study for about 6 months. The entire study took about 8 months to complete.

When the study ended in October 2022, 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?

Did participants have immune responses to specific strains of the COVID-19 virus after they got a booster shot of COVID-19 vaccine?

To answer this question, researchers checked the participants' **antibody levels** against the following **strains of the COVID-19 virus** before and after they got their BNT, BNT OMI, or bivalent BNT plus BNT OMI COVID-19 vaccine:

- Original strain.
- Omicron BA.1 strain.
- Omicron BA.4/BA.5 strain.

A booster shot of **BNT**, **BNT OMI**, or bivalent **BNT plus BNT OMI** COVID-19 vaccine given at 30 or 60 mcg led to the following results in this study:

- Participants in all the vaccine groups had strong **immune responses** to the original, Omicron BA.1, and Omicron BA.4/BA.5 strains of the COVID-19 virus.

- The **antibody levels** against the Omicron BA.1 strain were higher among participants in the BNT OMI and bivalent BNT plus BNT OMI groups than participants in the BNT groups.

- More participants had an at least **4-fold rise in immune responses** to the original, Omicron BA.1, and Omicron BA.4/BA.5 strains of the COVID-19 virus at **1 month** after their booster shot than the **other time points** across all vaccine groups at either 30 or 60 mcg strength, except for the BNT OMI groups.
    - For most of the BNT OMI groups, the participants' 4-fold rise in immune responses to the Omicron BA.1 and Omicron BA.4/BA.5 strains of the COVID-19 virus at **1 month** and at **6 months** after their booster shot were similar.

      The results for the BNT OMI groups may be due to ongoing COVID-19 infection in some participants.
    - For the BNT OMI 60 mcg group, more participants had an at least 4-fold rise in immune responses to the original strain of the COVID-19 virus at **6 months** after their booster shot than at **1 month** after their booster shot.
- There was no steady pattern of a drop in the antibody levels against the COVID-19 virus strains after reaching the highest antibody levels 1 month after the booster shot. The reasons for this may be the ongoing COVID-19 infection in some participants and the small number of participants in this study.

These results mean that, for healthy adults aged 60 years and older who had already gotten 3 doses of the BNT COVID-19 vaccine before:

A fourth dose or booster shot of the **BNT**, **BNT OMI**, or bivalent **BNT plus BNT OMI** COVID-19 vaccine may offer protection against the original, Omicron BA.1, and Omicron BA.4/BA.5 strains of the COVID-19 virus.

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

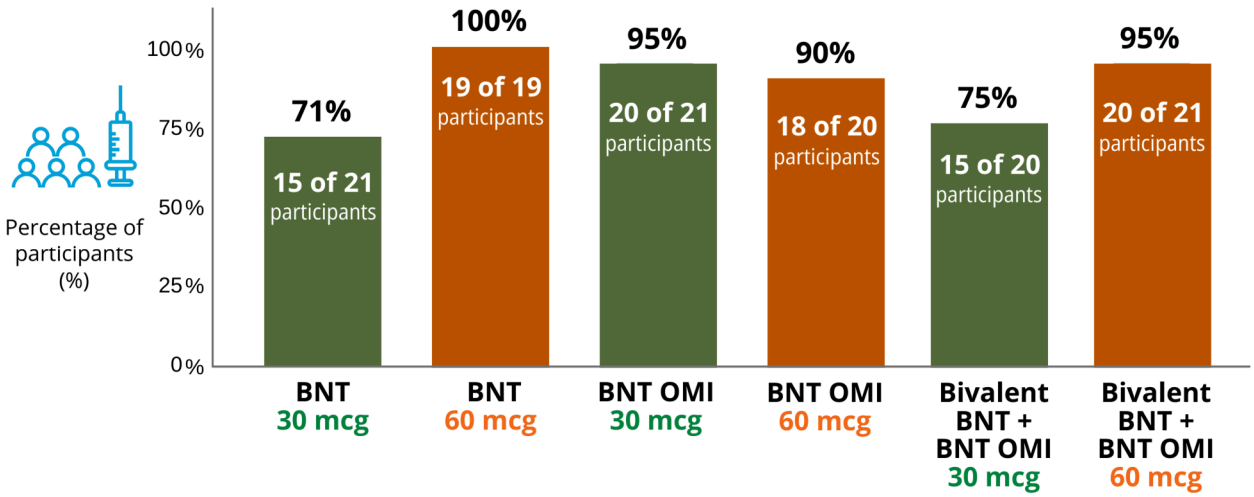
To answer this question, researchers checked the electronic diary records of participants.

Within 7 days after the booster shot, **71%** to **100%** of participants across the vaccine groups had at least 1 injection site reaction of any redness, swelling, or pain.

Figure 2 below shows these results.

Most of these injection site reactions were mild or moderate in severity and went away after about 1 to 3 and a half days. The most common injection site reaction was pain.

Figure 2. How many participants had any redness, swelling, or pain at the injection site within 7 days after the booster shot?



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

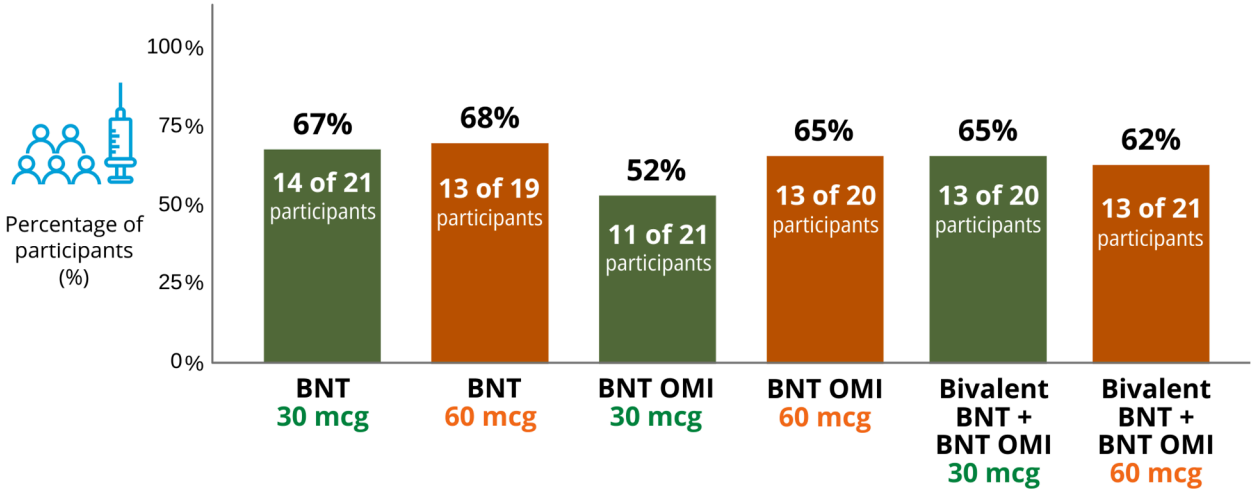
To answer this question, researchers checked the electronic diary records of participants.

Within 7 days after the booster shot, **52%** to **68%** of participants across the vaccine groups had at least 1 symptom of any fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain.

Figure 3 below shows these results.

Most of these symptoms were mild or moderate in severity and went away after about 1 to 3 days. The most common symptom was tiredness.

Figure 3. How many participants had any fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain within 7 days after the booster shot?



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.

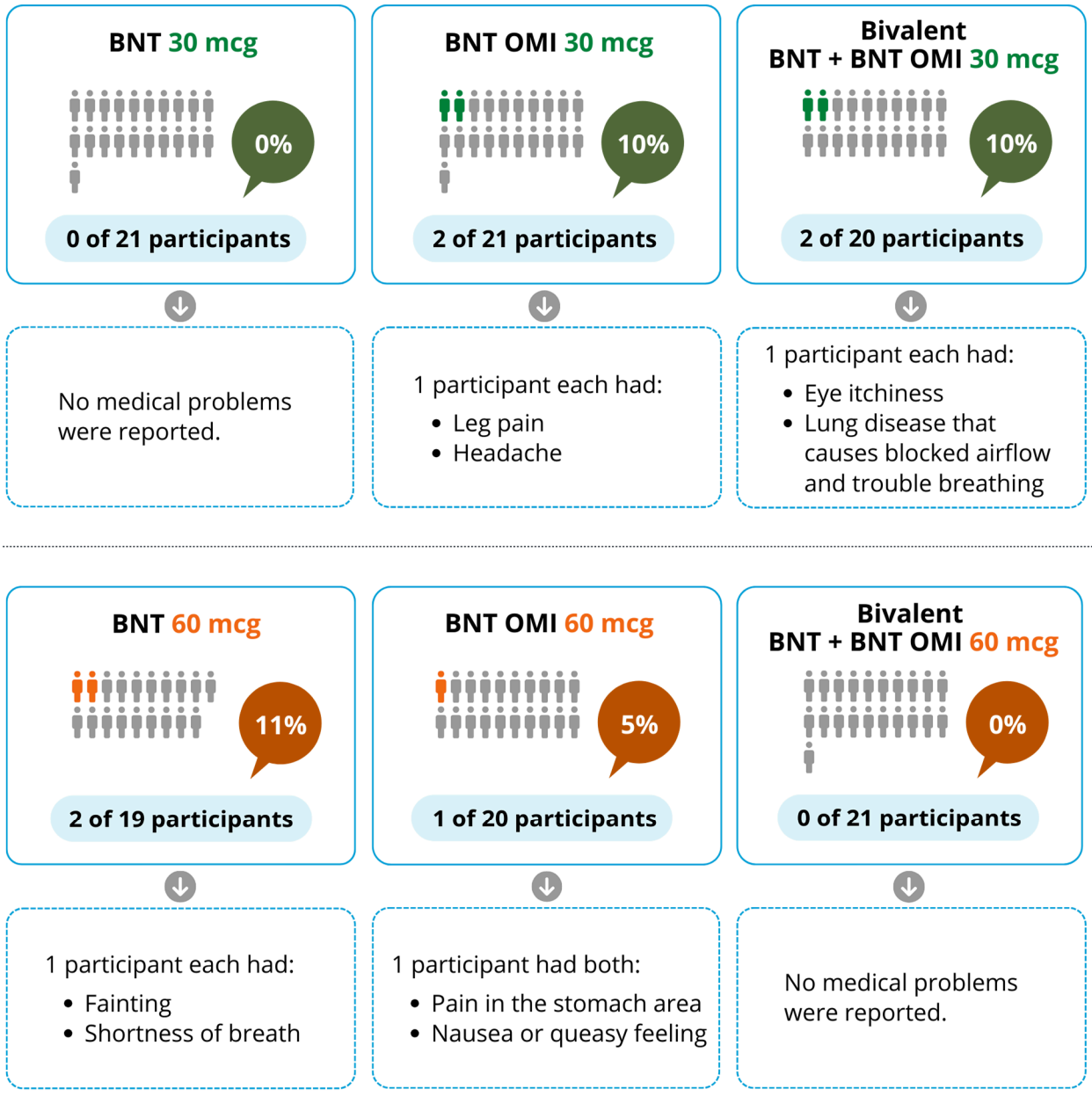
Overall, no participant left the study early because of a medical problem they had during the study.

How many participants had a medical problem within 1 month after the booster shot?

Within 1 month after the booster shot, no more than **11%** of participants in any of the vaccine groups had at least 1 medical problem.

Figure 4 below shows these results. It also lists all the medical problems reported by participants within 1 month after the booster shot.

Figure 4. How many participants had a medical problem within 1 month after the booster shot?



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 a serious medical problem within 6 months after the booster shot?

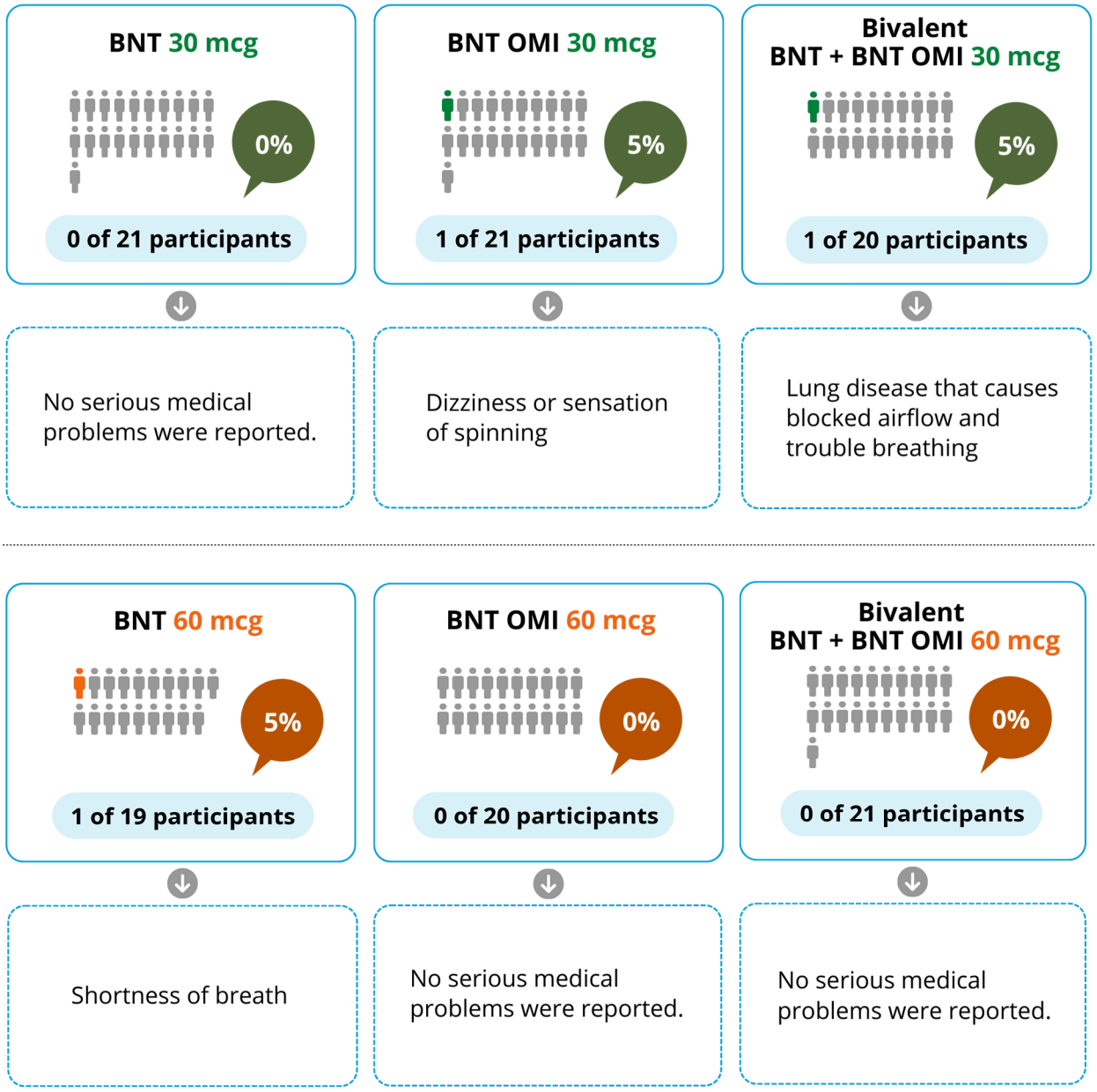
Within 6 months after the booster shot, no more than **5%** of participants in any of the vaccine groups had at least 1 serious medical problem.

Figure 5 below shows these results. It also lists all the serious medical problems reported by participants within 6 months after the booster shot.

Researchers do not believe that any of the serious medical problems seen in the participants were related to the COVID-19 vaccine given in this study.

No participant died during the study.

Figure 5. How many participants had a serious medical problem within 6 months after the booster shot?



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 **C4591031 SSF**

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

www.clinicaltrials.gov	Use the study identifier **NCT04955626**
www.clinicaltrialsregister.eu	Use the study identifier **2021-005197-25**

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

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