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:	Pfizer Inc.
Vaccine Studied:	RSV Subunit and Influenza modRNA Combination Vaccine (PF-07941314)
Protocol Number:	C5401001
Dates of Study:	09 March 2023 to 27 September 2023
Title of this Study:	A Study to Learn About Combination Vaccines Against Respiratory Syncytial Virus (RSV) and Influenza (Flu) in Older Adults [A Study to Evaluate the Safety, Tolerability, and Immunogenicity of Respiratory Combination Vaccine Candidates in Older Adults]
Date of this Report:	23 September 2024

– Thank You –

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

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

Why was this study done?

What are respiratory syncytial virus (RSV) and influenza (flu) illnesses?

The **RSV** and **flu viruses** are common viruses that cause infections of the respiratory tract (nose, throat, and lungs).

- RSV and flu illnesses may range from mild cold-like symptoms – runny nose, sore throat, cough, fever, body aches, or tiredness – to a severe respiratory tract infection such as pneumonia.
- Older adults are more likely to develop severe RSV or flu illnesses, which may lead to hospitalization or death.

What are RSV prefusion F (RSVpreF) subunit vaccine and influenza modified RNA (flu modRNA) vaccine?

A **vaccine** can help the body's defense system (immune system) to fight off a virus and prevent an infection or disease.

A **modified RNA vaccine** can help the body to make a protein that the immune system can recognize and use to fight off a virus.

The injectable vaccines given in this study are described below.

RSV prefusion F (RSVpreF) subunit vaccine

RSVpreF vaccine (also known as Abrysvo®) is designed to protect against 2 different types (or strains) of the RSV virus. These 2 strains are called RSV A and RSV B.

During this study, health authorities in Argentina (where this study was done) and other countries approved RSVpreF vaccine for use in adults 60 years of age and older to protect against RSV illness. RSVpreF vaccine was also approved for use in pregnant people to prevent RSV illness in their babies from birth to 6 months of age.

Influenza Modified RNA (flu modRNA) vaccine

The **flu modRNA** vaccine is also called **q**uadrivalent **i**nfluenza **R**NA **v**accine (**qIRV**). A **quadrivalent** vaccine can target 4 strains of a virus. The flu modRNA is designed to protect against 4 different strains of flu viruses. These include:

- 2 types of influenza A strains (H1N1 and H3N2), and
- 2 types of influenza B strains (B strain 1 and B strain 2).

The use of flu modRNA vaccine in this study was investigational, which means it was not approved for use outside of research studies.

Health authorities from different countries recommend people get a **flu vaccine** every year. Flu viruses constantly change (mutate), which leads to new strains of the flu virus. Each year before flu season starts, scientists check which flu strains are spreading at the time and update flu vaccines that can protect against these most common flu strains.

RSVpreF and flu modRNA combination vaccine

This combination vaccine is **RSVpreF** vaccine plus **flu modRNA** vaccine given as 1 shot. The **RSVpreF and flu modRNA combination vaccine** is designed to protect against the virus strains listed below:

- 2 RSV virus strains: RSV A and RSV B strains
- 4 flu virus strains: 2 A strains (H1N1 and H3N2) and 2 B strains

The RSVpreF and flu modRNA combination vaccine was studied to find out if it can help protect against RSV and flu illnesses.

The RSV and flu viruses can spread (circulate) at the same place and time, and they tend to spread more easily in the fall and winter months. Because the RSV and flu viruses often circulate at the same time, it might be possible in the future to schedule the RSV and flu vaccinations at the same time of the year. Combining the 2 vaccines (RSV and flu) into a single shot would need fewer injections compared to giving the 2 vaccines separately.

In this study, researchers tested different vaccines in 2 parts:

- In **Substudy A**, the **RSVpreF and flu modRNA combination** vaccine given as 1 shot was compared with **flu modRNA** vaccine (1 shot) and **RSVpreF** vaccine (1 shot) given **separately** about 1 month apart.
- In **Substudy B**, 2 different formulations (mixtures) of **RSVpreF and flu modRNA combination** vaccine were compared.

In this study, both ways of giving **RSVpreF** vaccine and **flu modRNA** vaccine (combined or separately) were **investigational**, which means they were not approved for use outside of research studies.

In this summary:

- The **RSVpreF vaccine** is called **"RSV shot"**.
- The **flu modRNA vaccine** is called **"flu shot"**.
- The combination of **RSVpreF vaccine** plus **flu modRNA vaccine** given together as a single shot is called **"RSV + flu shot"**.

What was the purpose of this study?

- The main goal of **Substudy A** was to find out if the **RSV + flu shot** combination is safe and can help to protect against RSV and flu viruses, similar to when the **flu shot** and **RSV shot** are given separately.
- The main goal of **Substudy B** was to find out if 2 different mixtures of the **RSV + flu shot** combination are safe.

To find out if the study vaccines are safe, researchers checked the participants' health during Substudy A and Substudy B. Researchers asked participants to report any local or systemic reactions within 7 days after vaccination and any other health problems throughout the study.

- **Local reactions** can happen in the area on the arm where the vaccine was injected (injection site).
- **Systemic reactions** are symptoms that involve the whole body or parts of the body other than the injection site.

Researchers wanted to know:

- **Can the RSV + flu shot combination help to protect against RSV and flu illnesses as well as when the flu shot and RSV shot are given separately? (**Substudy A only)
- **How many participants had local or systemic reactions within 7 days after vaccination?** (Substudies A and B)
- **How many participants had medical problems within 1 month after vaccination?** (Substudies A and B)
- **How many participants had serious medical problems during the study?** (Substudies A and B)

What happened during the study?

How was the study done?

Participants joined 1 of 2 parts: Substudy A or Substudy B.

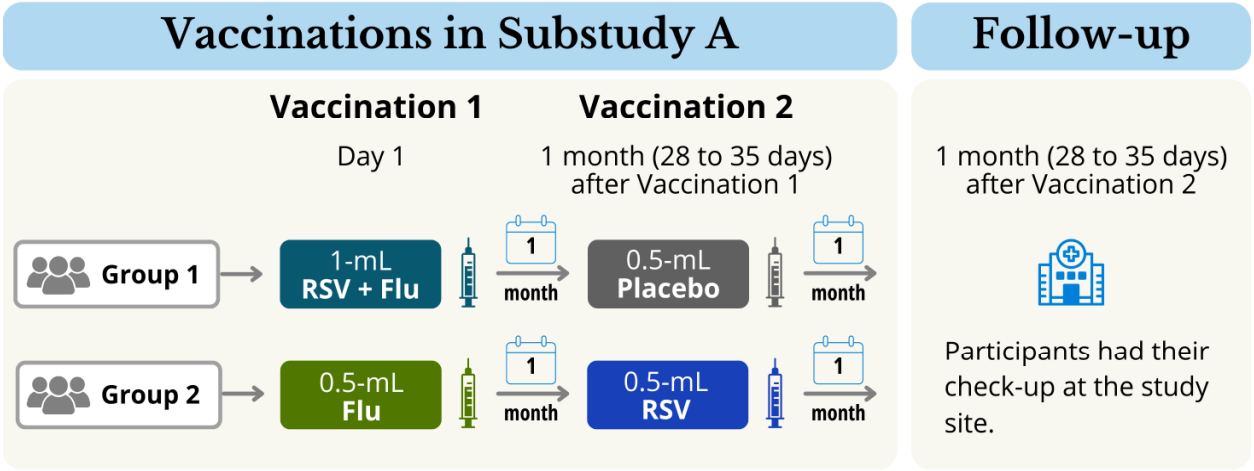
Substudy A:

Researchers used a computer program to randomly assign participants to 1 of 2 groups (by chance).

- **Group 1:** Participants got the **RSV + flu shot** as Vaccination 1 on Day 1. About 1 month later, they got a **placebo shot** as Vaccination 2. A **placebo** does not have active ingredients in it and will cause no effect.
- **Group 2:** Participants got the **flu shot** as Vaccination 1 on Day 1. About 1 month later, they got the **RSV shot** as Vaccination 2.

All participants in Substudy A had a follow-up visit about 1 month after Vaccination 2. Figure 1 below shows what happened in Substudy A.

Figure 1. What happened in Substudy A?



In the figure above, **mL** means milliliter.

Substudy B:

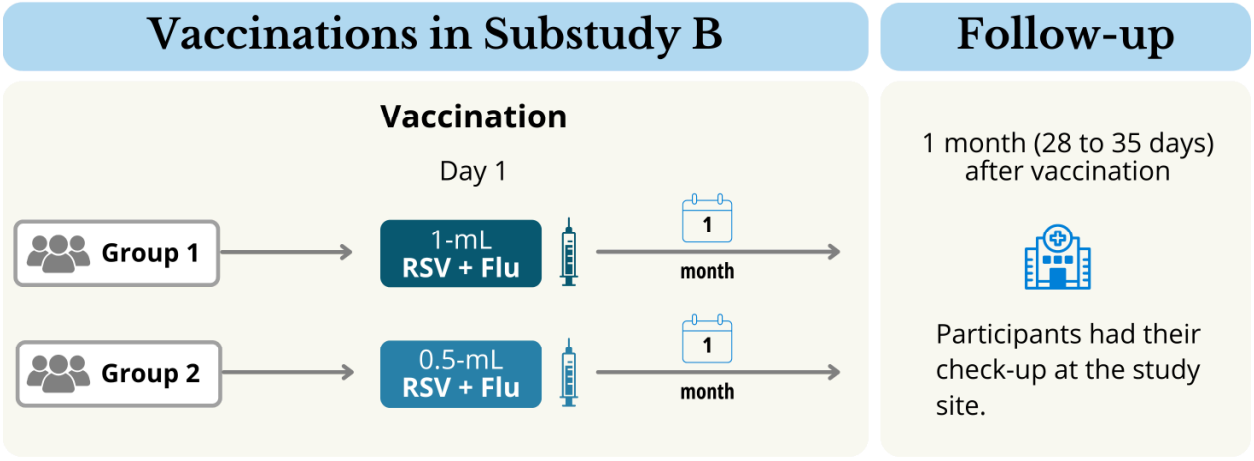
Researchers used a computer program to randomly assign participants to 1 of 2 groups (by chance).

- **Group 1:** Participants got the **1-mL** mixture of **RSV + flu shot** on Day 1. This was the same **RSV + flu shot** combination given to Group 1 participants in Substudy A.
- **Group 2:** Participants got the **0.5-mL** mixture of **RSV + flu shot** on Day 1.

Both the 1-mL and 0.5-mL mixtures had the same amount of RSV shot and flu shot. The only difference was that the 1-mL mixture given to Group 1 also had sterile water. This means that the 1-mL mixture given to Group 1 was less concentrated compared to the 0.5-mL mixture given to Group 2.

Researchers checked the safety of the first few participants in each group before more participants in each group were vaccinated in Substudy B. All participants in Substudy B had a follow-up visit about 1 month after vaccination. Figure 2 below shows what happened in Substudy B.

Figure 2. What happened in Substudy B?



In the figure above, **mL** means milliliter.

During Substudy A and Substudy B:

Researchers took samples of blood from participants for testing. Throughout the study, researchers also checked the participants' health and asked them how they were feeling. Participants also had an electrocardiogram (ECG) test, which looks at the electrical activity in the heart.

Both substudies were **observer-blinded**. This means only the healthcare staff who gave the injections knew which group the participants were in. The participants and researchers did not know which group the participants were in.

Where did this study take place?

The Sponsor ran Substudy A and Substudy B at 1 location in Argentina.

When did this study take place?

Substudy A began on 09 March 2023 and ended on 20 July 2023.

Substudy B began on 19 July 2023 and ended on 27 September 2023.

Who participated in this study?

The study included healthy adults who met the requirements, such as:

- **Substudy A:** They must be 60 years of age or older.
- **Substudy B:** They must be 50 years of age or older.

They must not have received any RSV vaccine at any time before joining this study. They must not have received any flu vaccine within 4 months (Substudy A) to 6 months (Substudy B) before joining this study.

Substudy A:

In total, 251 participants started Substudy A.

- A total of 116 men (46.2%) and 135 women (53.8%) participated.
- Participants were between the ages of 60 and 86 years.

Out of the 251 participants, all (100%) received Vaccination 1 and 237 (94.4%) received Vaccination 2 in this study.

A total of 233 out of 251 participants (92.8%) finished the study. A total of 18 out of 251 participants (7.2%) did not finish the study after Vaccination 1 or Vaccination 2, with the most common reason being that participants chose to leave the study before it was over.

Substudy B:

In total, 204 participants started Substudy B.

- A total of 108 men (53.2%) and 95 women (46.8%) participated.
- Participants were between the ages of 50 and 87 years.

Out of the 204 participants, 203 (99.5%) received their vaccination in this study. A total of 201 out of 203 participants (98.5%) finished the study. A total of 2 out of 203 participants (1.0%) did not finish the study after their vaccination because they did not want to undergo the study procedures, or they were no longer available to do so.

How long did the study last?

For Substudy A, each participant was in the study for about 2 months. For Substudy B, each participant was in the study for about 1 month. The entire study took about 6 months to complete.

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

What were the results of the study?

Can the RSV + flu shot combination help to protect against RSV and flu illnesses as well as when the flu shot and RSV shot are given separately? (Substudy A only)

To answer this question, researchers measured the **Substudy A** participants' **antibody levels** against the RSV and flu viruses.

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

Antibody levels against the RSV and flu virus strains that are being targeted by the study vaccines were measured **before** and 1 month **after** each vaccination in Substudy A.

- 2 **RSV virus strains:** RSV A and RSV B strains
- 4 **flu virus strains:** 2 A strains (H1N1 and H3N2) and 2 B strains

Researchers then compared the **antibody levels** of participants in **Group 1** (given **RSV + flu shot** combination) with the antibody levels of participants in **Group 2** (given **flu shot** and **RSV shot** separately 1 month apart).

One (1) month after each vaccination in **Substudy A**, the RSV and flu virus **antibody levels** of participants given **RSV + flu shot** combination were found to be **not different** or **not worse than** those seen in participants given **flu shot** and **RSV shot** separately.

This means that the **RSV + flu shot** given as a combination may produce immune responses to help protect healthy adults 60 years of age and older against RSV and flu illnesses **as well as** when the **flu shot** and **RSV shot** are given separately (1 month apart).

How many participants had local or systemic reactions within 7 days after vaccination?

(Substudies A and B)

Participants recorded on their electronic diary or app in their phone if they had these reactions within 7 days after vaccination.

- **Local reactions:** Redness, swelling, or pain at the injection site
- **Systemic reactions:** Fever, tiredness, headache, vomiting, nausea, diarrhea, chills, muscle pain, or joint pain

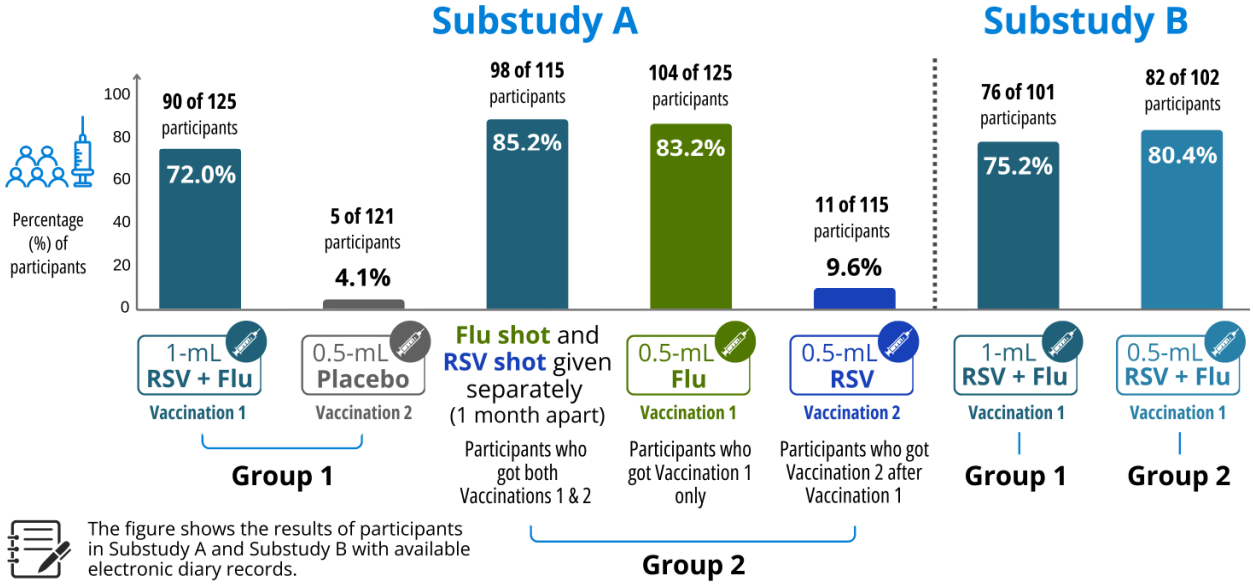
Local reactions:

Substudy A:

The left side of Figure 3 below shows how many participants in Substudy A had any local reactions within 7 days after each vaccination.

- The percentage of participants in **Group 1** with any local reactions after their **RSV + flu shot** combination (72.0%) was lower than that of participants in **Group 2** who got both vaccinations (**flu shot** and **RSV shot**) given separately (85.2%).
- The percentage of participants in **Group 1** with any local reactions after their **RSV + flu shot** combination (72.0%) was lower than that of **Group 2** after their **flu shot** (83.2%) and higher than that of **Group 2** after their **RSV shot** (9.6%).
- The percentage of participants in **Group 1** with any local reactions after their **placebo shot** was 4.1%.

Figure 3. How many participants had any local reactions within 7 days after each vaccination?



Substudy B:

The right side of Figure 3 above shows how many participants in Substudy B had any local reactions within 7 days after vaccination.

- The percentage of participants in **Group 1** with any local reactions after their **1-mL RSV + flu shot** (75.2%) was lower than that of **Group 2** after their **0.5-mL RSV + flu shot** (80.4%).

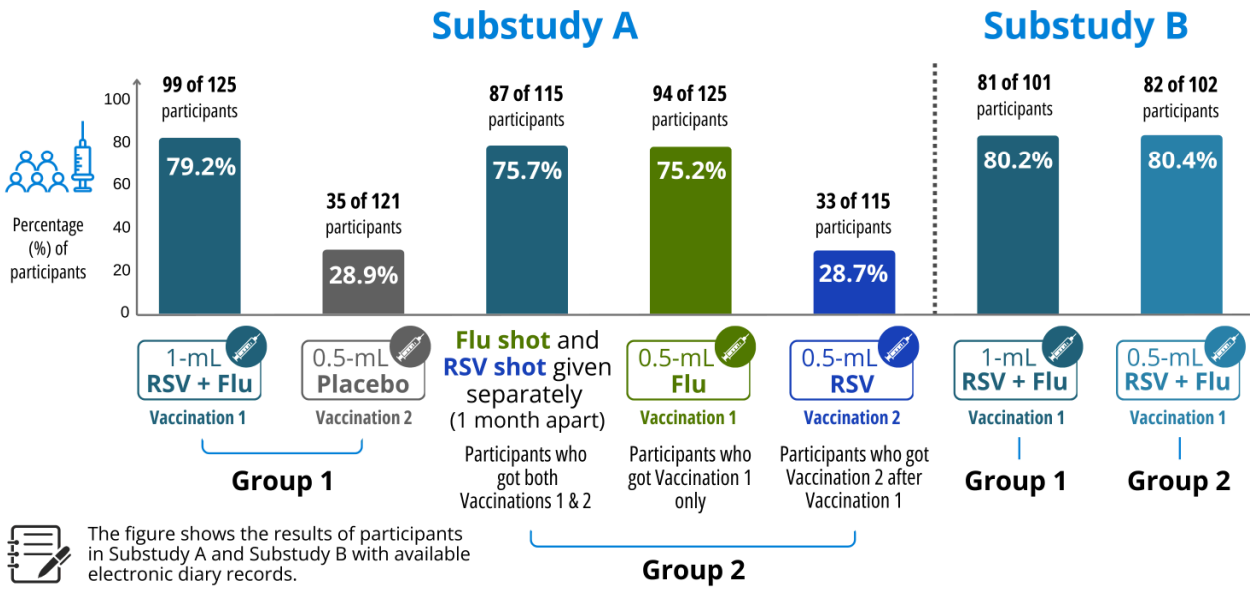
Systemic reactions:

Substudy A:

The left side of Figure 4 below shows how many participants in Substudy A had any systemic reactions within 7 days after each vaccination.

- The percentage of participants in **Group 1** with any systemic reactions after their **RSV + flu shot** combination (79.2%) was similar to that of participants in **Group 2** who got both vaccinations (**flu shot** and **RSV shot**) given separately (75.7%).
- The percentage of participants in **Group 1** with any systemic reactions after their **RSV + flu shot** combination (79.2%) was similar to that of **Group 2** after their **flu shot** (75.2%) and higher than that of **Group 2** after their **RSV shot** (28.7%).
- The percentage of participants in **Group 1** with any systemic reactions after their **placebo shot** was 28.9%.

Figure 4. How many participants had any systemic reactions within 7 days after each vaccination?



Substudy B:

The right side of Figure 4 above shows how many participants in Substudy B had any systemic reactions within 7 days after vaccination.

- The percentage of participants in **Group 1** with any systemic reactions after their **1-mL RSV + flu shot** (80.2%) was similar to that of **Group 2** after their **0.5-mL RSV + flu shot** (80.4%).

Substudy A and Substudy B:

Most of the **local reactions and systemic reactions** were mild or moderate in severity and lasted about 1 to 3 days.

The most common local reaction was **injection site pain**. The most common systemic reactions were **tiredness**, **muscle pain**, and **headache**.

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.

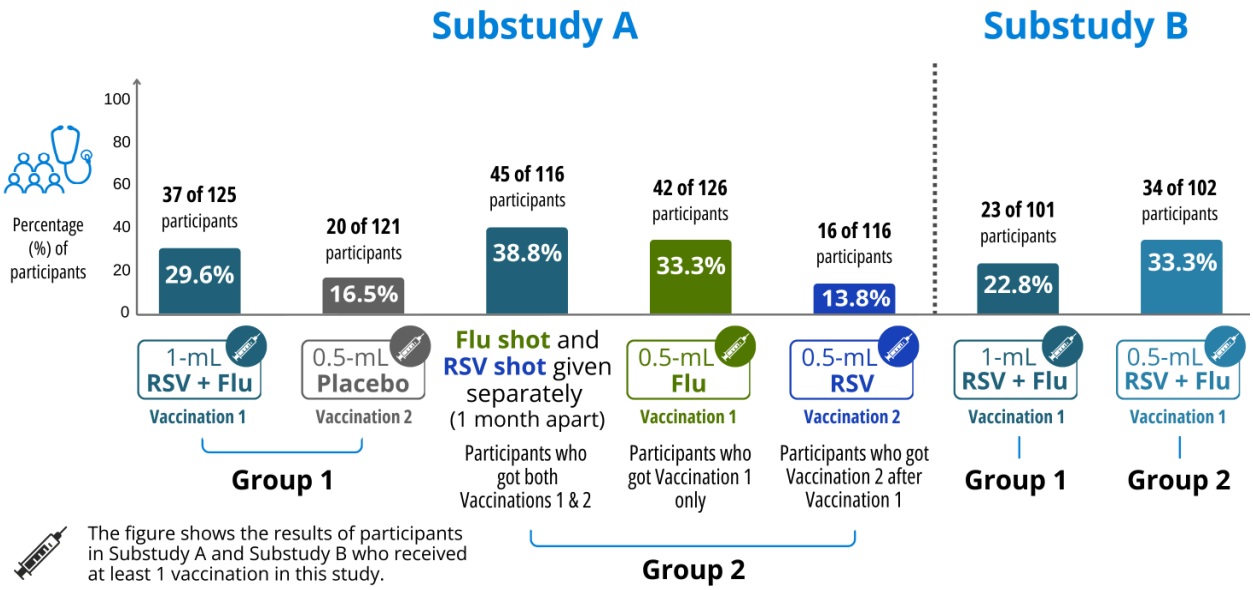
How many participants had medical problems within 1 month after vaccination? (Substudies A and B)

Substudy A:

The left side of Figure 5 below shows how many participants in Substudy A reported at least 1 medical problem within 1 month after each vaccination.

- The percentage of participants in **Group 1** with medical problems after their **RSV + flu shot** combination (29.6%) was lower than that of participants in **Group 2** who got both vaccinations (**flu shot** and **RSV shot**) given separately (38.8%).
- The percentage of participants in **Group 1** with medical problems after their **RSV + flu shot** combination (29.6%) was lower than that of **Group 2** after their **flu shot** (33.3%) and higher than that of **Group 2** after their **RSV shot** (13.8%).
- The percentage of participants in **Group 1** with medical problems after their **placebo shot** was 16.5%.

Figure 5. How many participants had at least 1 medical problem within 1 month after each vaccination?



In Substudy A, the most common medical problem within 1 month after each vaccination – reported by at least 10% of participants in either group – was a build-up of mucus (phlegm) in the airways (nose, sinuses, or throat). This medical problem was seen in:

- 15 out of 125 participants (12.0%) in **Group 1** after their **RSV + flu shot** and 6 out of 121 participants (5.0%) after their **placebo shot**.
- 14 out of 116 participants (12.1%) in **Group 2** after their **flu shot** and **RSV shot** given separately.

A total of 3 participants in Substudy A left the study because of a medical problem. Of these 3 participants:

- 1 participant in **Group 1** left the study because of asthma within 1 month after vaccination with the **RSV + flu shot** combination.
- 2 participants in **Group 2** left the study because of medical problems within 1 month after vaccination with the **flu shot** and did not receive the **RSV shot**. Of these 2 participants, 1 left the study because of an ECG finding of extra heartbeats that start in the lower chambers of the heart. The other participant left the study because of high blood pressure.

Researchers believe that these medical problems were not related to the study vaccine.

Substudy B:

The right side of Figure 5 above shows how many participants in Substudy B reported at least 1 medical problem within 1 month after vaccination.

- The percentage of participants in **Group 1** with medical problems after their **1-mL RSV + flu shot** (22.8%) was lower than that of **Group 2** after their **0.5-mL RSV + flu shot** (33.3%).

In Substudy B, the most common medical problems within 1 month after vaccination – those reported by more than 2% of participants in either group – are listed below.

- A build-up of mucus (phlegm) in the airways (nose, sinuses, or throat) was reported by:
    - 4 out of 101 participants (4.0%) in **Group 1** after their **1-mL RSV + flu shot**, and
    - 12 out of 102 participants (11.8%) in **Group 2** after their **0.5-mL RSV + flu shot**.
- Flu-like illness was reported by:
    - 2 out of 101 participants (2.0%) in **Group 1** after their **1-mL RSV + flu shot**, and
    - 9 out of 102 participants (8.8%) in **Group 2** after their **0.5-mL RSV + flu shot**.
- Chest pain was reported by:
    - 2 out of 101 participants (2.0%) in **Group 1** after their **1-mL RSV + flu shot**, and
    - 3 out of 102 participants (2.9%) in **Group 2** after their **0.5-mL RSV + flu shot**.

No participant in Substudy B left the study because of a medical problem within 1 month after vaccination with **1-mL** or **0.5-mL RSV + flu shot** combination.

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 during the study? (Substudies A and B)

Substudy A:

None of the 125 participants (0%) in **Group 1** had a serious medical problem or died during the study.

A total of 2 out of 116 participants (1.7%) in **Group 2** reported serious medical problems during the study. Of these 2 participants:

- 1 participant had a head injury and fainting 1 day after their **flu shot**.
- 1 participant had heart and lung failures 1 day after their **RSV shot**. The participant died from these serious medical problems.

After the 1-month follow-up visit, 1 participant reported serious medical problems. The participant had heart failure and blockage of the heart’s arteries due to a build-up of fatty deposits (plaque).

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

Substudy B:

A total of 2 out of 101 participants (2.0%) in **Group 1** reported serious medical problems within 1 month after vaccination with **1-mL RSV + flu shot** combination. Of these 2 participants:

- 1 participant had a heart attack.
- 1 participant had a brain bleed.

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

None of the 102 participants (0%) in **Group 2** had a serious medical problem within 1 month after vaccination with **0.5-mL RSV + flu shot** combination.

No participant in **Group 1** or **Group 2** died during the study.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C5401001**

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

www.clinicaltrials.gov	Use the study identifier **NCT05788237**

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