

# Real World Impact of COVID-19 Vaccines and Updates on Predominant SARS-CoV-2 Variant of Concern



**Chen Yi-ching M.D.**  
**Dept. of Pediatrics, Chang Gung Memorial Hospital**

# Outline



## **Omicron variant updates**

- Detection of the Omicron Variants**
- Reasons of rapid expansion**
- Decreased disease severity**

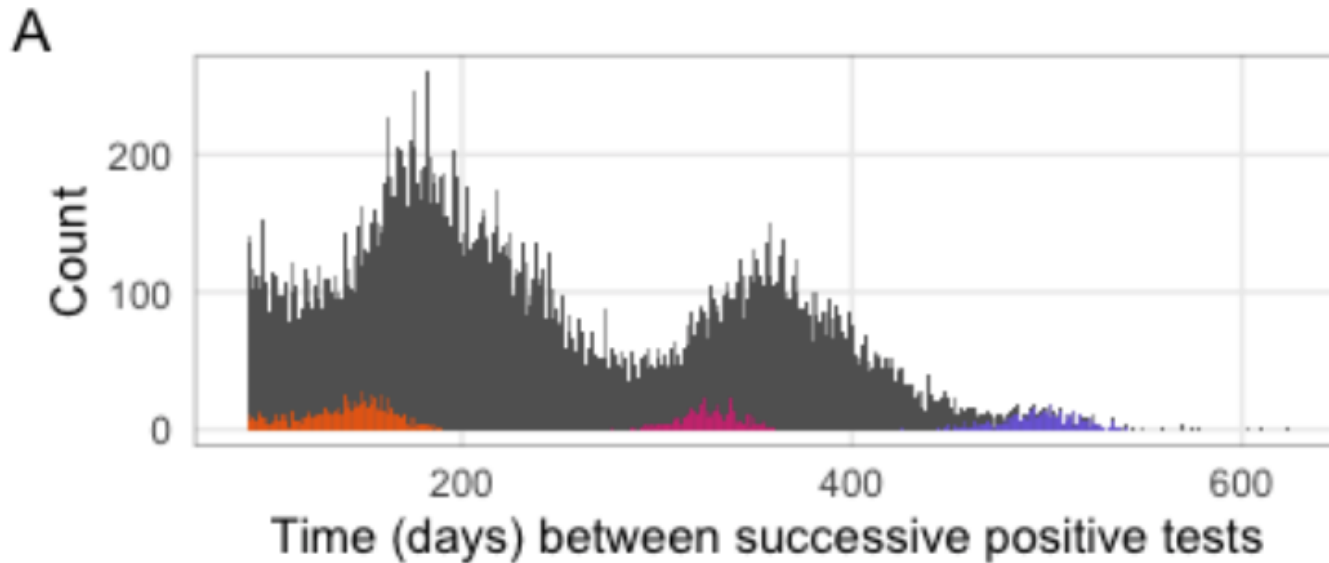


## **Introduction Vaccine Effectiveness**



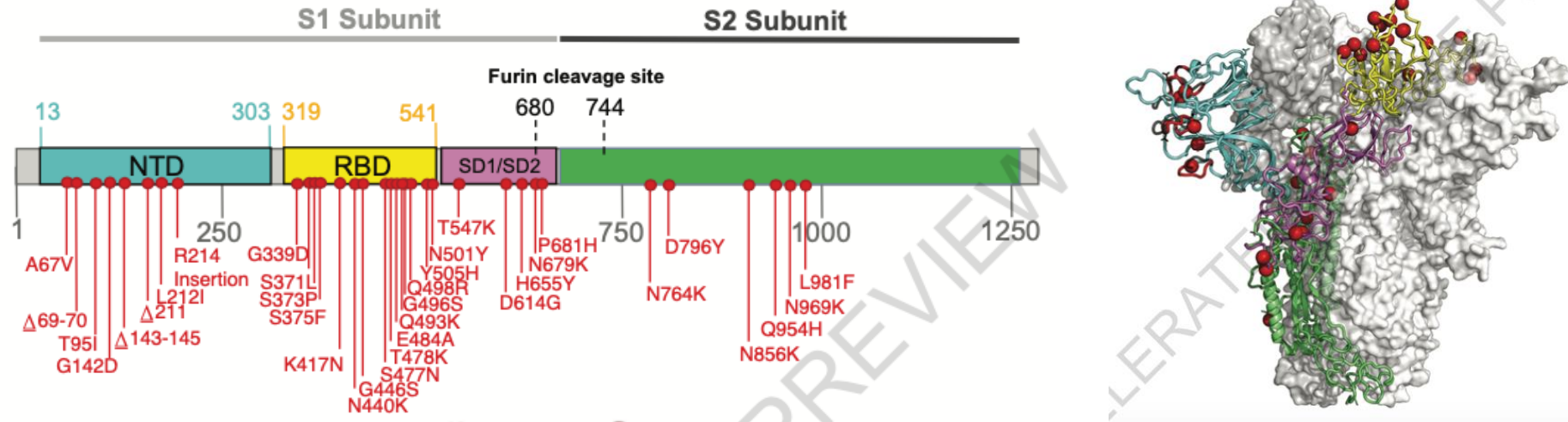
## **Benefits from the booster dose of COVID-19 vaccine**

# First Detection of Omicron Variant in Africa



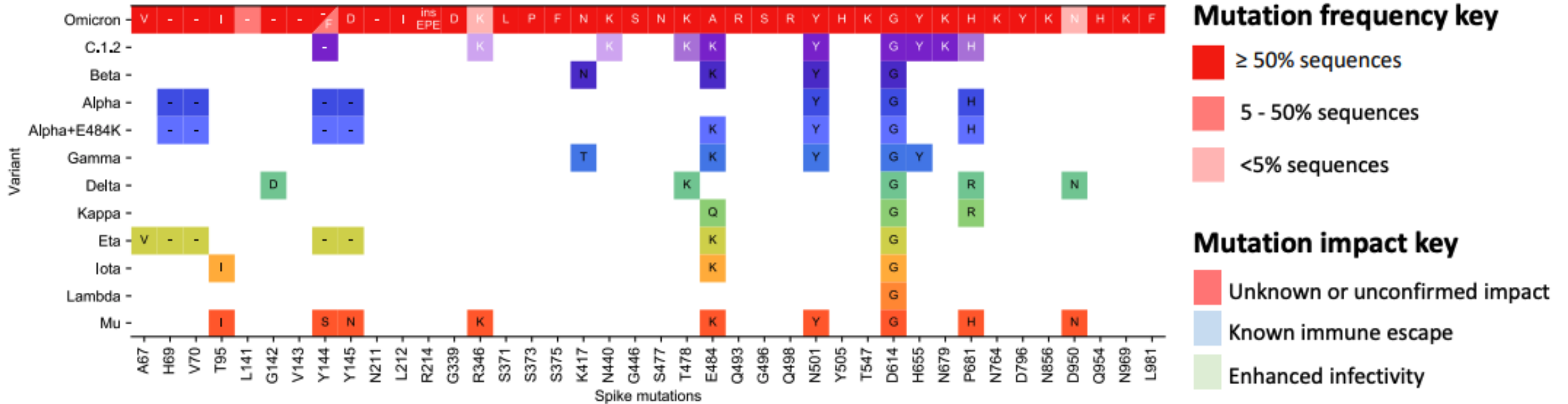
- B.1.1.529 was first detected in specimens collected on **November 11, 2021** in **Botswana** and on **November 14, 2021** in **South Africa**.
- On **November 24, 2021**, South Africa reported the identification of a new SARS-CoV-2 variant, B.1.1.529, to the World Health Organization (WHO).

# Omicron Mutation Lineage Profile



- 45-52 amino acid changes (including deletions) across the whole genome
  - **26-32** changes in **spike protein**, **15** amino acid substitution in **RBD**
- Key Amino Acid Substitutions in Spike Protein (RBD substitutions in bold type): A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, **G339D**, **S371L**, **S373P**, **S375F**, **K417N**, **N440K**, **G446S**, **S477N**, **T478K**, **E484A**, **Q493R**, **G496S**, **Q498R**, **N501Y**, **Y505H**, **T547K**, **D614G**, **H655Y**, **N679K**, **P681H**, **N764K**, **D796Y**, **N856K**, **Q954H**, **N969K**, **L981F**
  - Does not possess the RdRp G671S change
    - Associated with a decreased in Ct value for Delta variants
  - Does possess the 69-70del
    - Causing the S-gene Target Failure (SGTF) and was previously seen in the Alpha VOC

# Omicron Spike Mutations Compared to other VOC/VOIs



- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked to immune escape

# Reasons for Omicron Rapid Spreading

- Increases in infections are most likely due to a combination of two factors:
  - Increased transmissibility**
  - The ability of the variant to evade immunity conferred by past infection or vaccination (e.g. **immune evasion**).

Scenario*	Inherent transmissibility relative to Delta	Immune escape relative to all prior strains
Faster growth (Higher transmission**. Mid escape)	1.6x	43%
Slower growth (Higher transmission. Low escape)	1.5x	10%
Faster growth (Unchanged transmission. High escape)	1.0x	85%
Slower growth (Lower transmission. Mid escape)	0.8x	50%

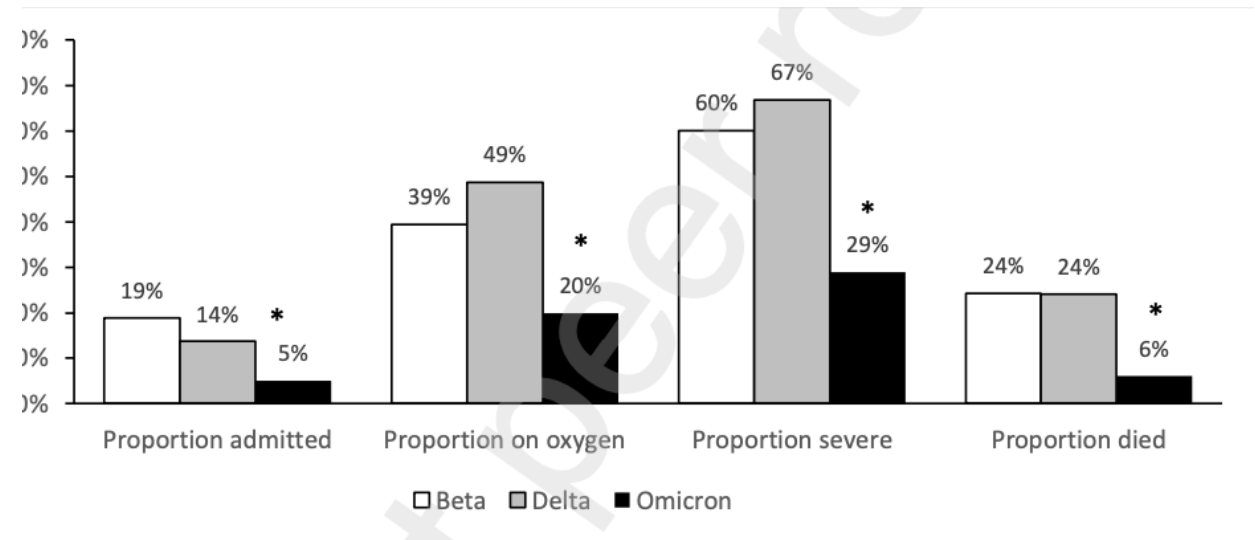
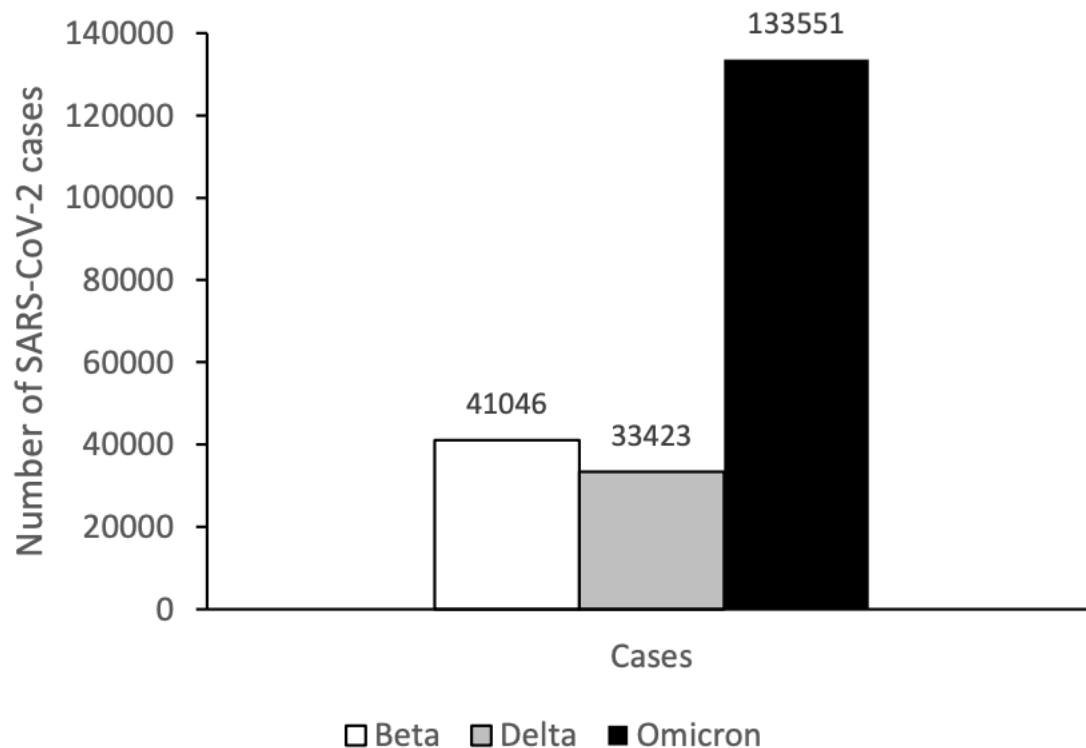
# Potential Impact of Rapid Increasing Cases

- Even if the proportion of infections associated with severe outcomes is lower than with previous variants, given the likely increase in number of infections, **the absolute numbers of people with severe outcomes could be substantial.**
- In addition, demand for ambulatory care, supportive care for treatment of mild cases, and infection control requirements, quarantining/isolation of exposed/infected workforce could also **stress the healthcare system.**
- These stresses likely will be in addition to the ongoing Delta variant infections and a rising burden of illness caused by other respiratory pathogens, such as influenza, which have begun circulating at greater frequencies



# Clinical Severity of Omicron Infection – South Africa

- In South Africa, patients admitted during the Omicron wave were **73% less** likely to have severe disease than those admitted during the Delta wave.
- Hospitalization rates for persons infected with Omicron:
  - 0.4% England, 0.6% Denmark





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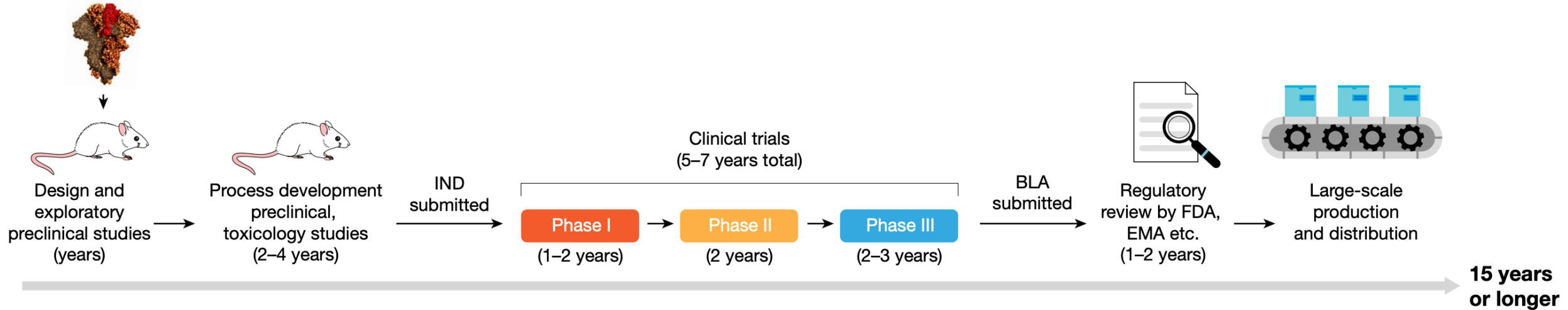
## **Introduction Vaccine Effectiveness**



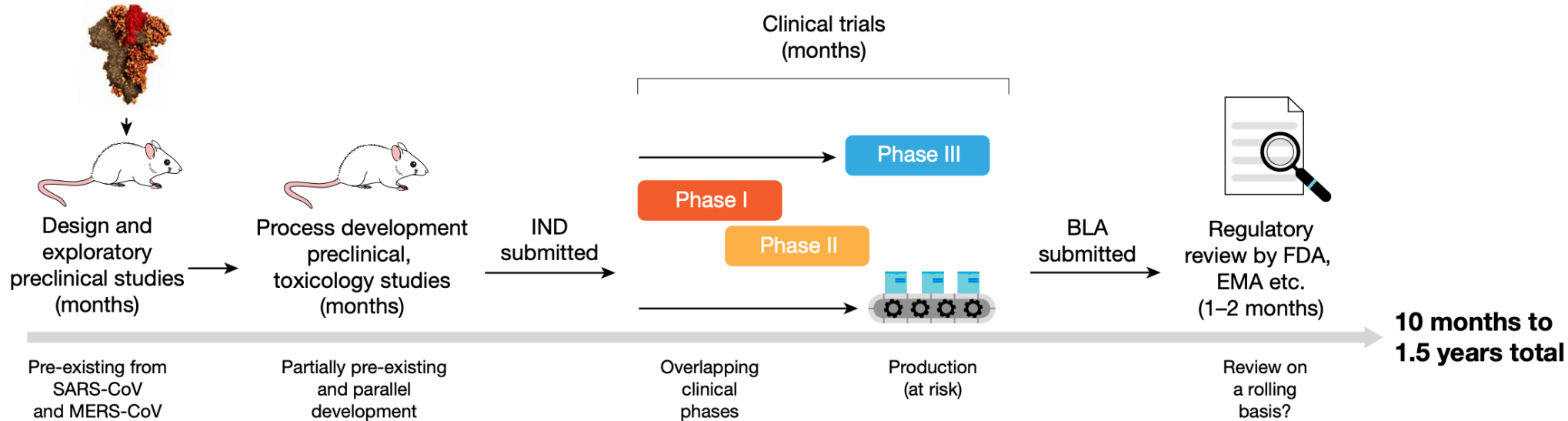
## **Benefits from the booster dose of COVID-19 vaccine**

# Traditional and accelerated vaccine-development pipelines

## Traditional development



## SARS-CoV-2 vaccine development



# How a new vaccine is developed, approved and manufactured

The Food and Drug Administration (FDA) sets rules for the three phases of clinical trials to ensure the safety of the volunteers. Researchers test vaccines with adults first.

## PHASE 1



**20-100  
healthy volunteers**



- Is this vaccine safe?
- Does this vaccine seem to work?
- Are there any serious side effects?
- How is the size of the dose related to side effects?

## PHASE 2



**several hundred  
volunteers**

- What are the most common short-term side effects?
- How are the volunteers' immune systems responding to the vaccine?

## PHASE 3



**hundreds or thousands  
of volunteers**

- How do people who get the vaccine and people who do not get the vaccine compare?
- Is the vaccine safe?
- Is the vaccine effective?
- What are the most common side effects?

**FDA licenses the vaccine only if:**

- It's safe and effective
- Benefits outweigh risks

Vaccines are made in batches called lots.



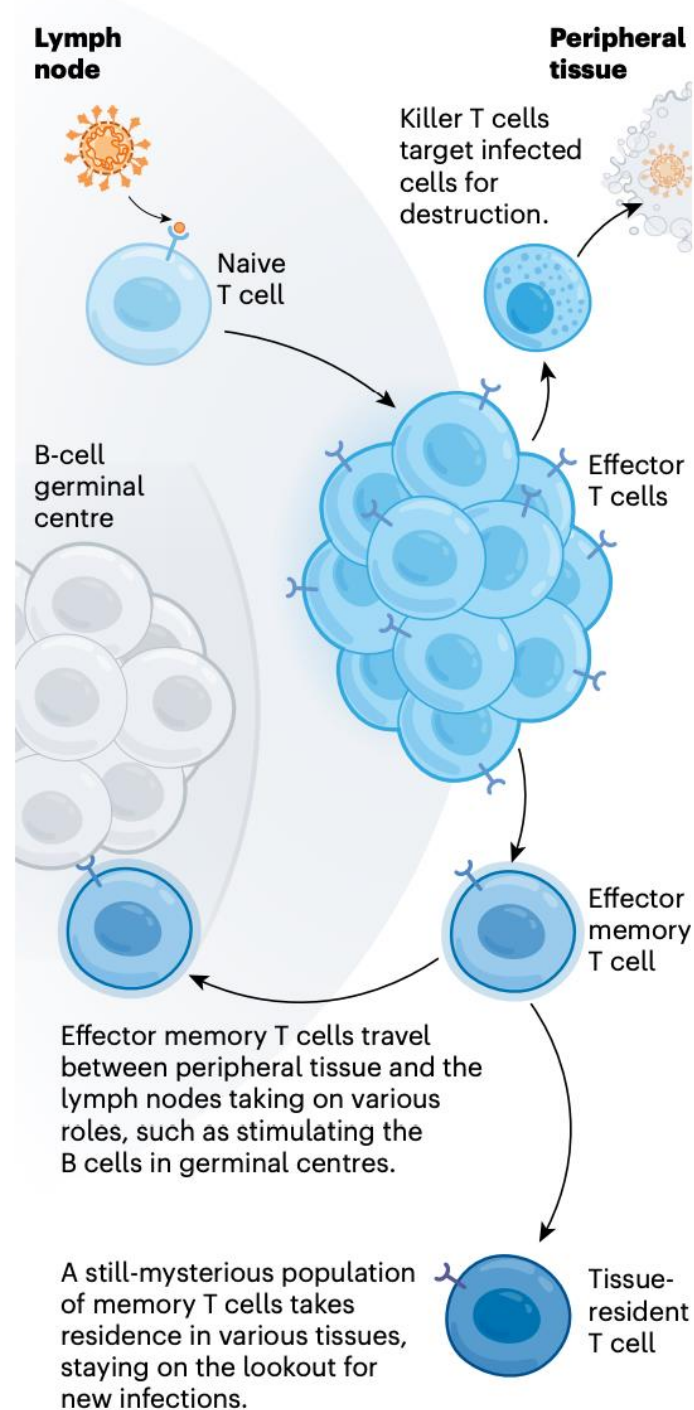
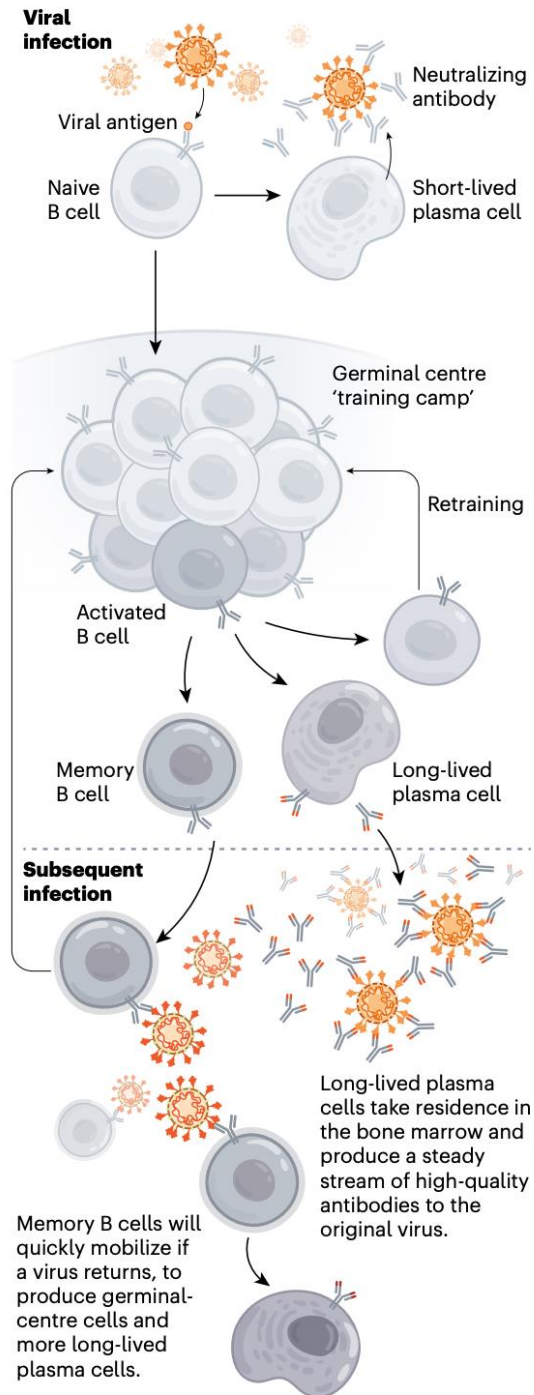
Manufacturers must test all lots to make sure they are safe, pure and potent. The lots can only be released once FDA reviews their safety and quality.

The FDA inspects manufacturing facilities regularly to ensure quality and safety.



**FOR MORE INFORMATION, VISIT [HTTPS://WWW.FDA.GOV/CBER](https://www.fda.gov/cber)**

# B cell immunity



# T cell immunity

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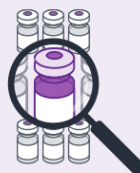
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# Vaccine Efficacy and Vaccine Effectiveness



## Vaccine efficacy

refers to how the vaccine performs in ideal conditions  
– controlled clinical trials.



## Vaccine effectiveness

refers to how the vaccine performs in the wider populations.

### 三、第三期臨床試驗的結果

#### mRNA-1273疫苗：

mRNA-1273疫苗由美國莫德納公司開發，第三期臨床試驗是從2020年7月27日開始收案，同步在美國多家醫學中心進行。有安慰劑對照組、雙盲的臨床試驗。收案對象是18歲以上成人，以28天的間隔接受兩劑安慰劑或疫苗。到2020年11月25日，大約是臨床試驗開始後4個月進行期中分析時，總共有30,420位受試者進行隨機分組，疫苗組與安慰劑組各15,210人。分析結果發表在2020年12月底《新英格蘭醫學期刊》<sup>[1]</sup>。有下面幾項重點：

1. 對有症狀的感染**保護力**：接種一劑疫苗14天後的保護力是92.1%。接種完二劑疫苗14天後的保護力達到94.1%。
2. 對重症的保護力：30個重症包括一個死亡病例全部都出現在安慰劑組，而接種二劑疫苗的受試者沒有任何重症病例，因此對重症的保護力達到100%。



# 與第三期臨床試驗相符！以色列大型實測：輝瑞疫苗打兩劑保護力達94%

文 / 中央社

2021-02-25

瀏覽數 35,200+

# Vaccine Efficacy and Vaccine Effectiveness



## Vaccine efficacy

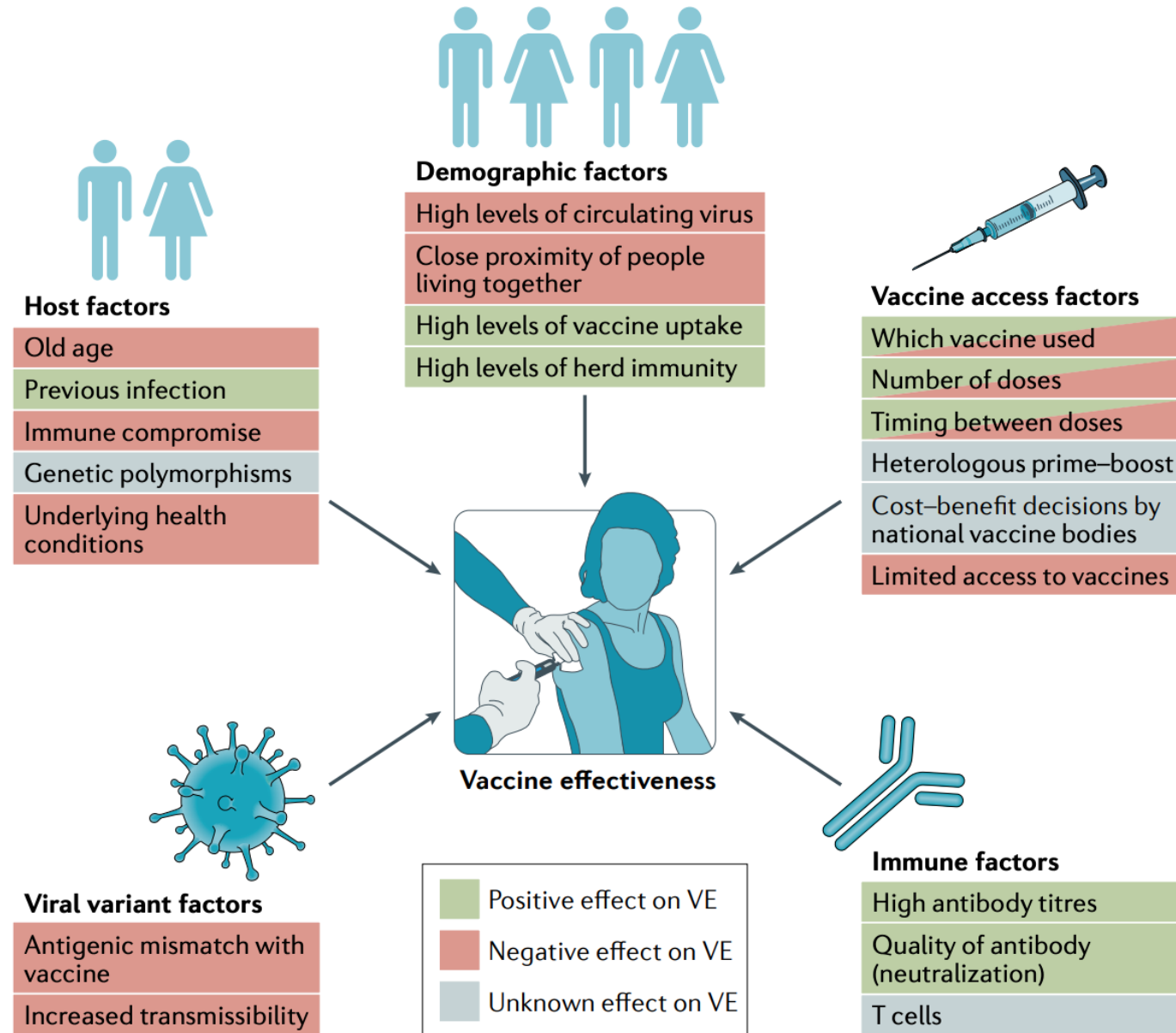
refers to how the vaccine performs in ideal conditions  
– controlled clinical trials.



## Vaccine effectiveness

refers to how the vaccine performs in the wider populations.

# Factors influencing vaccine effectiveness



**Safety**



**Immunogenicity**



**Efficacy**

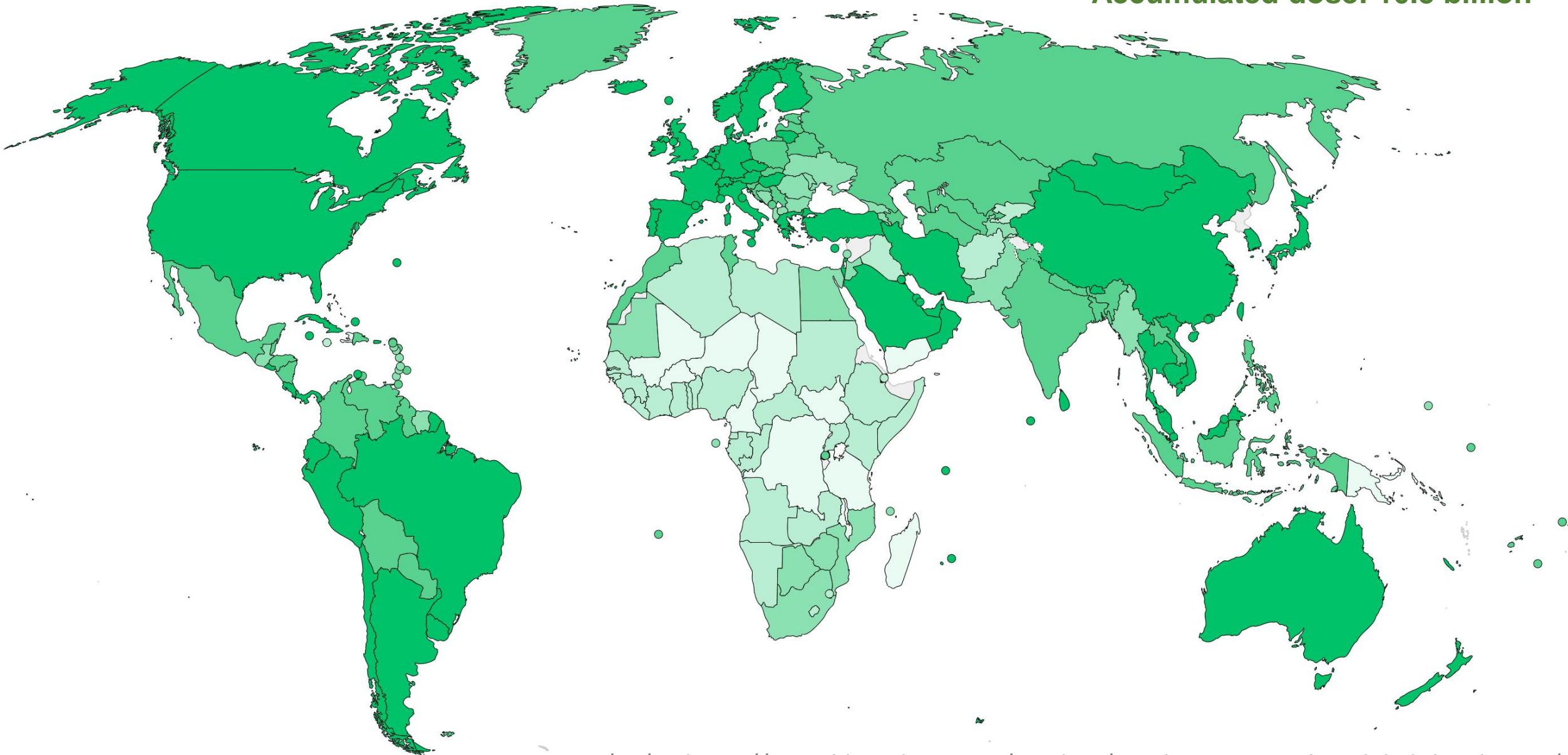


**Effectiveness**

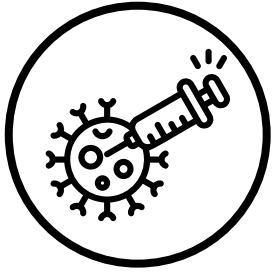
# World Map of COVID-19 Vaccine

no data 10 50 100 150 doses per 100 people

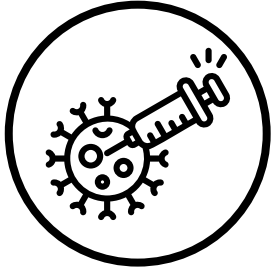
Accumulated dose: 10.5 billion



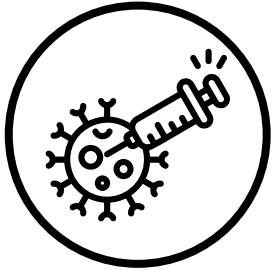
# Key Factor of COVID-19 Vaccine



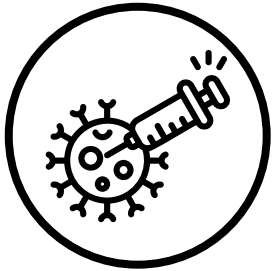
**Safe and effective**



**Prevent people getting sick or severely ill**

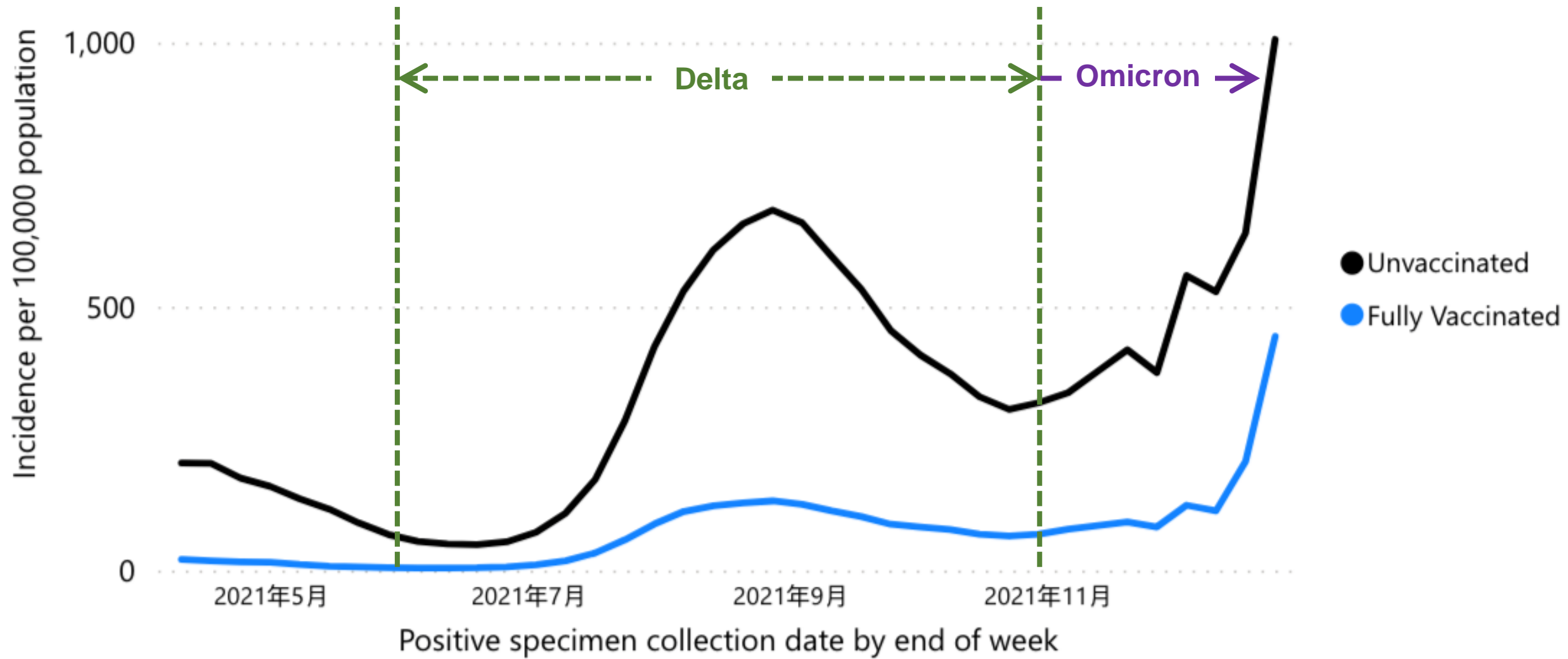


**Protect people around you**



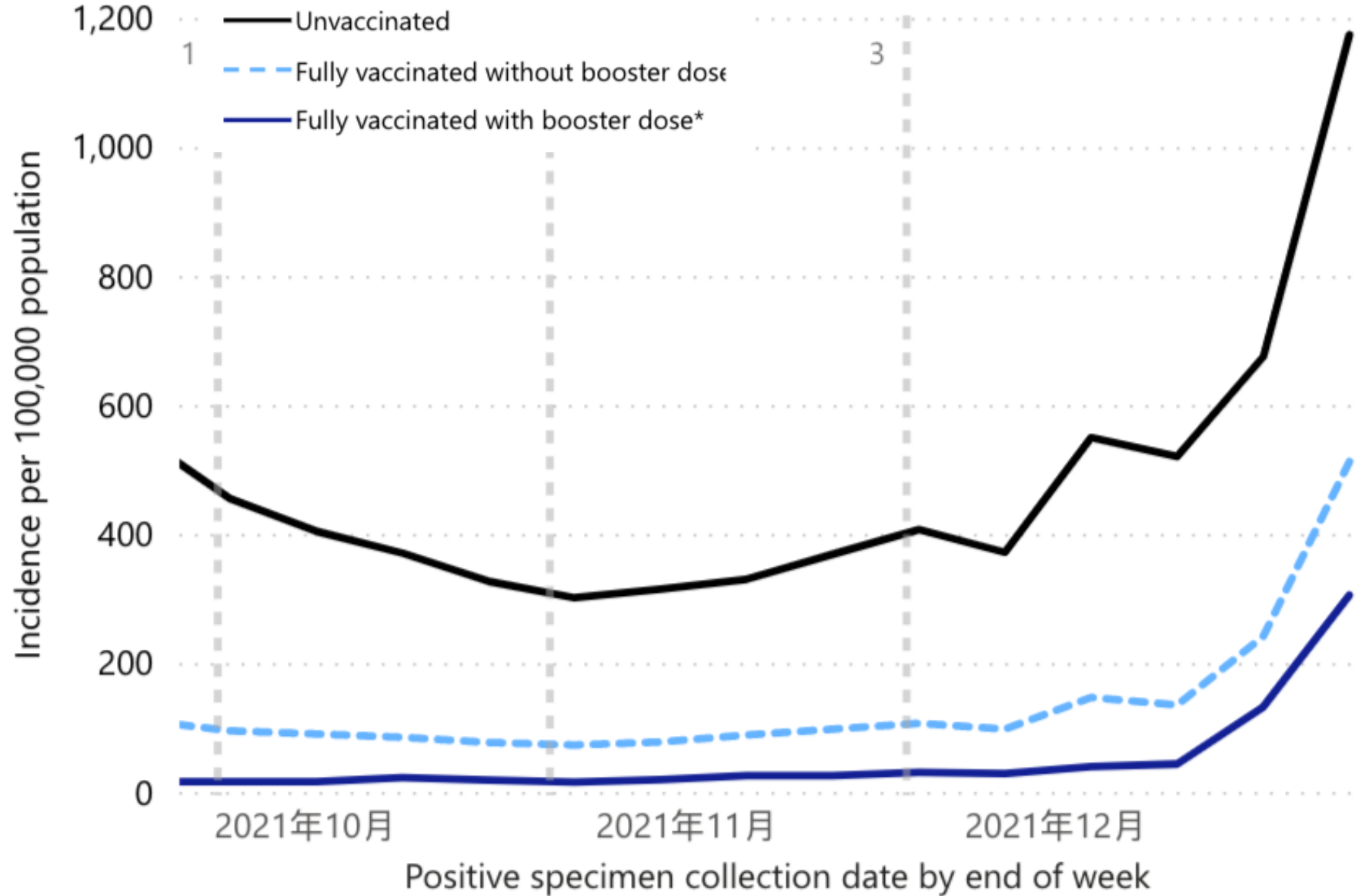
**No vaccine is 100% effective  
(breakthrough infection)**

# COVID-19 Incidence Rate by Vaccination Status, USA



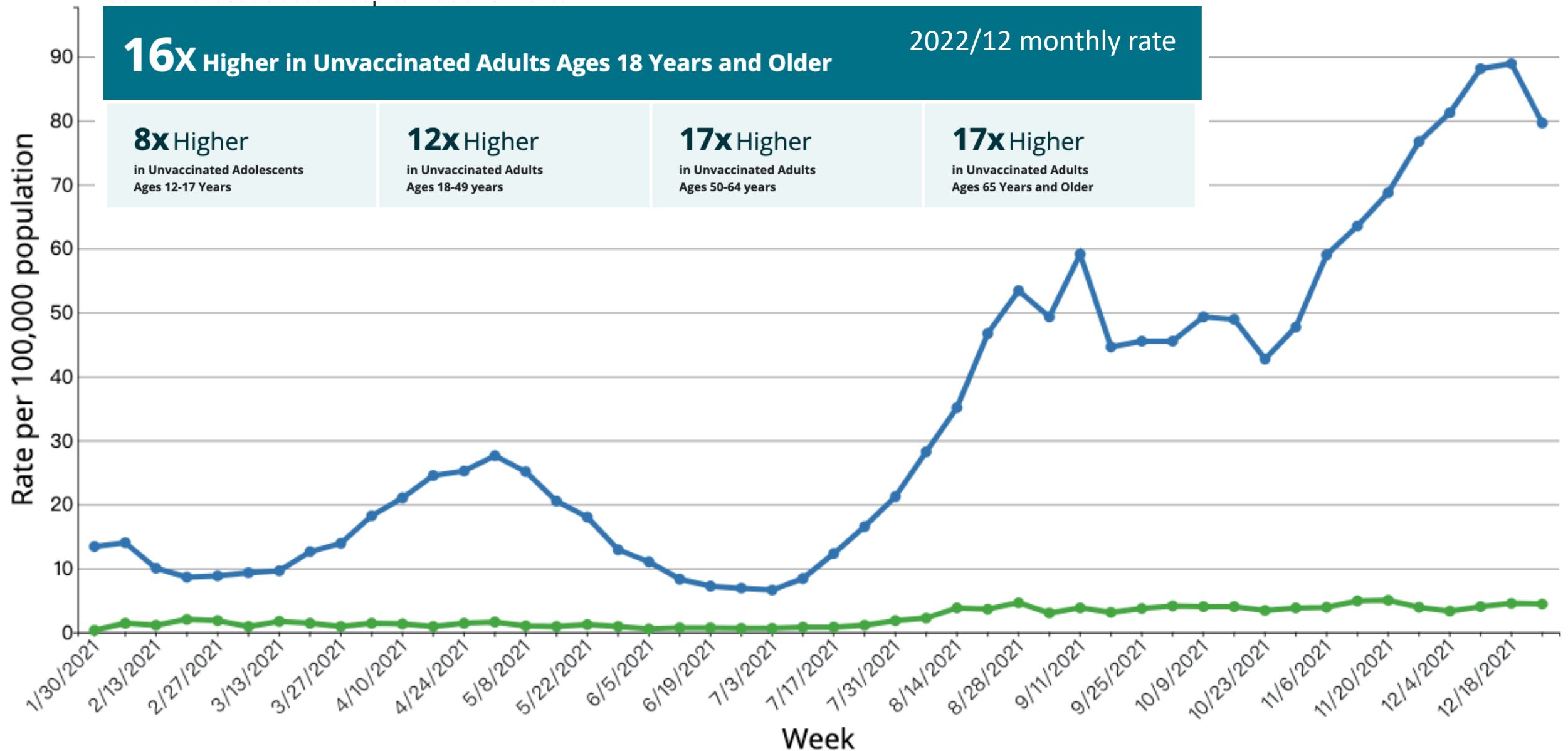


# COVID-19 Incidence Rate by Vaccination Status, USA

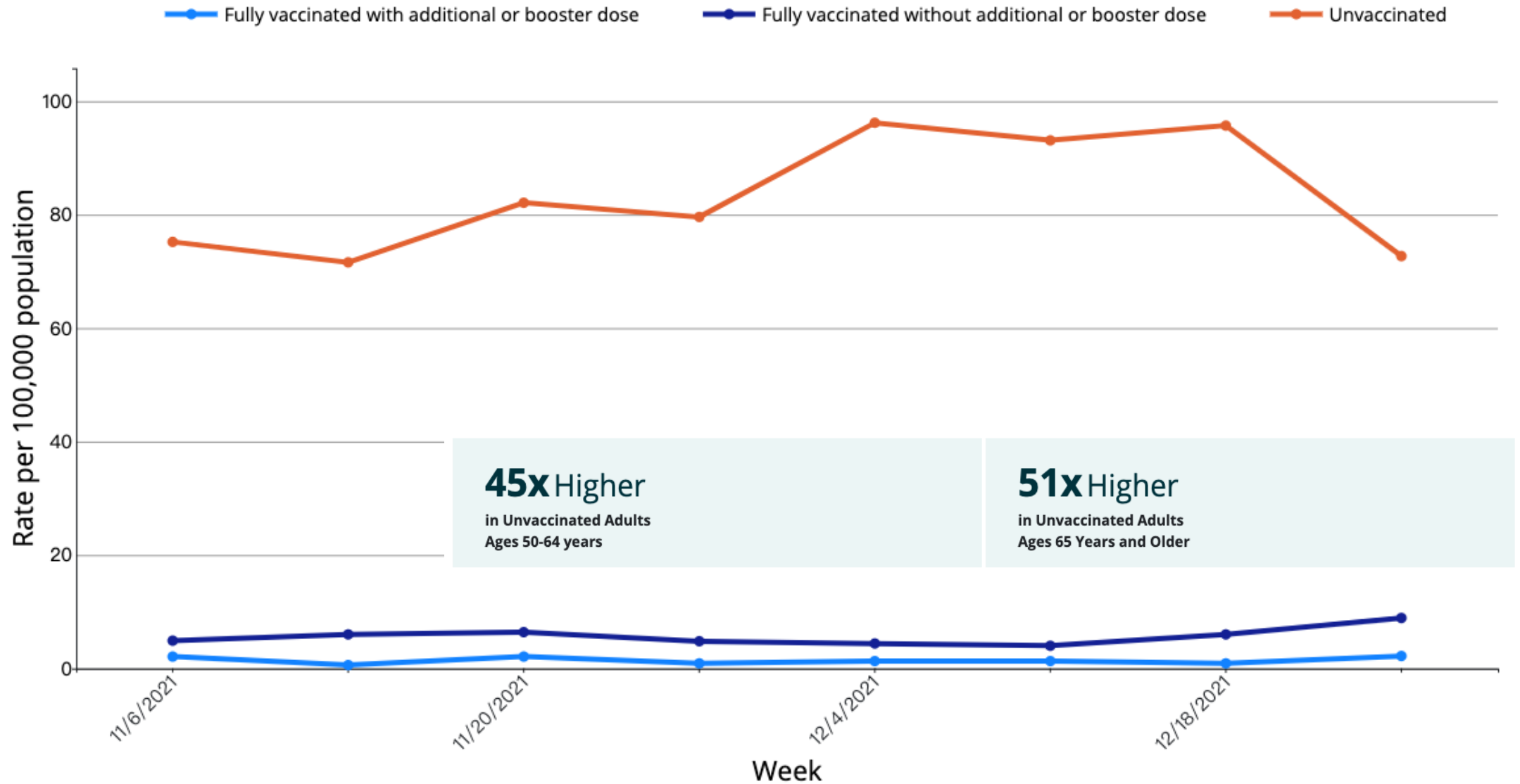


# COVID-19 Hospitalization Rate by Vaccination Status, USA

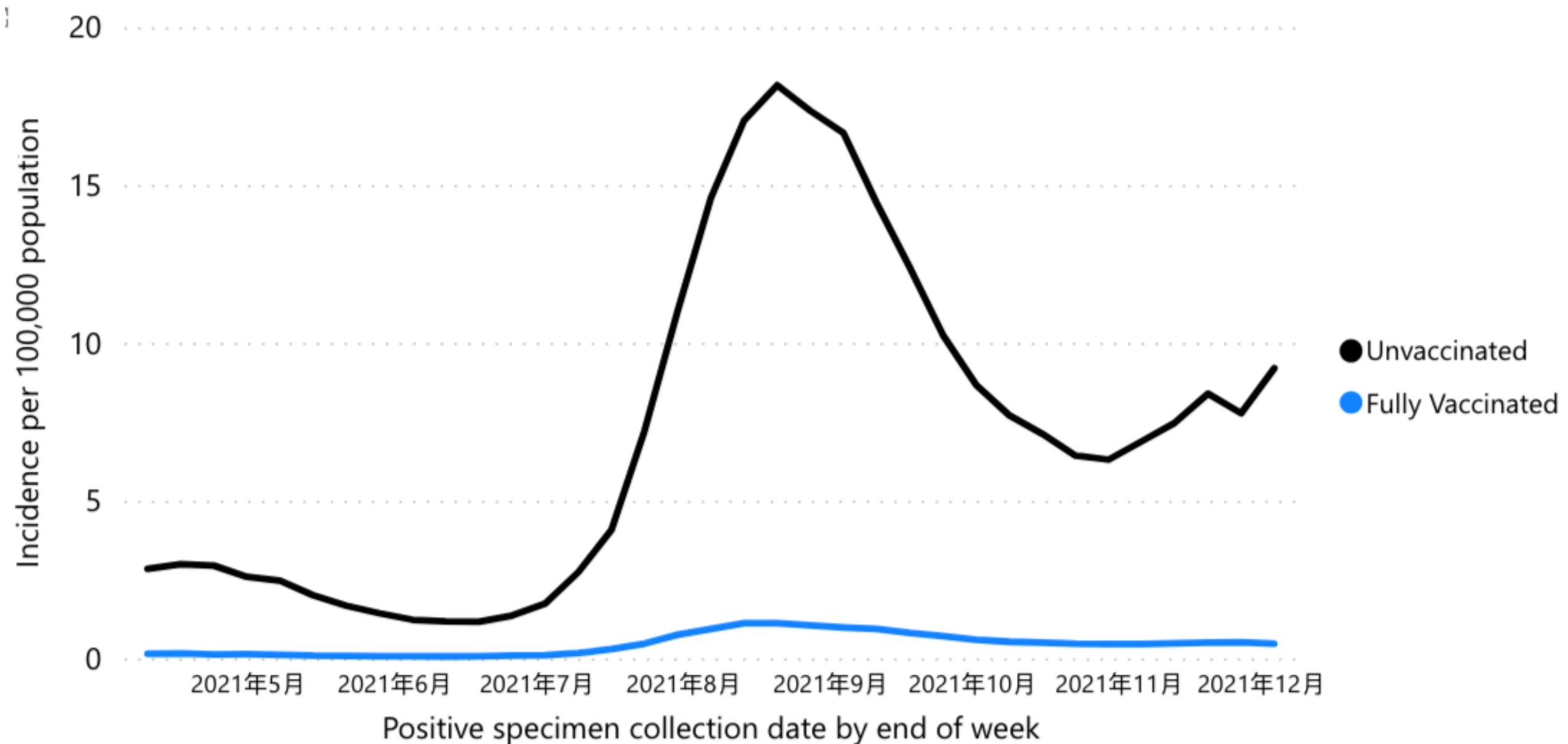
Rate in Fully Vaccinated Persons      Rate in Unvaccinated Persons



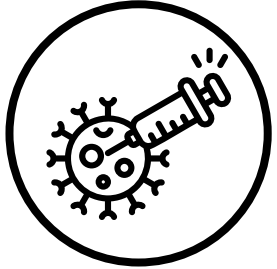
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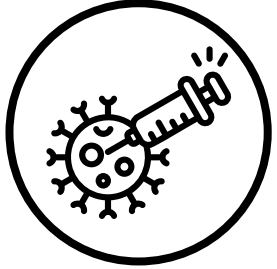
# COVID-19 Mortality Rate by Vaccination Status, USA



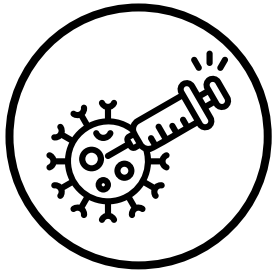
# What If You Didn't Receive COVID-19 Vaccination ?



**Greater risk of testing positive for COVID-19**



**Greater risk of hospitalization**



**Greater risk of dying from COVID-19**

# Vaccine Effectiveness Surveillance

## How CDC Monitors COVID-19 Vaccine Effectiveness

CDC uses several approaches to monitor COVID-19 vaccine effectiveness in real-world conditions. Some examples of the systems CDC uses are listed in the table below.

Select systems used by CDC and partners to monitor vaccine effectiveness

Outcome monitored	Population monitored	Monitoring system
Infection	Long-term care facility residents	<a href="#">NHSN</a>
Infection	Healthcare providers, first responders, and frontline workers	<a href="#">HEROES/RECOVER</a>
Infection	Children ages 4 months – 17 years	<a href="#">PROTECT</a>
Infection	Individuals tested at participating pharmacies	<a href="#">ICATT</a>
Hospitalization	Hospitalized children and adolescents ages 18 and younger	<a href="#">Overcoming COVID-19</a>
Hospitalization	Hospitalized adults ages 18 and older	<a href="#">IVY</a>

Research and analysis

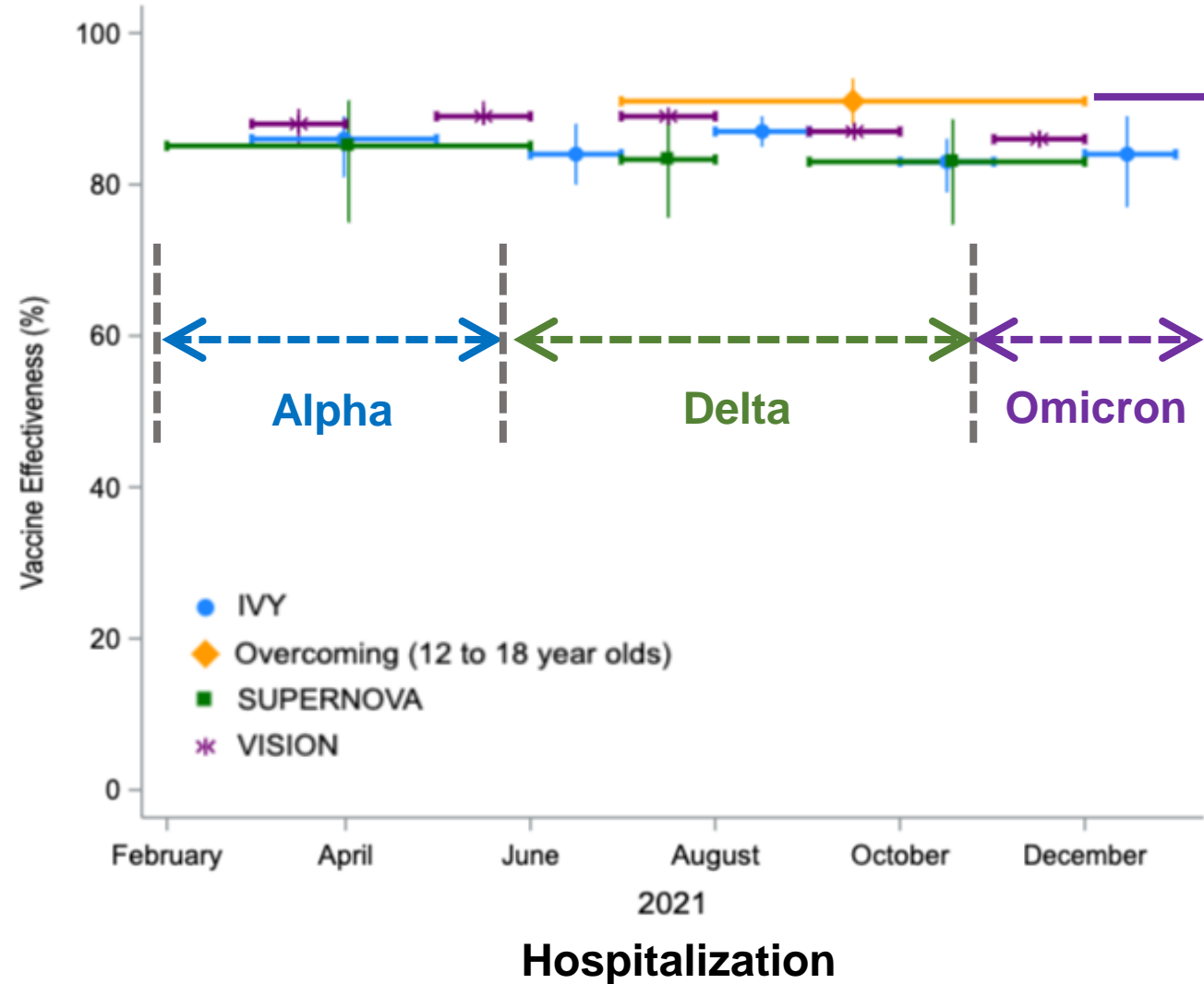
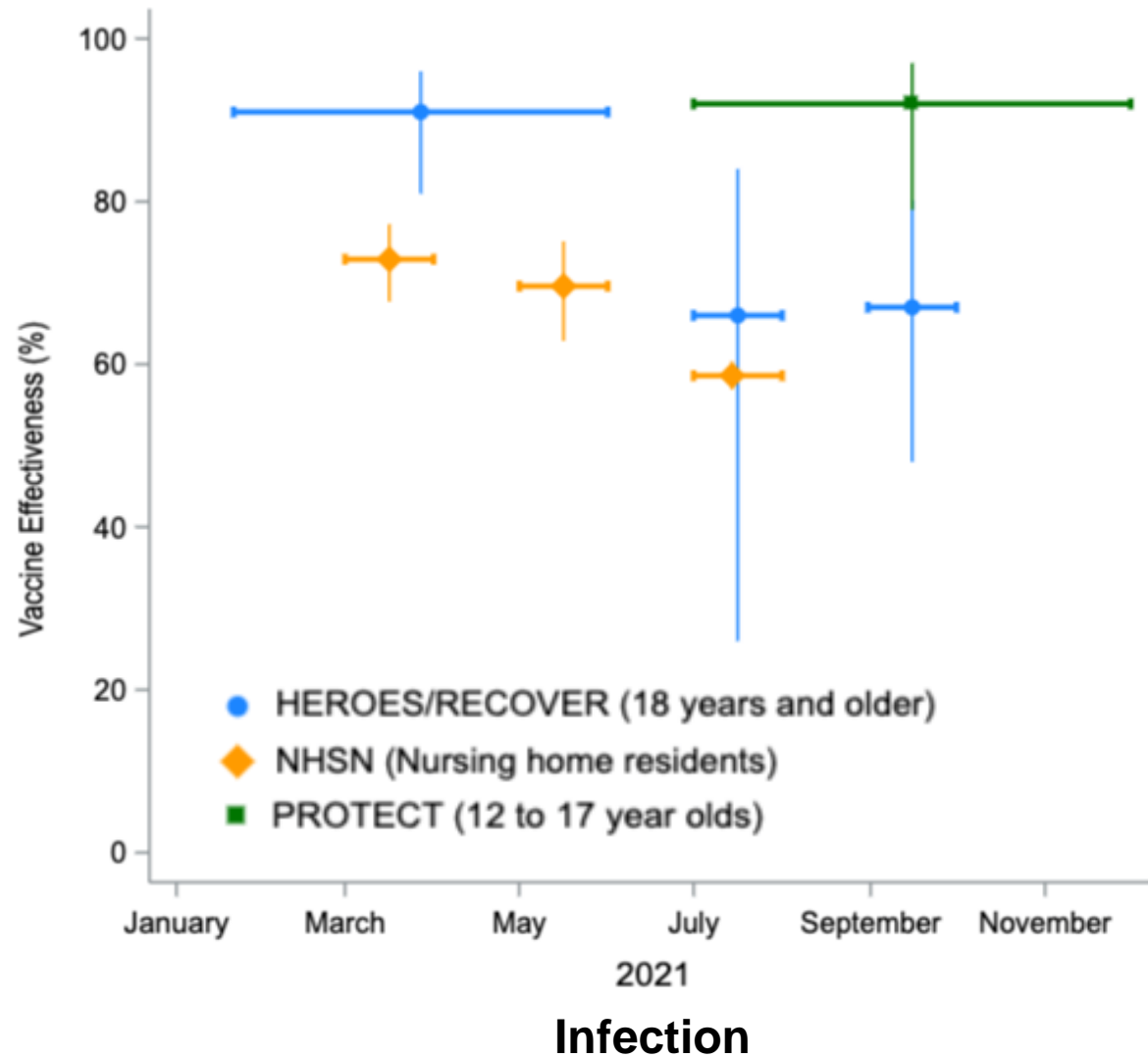
## COVID-19 vaccine surveillance reports (weeks 19 to 38)

Data on the real-world effectiveness and impact of the COVID-19 vaccines.



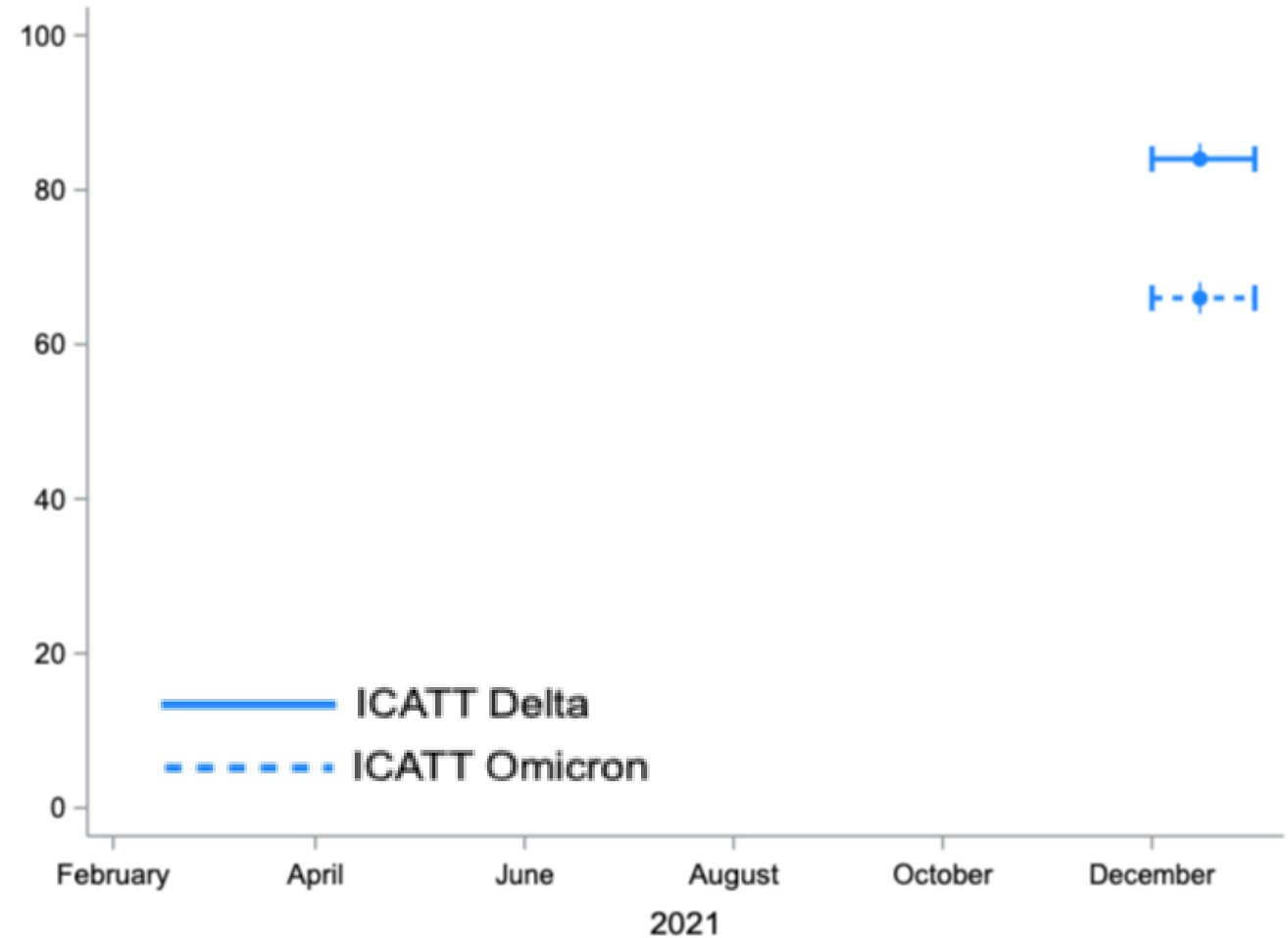
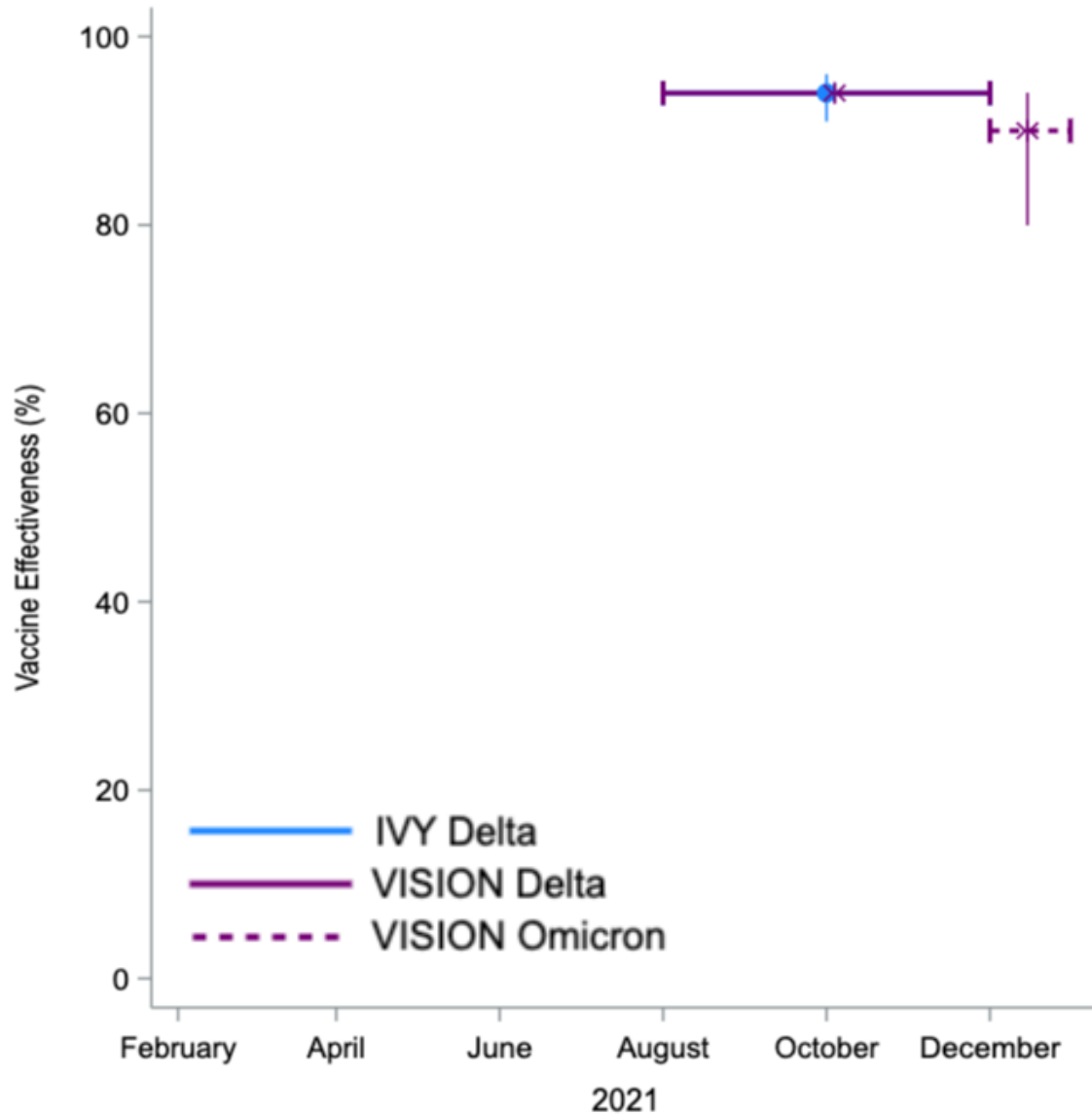
<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/index.html>

# Primary Series Vaccine Effectiveness Against Infection & Hospitalization





# Booster Vaccine Against Infection

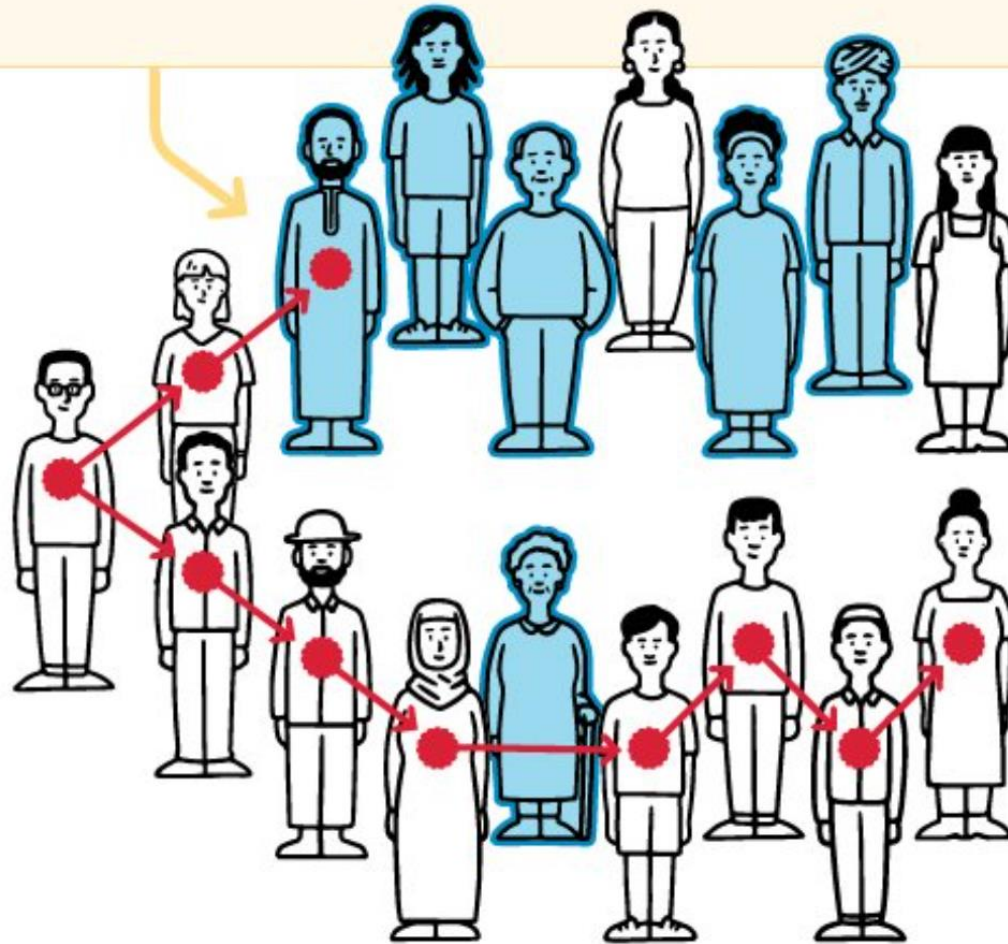


# Breakthrough Infection Rate, Minnesota, USA

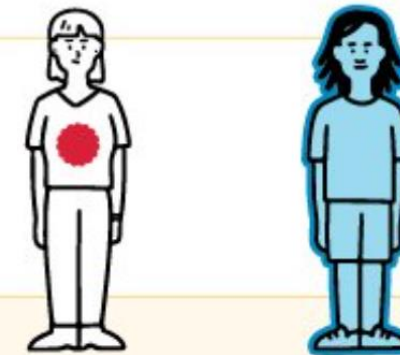
Total number of fully vaccinated Minnesotans age 5 and older (as of the week beginning 1/9/2022)*		3,532,622
	Number of vaccine breakthrough cases	Percent of fully vaccinated people
Total cases	347,831	9.846%
Total cases hospitalized**	9,037	0.256%
Total deaths***	1,601	0.045%

# COVID-19 Hospitalization Rate by Vaccination Status, USA

Vaccines do not provide full (100%) protection, so breakthrough infections can happen.



But as more people get vaccinated, it is expected fewer people will come into contact with the virus.



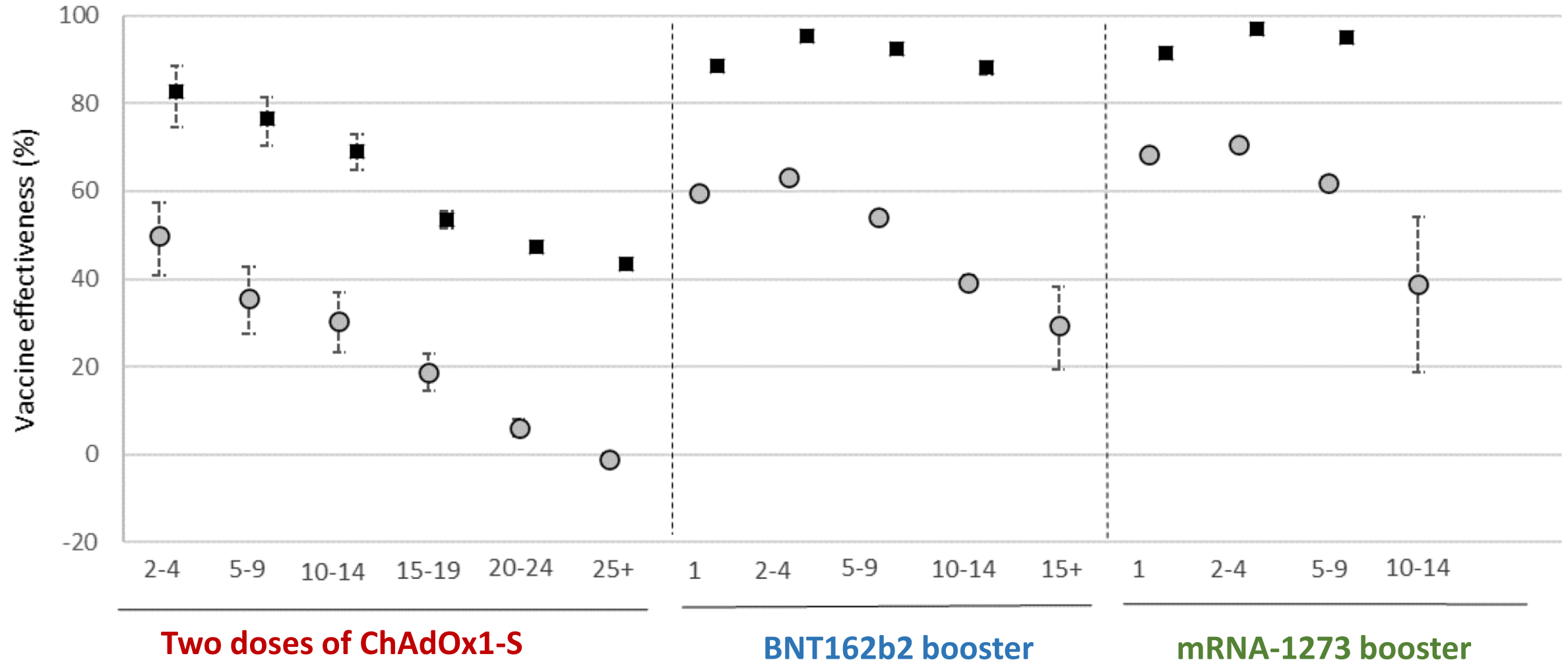
INFECTED

VACCINATED

# Estimated Vaccine Effectiveness Against Omicron Variant, UK

Vaccine effectiveness against symptomatic disease

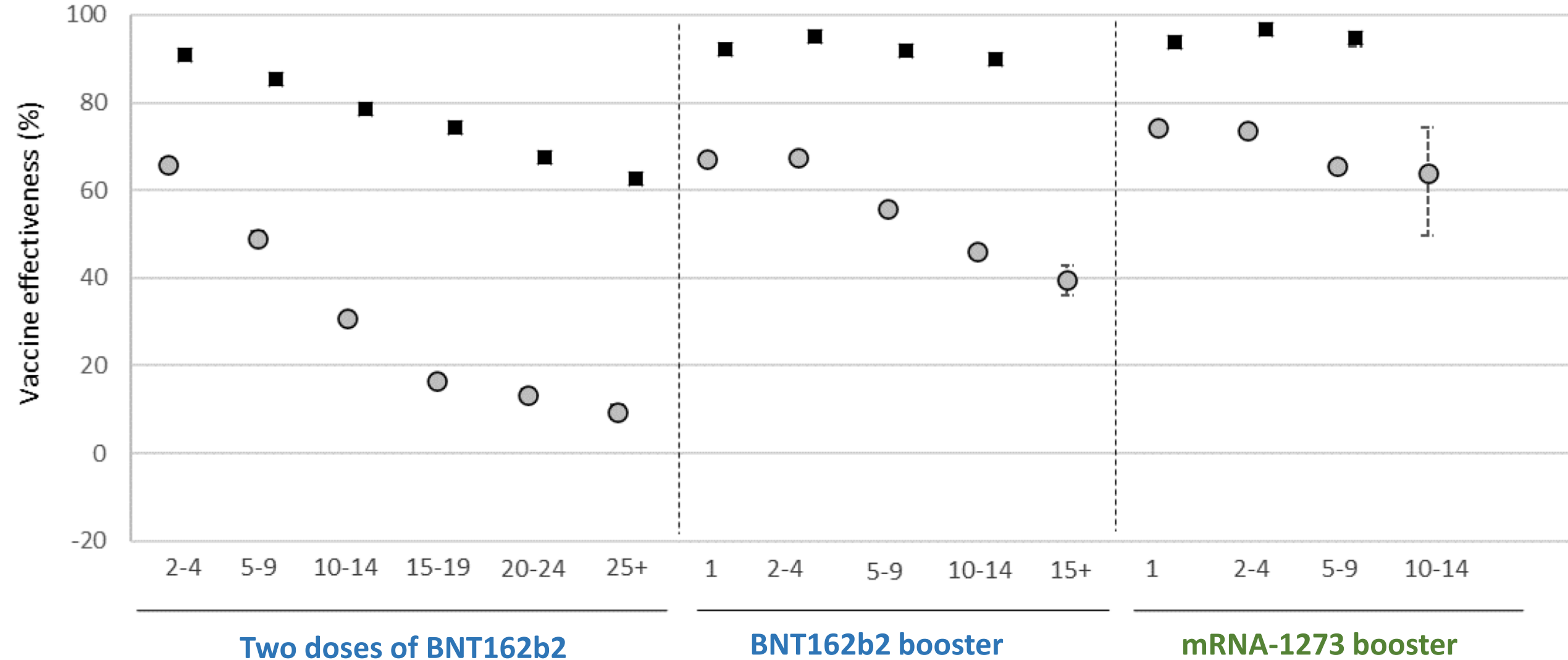
Two doses of ChAdOx1-S with a BNT162b2 or mRNA-1273 booster dose



# Estimated Vaccine Effectiveness Against Omicron Variant, UK

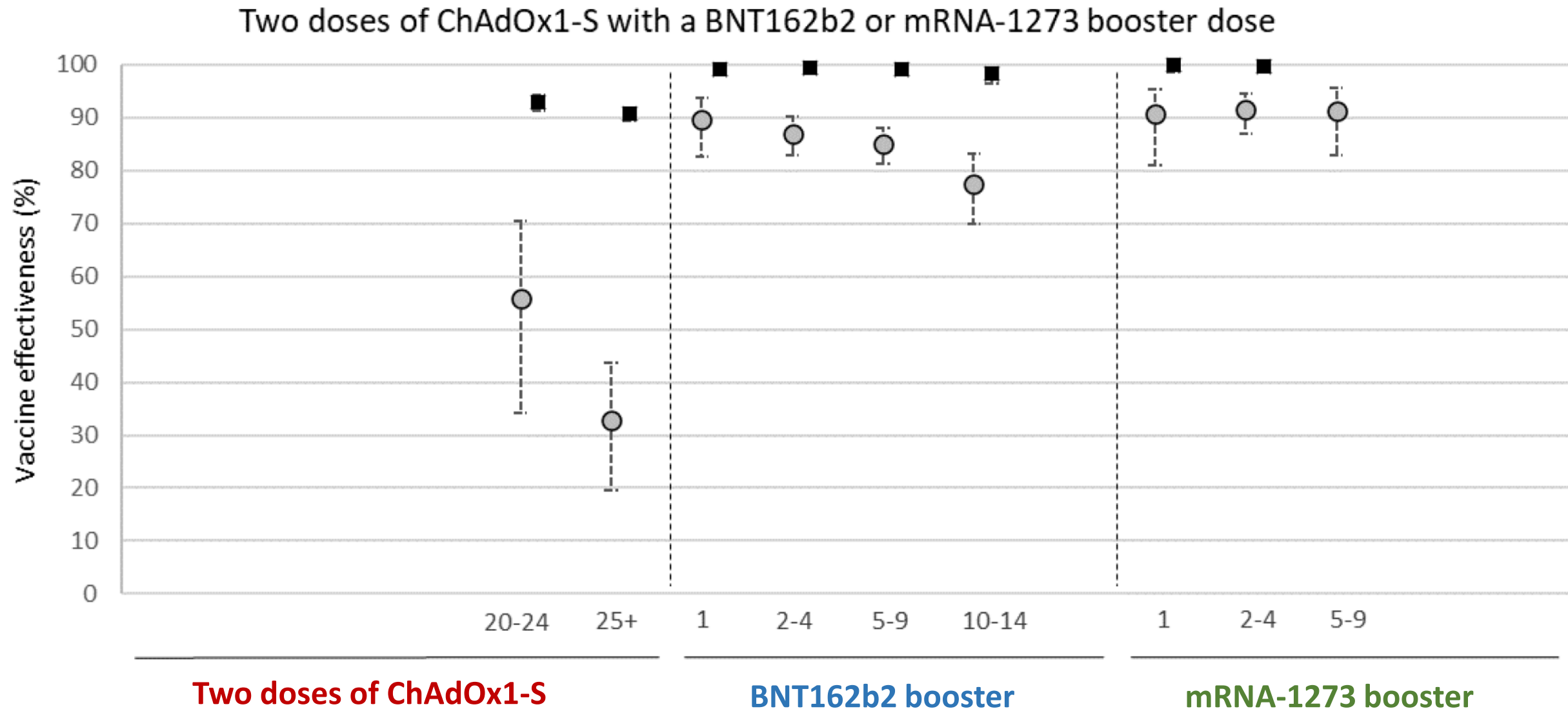
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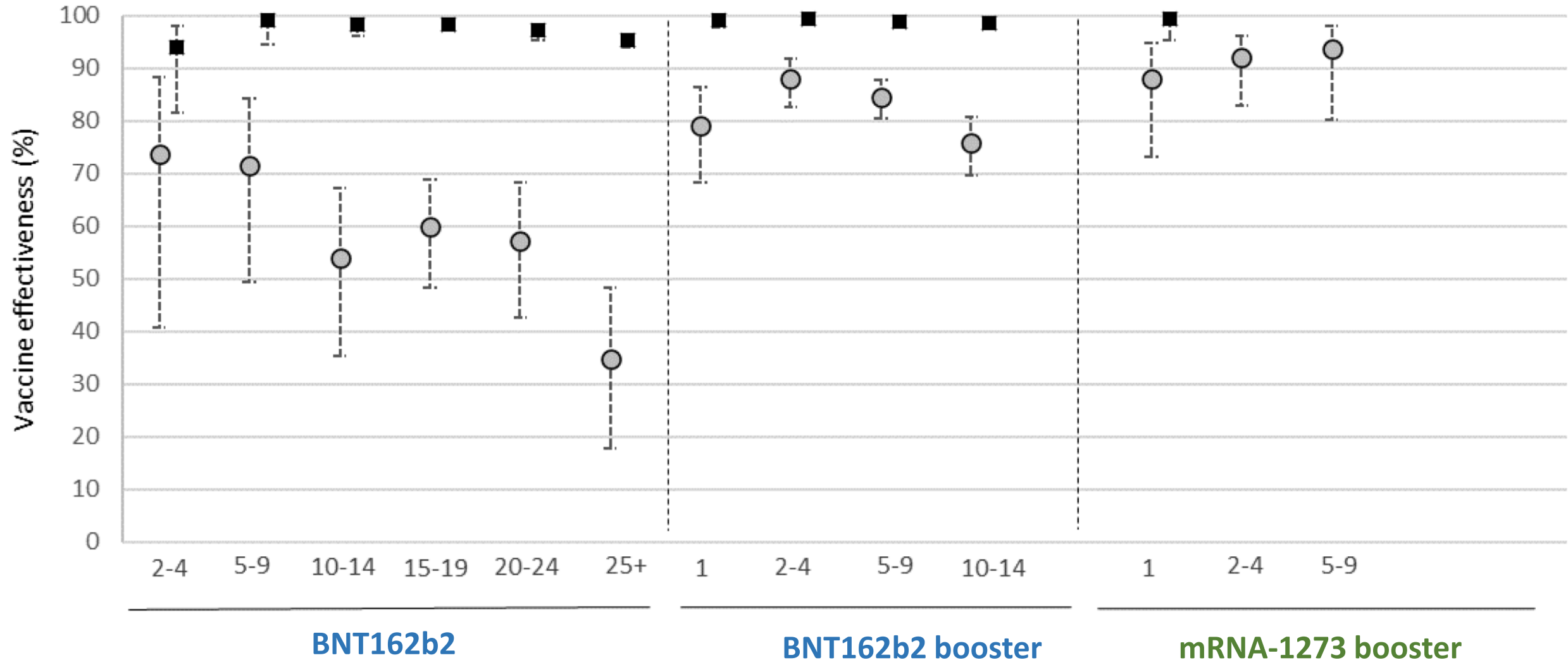
## Vaccine effectiveness against hospitalization



# Estimated Vaccine Effectiveness Against Omicron Variant, UK

## Vaccine effectiveness against hospitalization

Two doses of BNT162b2 with a BNT162b2 or mRNA-1273 booster dose





# Estimated Vaccine Effectiveness Against COVID-19, UK

## Vaccine effectiveness against Mortality

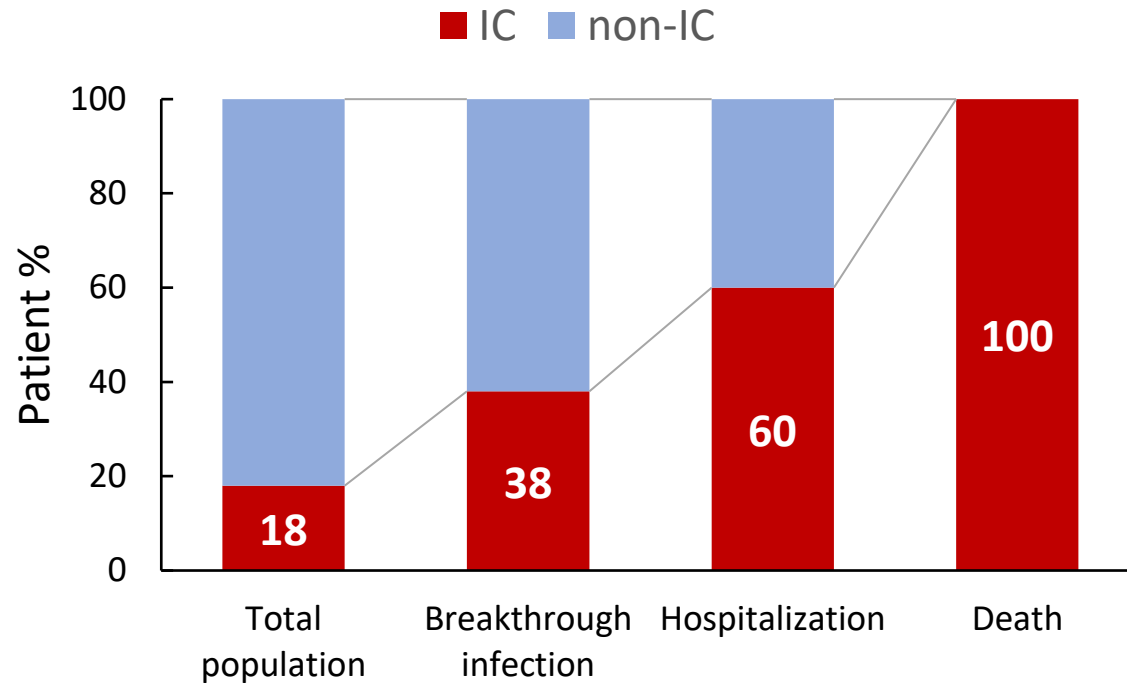
- High levels of protection (over 90%) are also seen against mortality with all 3 vaccines and against both the Alpha and Delta variants with relatively limited waning.
- VE against mortality with the Omicron variant has been estimated for those aged 50 years and older:

<b>Dose</b>	<b>Interval after dose</b>	<b>OR versus symptomatic disease</b>	<b>HR versus mortality</b>	<b>VE versus mortality</b>
2	25+ weeks	0.93 (0.9 to 0.96)	0.45 (0.19 to 1.03)	59% (4 to 82)
3	2+ weeks	0.41 (0.39 to 0.42)	0.12 (0.06 to 0.24)	95% (90 to 98)

# Poor Immunogenicity in immunocompromised patients

US HealthVerity database (12/10/2020-7/8/2021)

N = 1,277,747



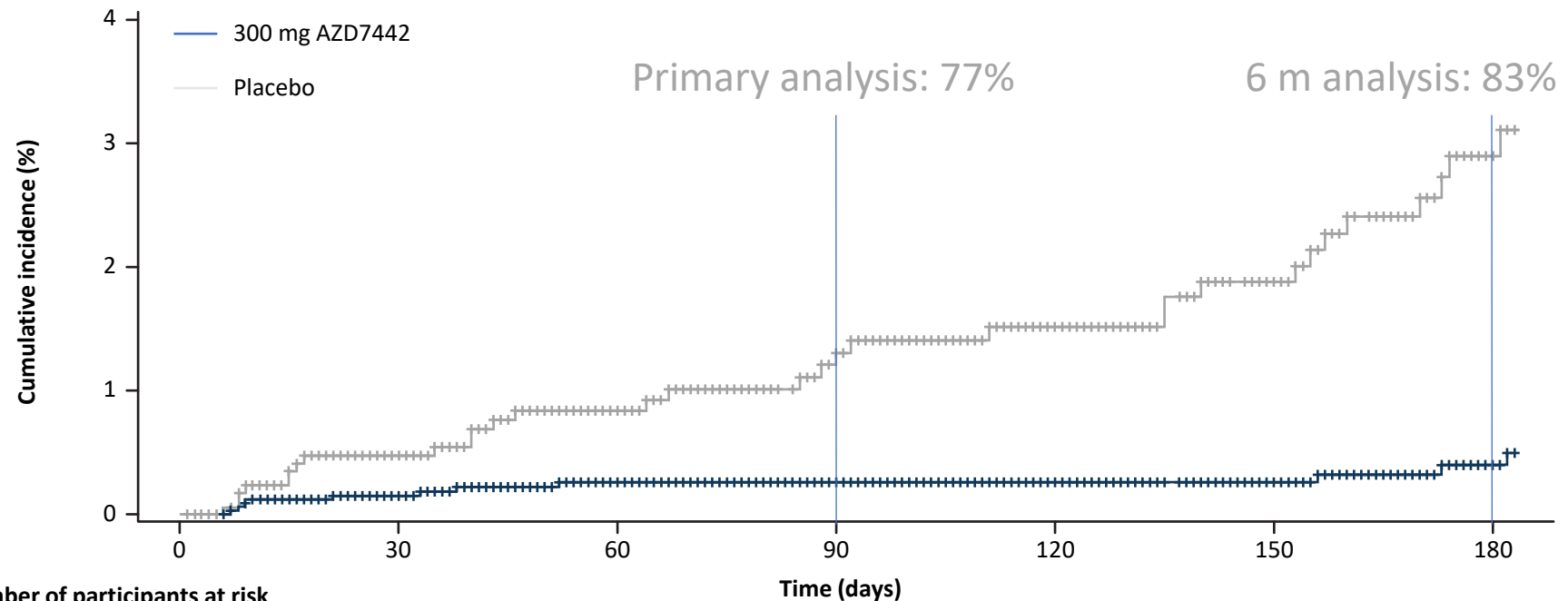
Population	IR per 100 person-year
Non-IC	0.34 (0.32-0.37)
IC	2.6X 0.89 (0.80-0.98)
HIV/AIDS	0.71 (0.15-2.07)
Solid malignancy	0.56 (0.40-0.70)
Bone marrow transplant	0.00 (NA)
Organ transplant	3.66 (1.19-8.54)
Rheumatologic condition	0.82 (0.62-1.06)
Primary Immunodeficiency	1.13 (0.45-2.33)
Other immune condition	0.27 (0.03-0.99)
CKD or ESRD	0.95 (0.75-1.19)
Hematological malignancy	1.09 (0.30-2.80)
IS medication usage ≥ 14 Days	0.48 (0.28-0.76)
antimetabolite usage ≥ 14 Days	1.48 (0.18-5.35)
> 1 IC condition	1.70 (1.41-2.03)

# Long-acting Monoclonal Antibody to prevent symptomatic illness

Primary outcome measures<sup>1</sup>

SARS-CoV-2 RT-PCR–positive symptomatic illness

Cumulative incidence of SARS-CoV-2 RT-PCR–positive symptomatic illness was lower for AZD7442 vs. placebo<sup>2,a</sup>



Number of participants at risk

AZD7442	3441	2957	2393	2054	1815	1667	1044
Placebo	1731	1483	1177	991	856	774	472

<sup>a</sup>Subjects who do not experience a primary endpoint event (and had not discontinued) are censored at Day 183. Subjects who were unblinded/vaccinated prior to an event are also censored at the earlier time of unblinding/vaccination.

RT-PCR = reverse transcriptase–polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TIXA/CILGA = tixagevimab/cilgavimab.

1. Study NCT04625725. ClinicalTrials.gov website; 2. Fact sheet for healthcare providers. Emergency Use Authorization (EUA) of EVUSHELD™ (tixagevimab co-packaged with cilgavimab). 2021.

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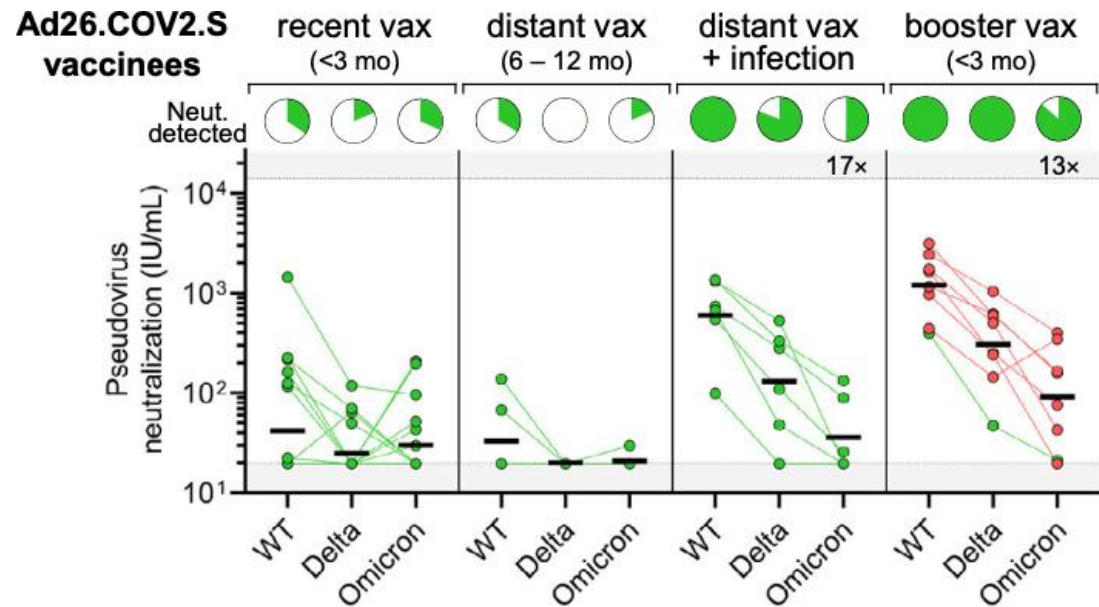
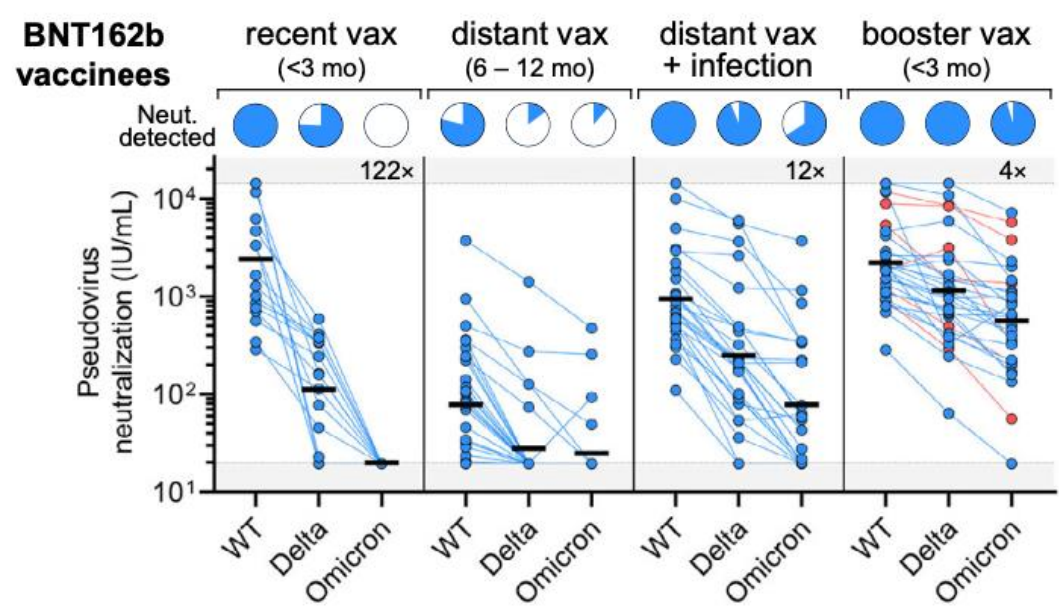
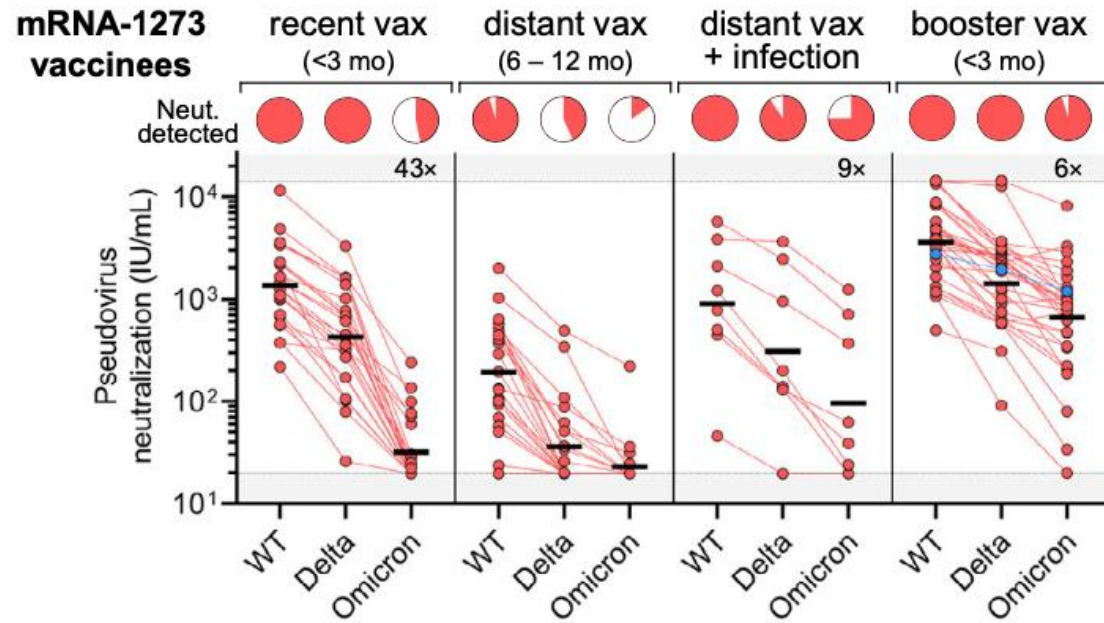


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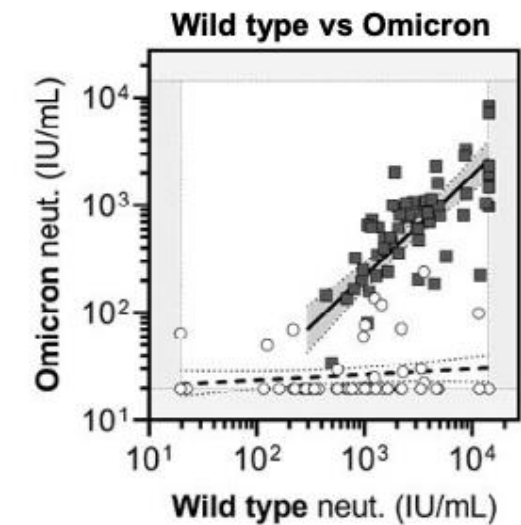
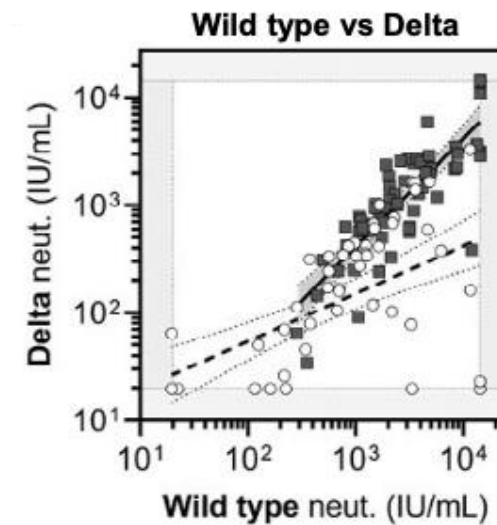
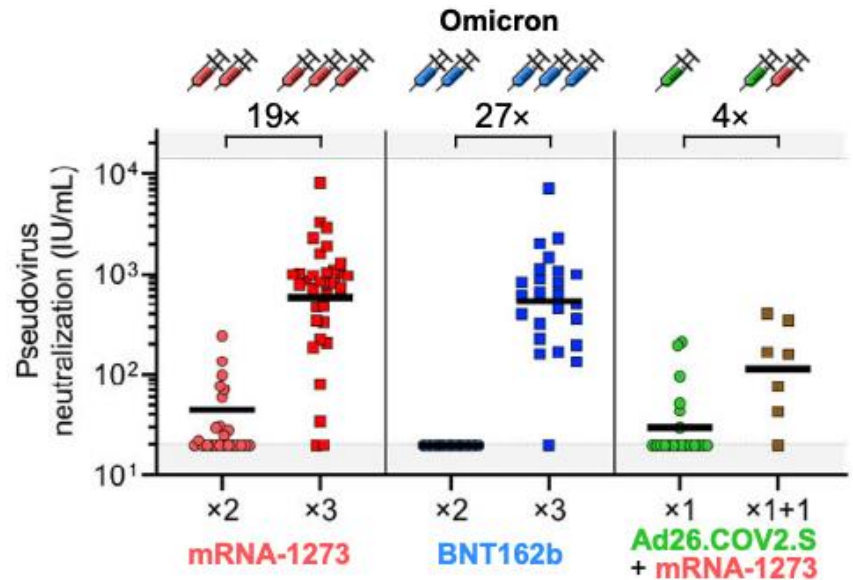
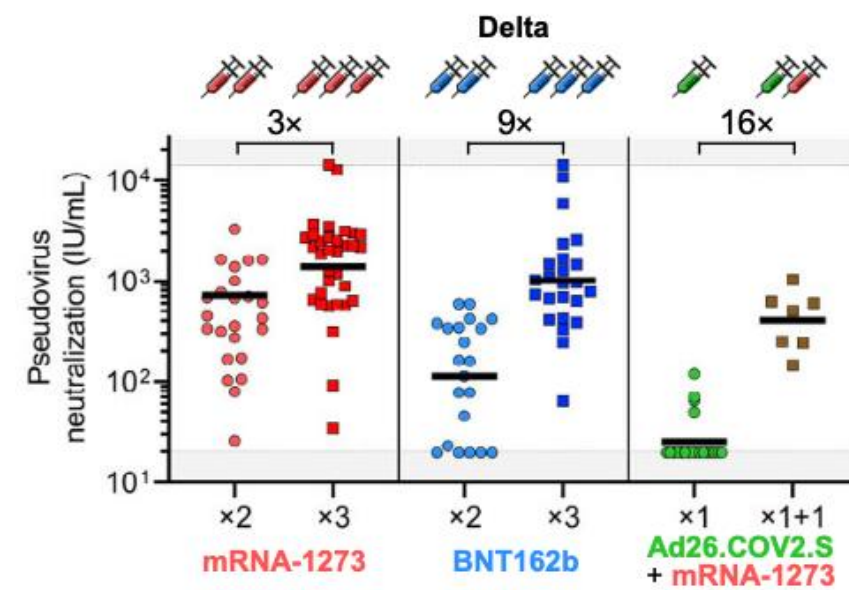
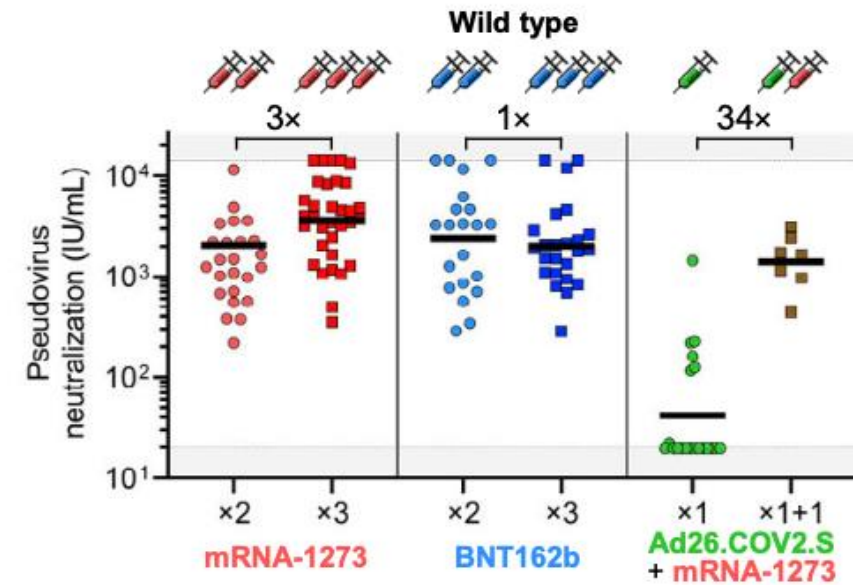


## **Benefits from the booster dose of COVID-19 vaccine**

# Neutralizing antibody demonstrate substantial escape by Omicron



# Booster Dose Increases Breadth and Cross-reactivity of Neutralizing Antibody Response







## *On the Origin of the Vaccine Inoculation.*

**T**HE most important discoveries, when familiarized to the mind, are contemplated with indifference. Who now wonders at the discovery of America, or the circulation of the blood? There is, however, a period between the conception of a discovery and its mature birth, fraught with more pangs than war or women know; and there is no light, in which the human mind can be viewed, more interesting than during this anxious period. Whenever, therefore, the author of any greatly useful invention details the progress of his own mind, during the completion of his plan, the history is perused with avidity. On these grounds, we conclude that our readers will be much gratified by the following narrative.

*“ I am induced to give the following concise History of the Origin of Vaccine Inoculation, from my frequently observing that those who only consider the subject cursorily, confound the casual Cow Pox with the Disease when excited by Inoculation.*

*Bond Street, May 6, 1801.*

*EDWARD JENNER.*

1796/06/14