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Covid-19: What's Next?

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หัวหน้า Tropical Medicine Cluster, Health Supercluster,
จุฬาลงกรณ์มหาวิทยาลัย
ผู้ช่วยผู้อำนวยการและรักษาการหัวหน้าฝ่ายวิจัยและบริการคลินิค
สถานเสาวภา สภากาชาดไทย

Disclosure (2016-2022)

Prof. Terapong Tantawichien: has received support for

Travel for International Conference (Bionet, Siam Pharm)
Lectureships (Zuellig Pharma.GlaxoSmithKline, Pfizer, MSD, Roche
Thai Meiji, Siam Pharm, Sanofi , Biovalys, Biogenetec……).
Advisory board for zoster vaccine/pneumococcal vaccine (MSD),
rabies vaccine (GSK), dengue vaccines (Sanofi, MSD, Takeda),
influenza vaccine(Sanofi)

Prof. Terapong Tantawichien: has received research funds from

Sanofi (C. difficile vaccine) 2016-17
Medico (Plant-derived influenza vaccine) 2017-18
MPH, Thailand (shorten rabies PET) 2019-20
NSTDA/Bionet (Asia)-Spearhead project
(Tdap: recombinant pertussis toxin)-2019-2023)
Sanofi (Rabies vaccine:VRV-12) 2020-2021
Sanofi (Rabies vaccine: VRV-14) 2020-2021
Baiya (Covid-19 vaccine) 2021-2023
Sanofi (Yellow fever vaccine) 2021-2025
Jansen (RSV vaccine) 2022-2024

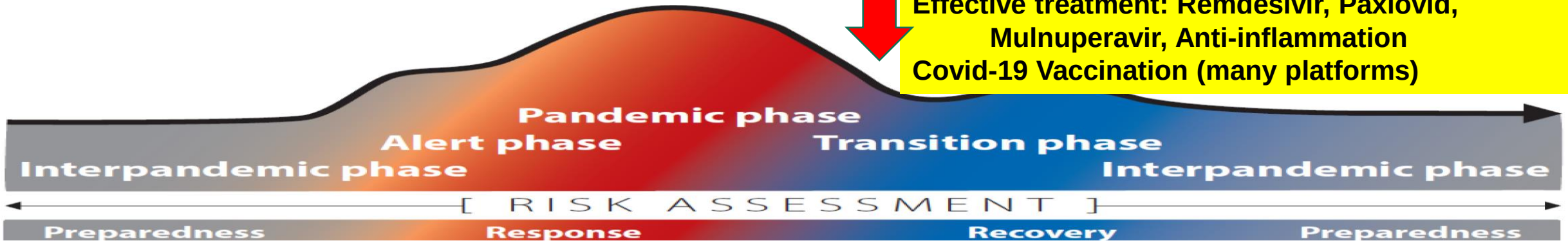
Covid-19: What's Next?

Overview:

- **Burden of covid-19 and future directions**
- **Strategies for Covid-19 vaccination:**
  - **Increased coverage of primary vaccination**
  - **Appropriate booster vaccination** *(Target population, types of vaccine, immune response, effectiveness, safety, interval, feasibility and acceptation.)*

Flattening pandemic COVID-19

Non-pharmacologic interventions: non-restriction?
Effective treatment: Remdesivir, Paxlovid, Mulnuperavir, Anti-inflammation
Covid-19 Vaccination (many platforms)



***Herd Immunity* (*population Immunity*):** Gained through **-Natural infection or Vaccination.**

Herd immunity threshold= 1-1/R0 COVID-19 R0 = 2-3= 60% delta 5-7 – **Omicron 8 (80-90%)**

Assume: ***long-life protection, homogenous population, no variant virus resist to antibody, T cell cross reactivity,*** *etc*

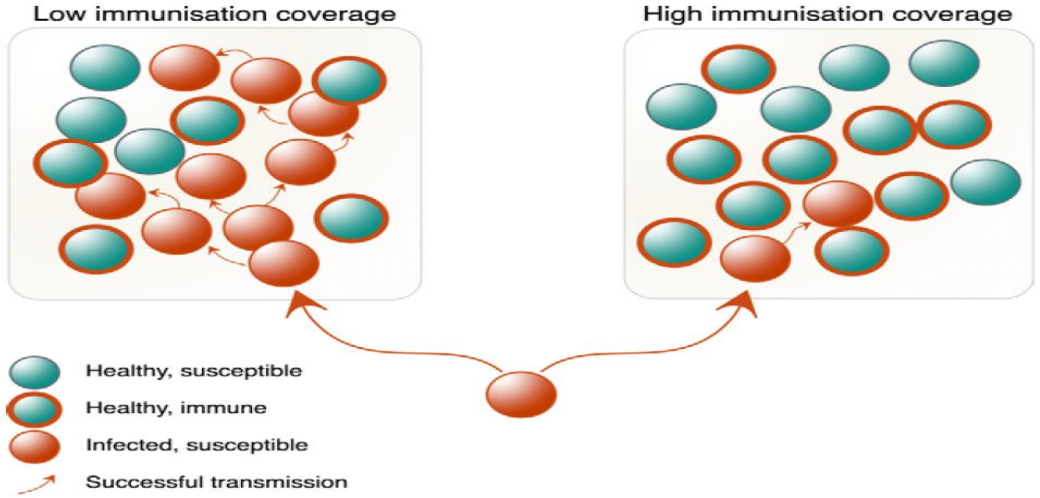


Figure 1. The double-edged sword of social life. When a sufficiently high proportion of a population is immune to a pathogen transmission to non- and poorly immunised individuals (e.g., the young the immunocompromised, and the weak responders to immunisation is blocked by the barrier formed by immunised individuals. Conversely when immunisation rate is insufficient, non-immunised individuals are at greater risk of becoming infected during social contacts.
doi:10.1371/journal.pbio.1001297.g001

The higher the vaccination rate and population immunity, the lower the number of hospitalizations and deaths

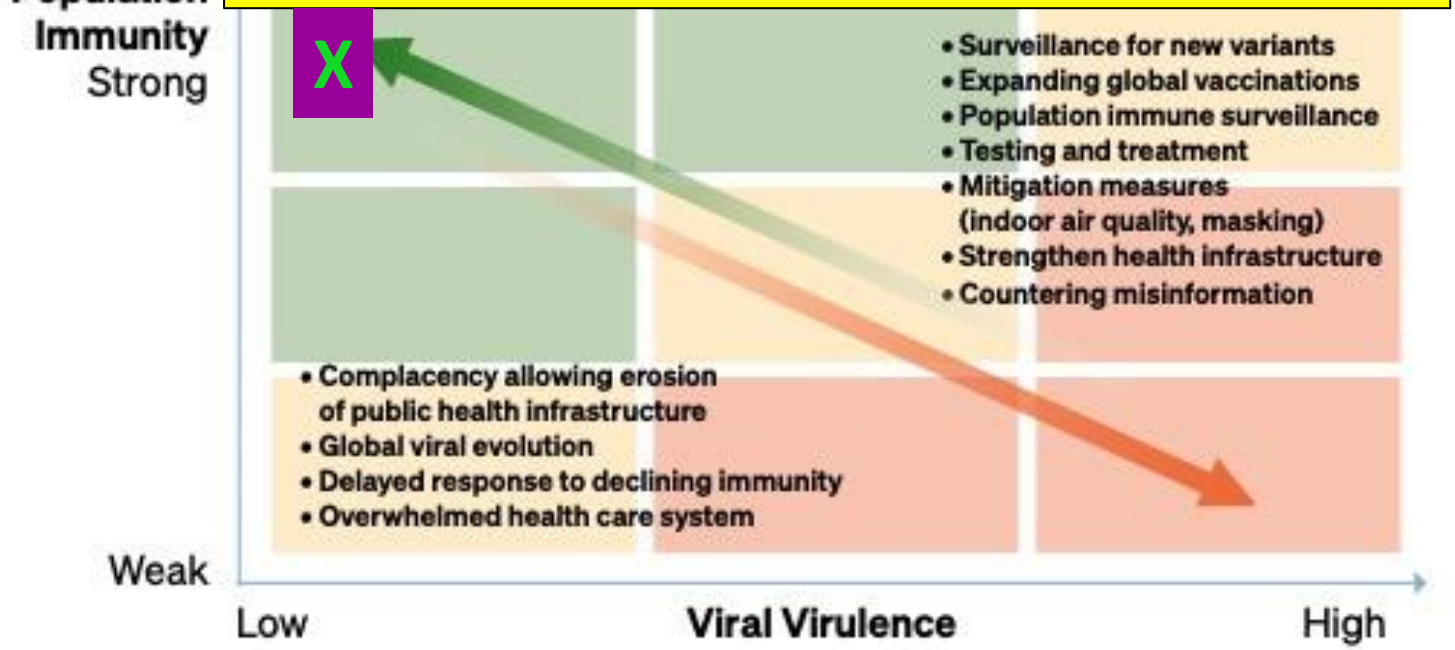
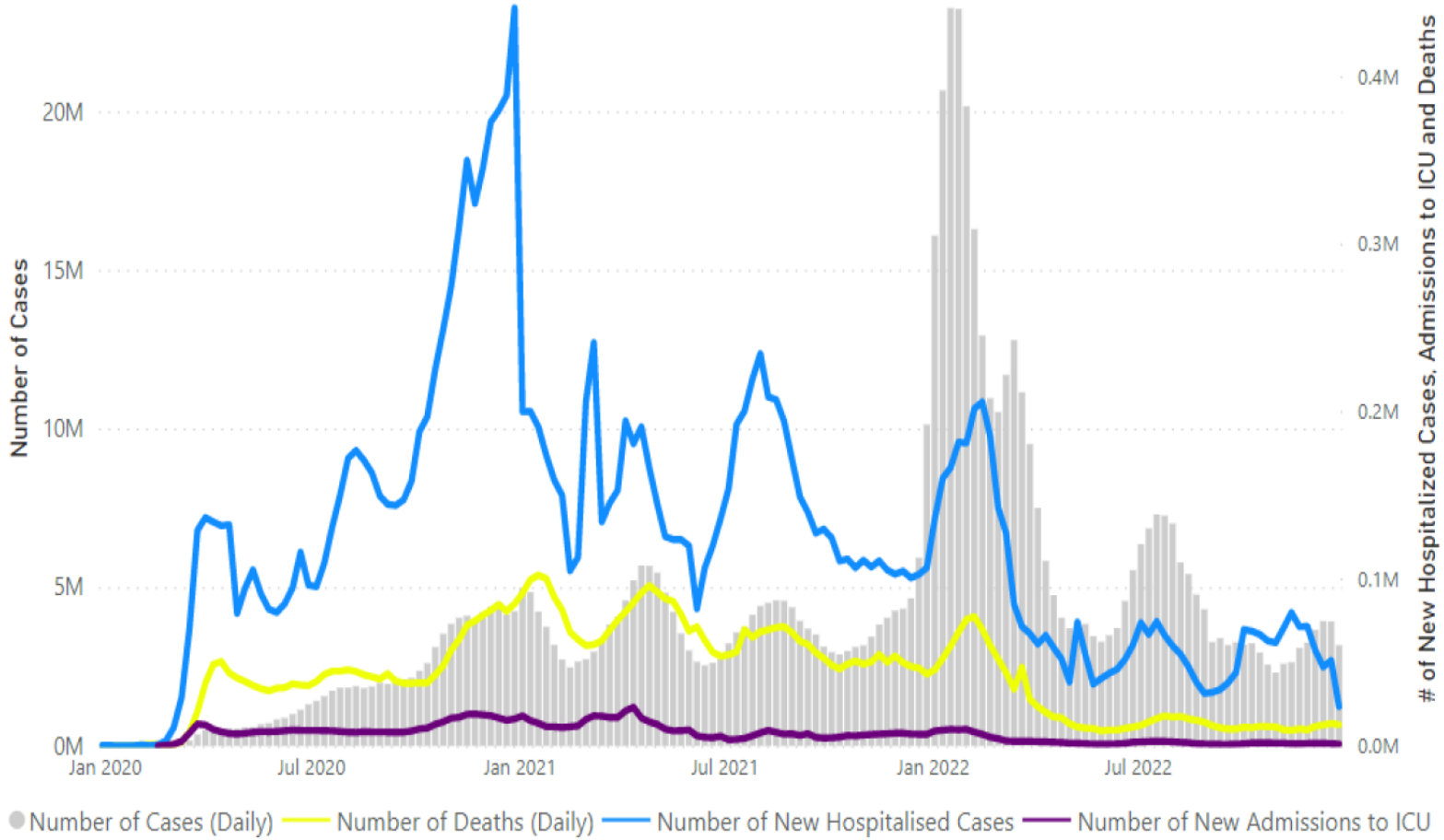
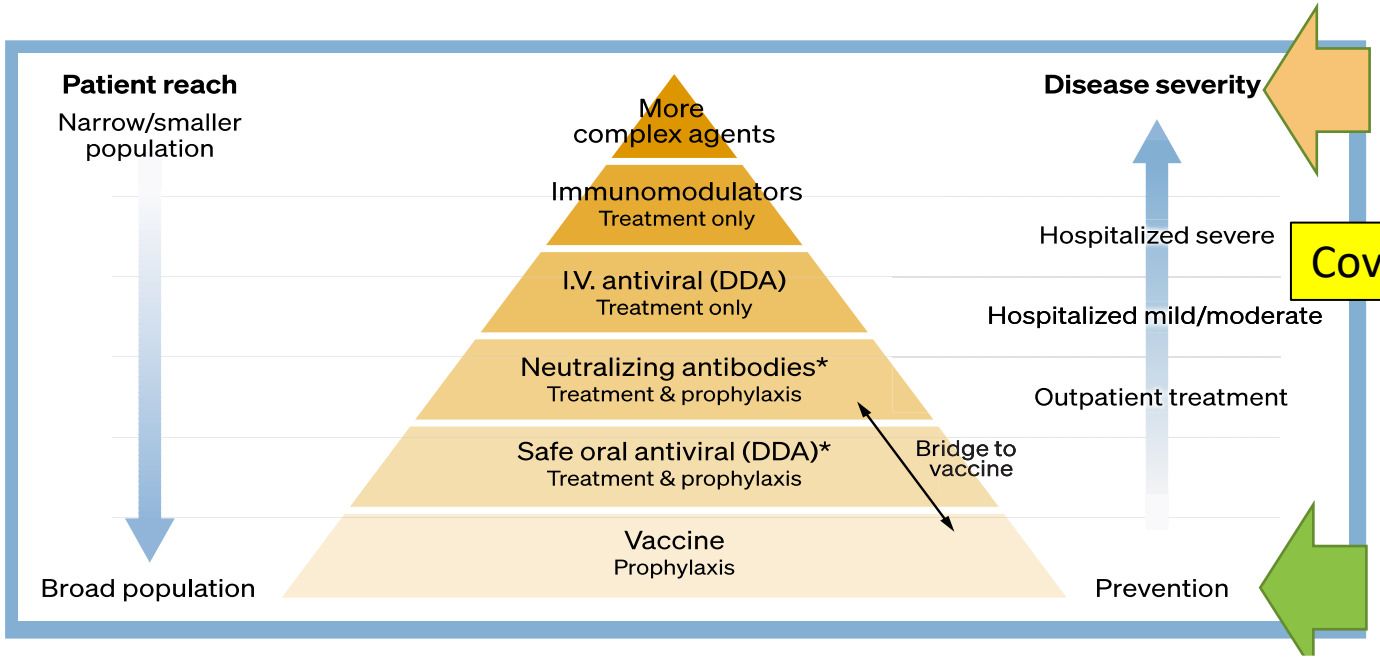


Figure 4. COVID-19 cases, deaths, hospitalizations, and ICU admissions reported weekly to WHO, as of 1 January 2023

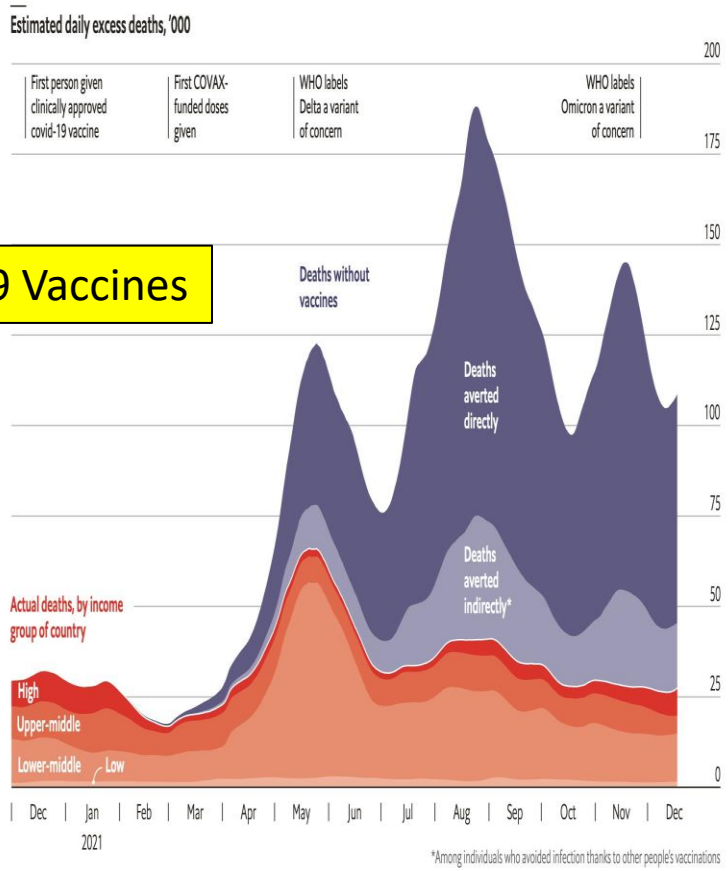


Note: Recent weeks are subject to reporting delays and should not be interpreted as a declining trend.

Vaccination and Treatment Options, by Disease Severity and Patient Reach



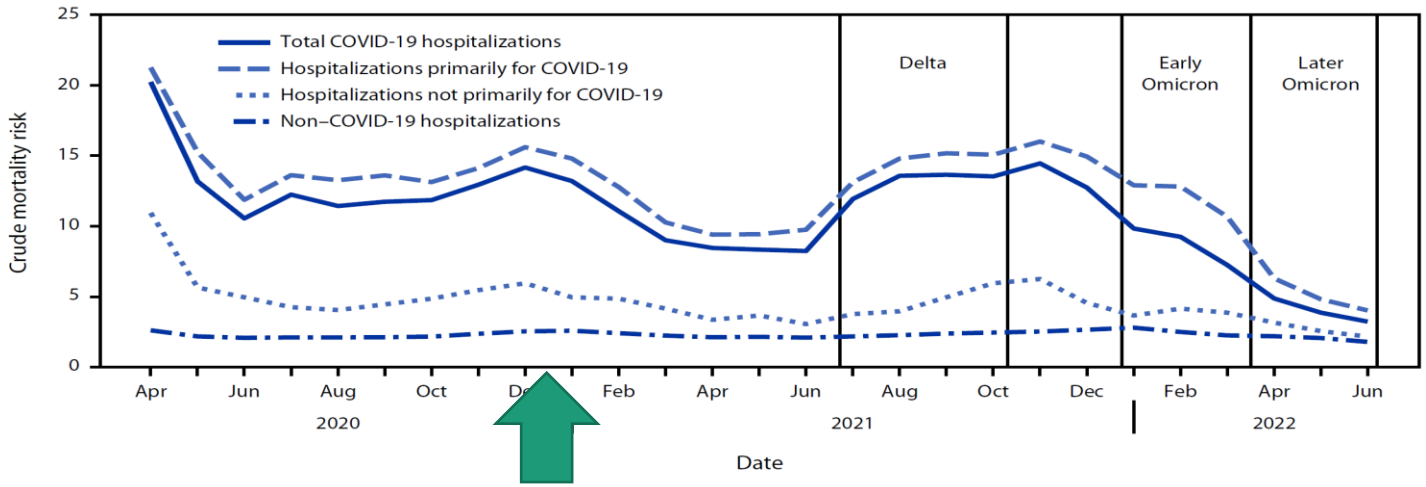
Covid-19 Vaccines



Deaths averted by vaccine

Actual death

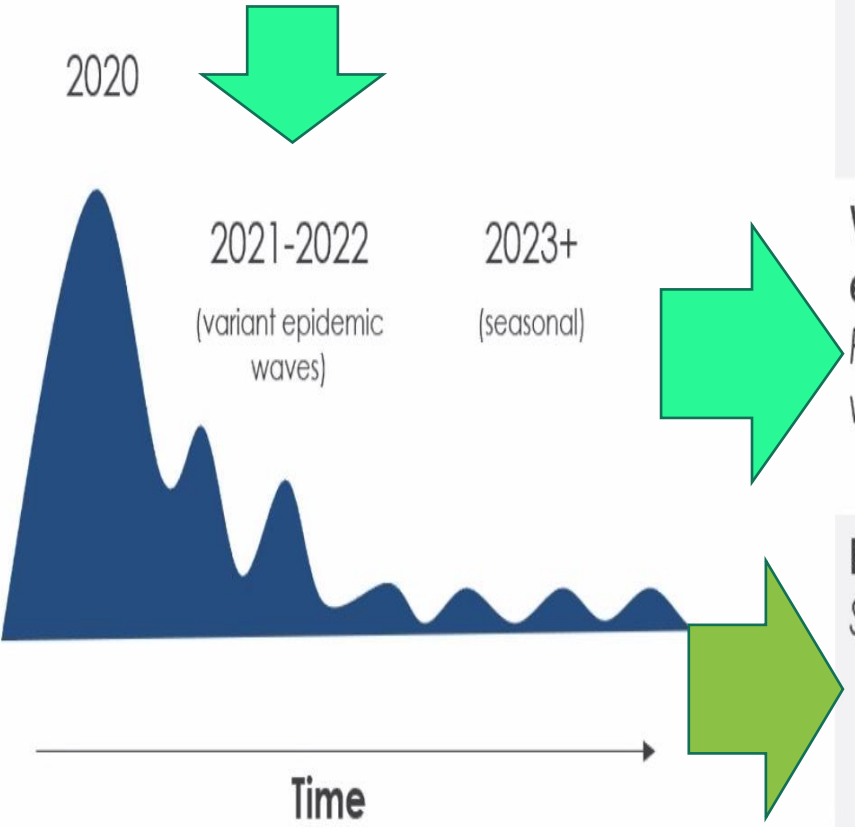
FIGURE. Crude mortality risk* for total COVID-19 hospitalizations, hospitalizations primarily for COVID-19, hospitalizations not primarily for COVID-19,† and non-COVID-19 hospitalizations — Premier Healthcare Database Special COVID-19 Release,§ United States, April 2022–June 2022¶



Based on official reported COVID-19 deaths, we estimated that **vaccinations prevented**...**19.8 million**...**deaths from COVID-19**... representing a **global reduction of 63% in total deaths** during the first year of COVID-19 vaccination.

and Sustaining the Next Normal A Roadmap for Living with COVID, March 2022

Post-pandemic immunity after immunization and natural infection will maintain endemic COVID-19 Immunity to human coronaviruses (natural infection): < 1 year



Stage	Focus for vaccines
Pandemic *Initial waves*	• Heavy focus on protecting high-risk populations • Mostly ancestral virus vaccine
Variant epidemics *Reinfection waves*	• Focus to suppressing transmission of variants • Speed & adaptability are critical
Endemic *Seasonal*	• Multi-valent approaches with broadest immunity • Focus on toddlers and seasonal protection against waning immunity in high-risk (e.g., 65+)

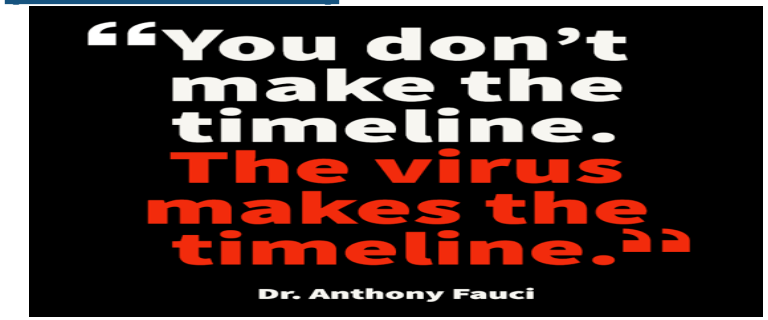
Non-pharmacologic interventions: non-restriction?
Effective treatment: Rem, Paxlovid, Mulnuperavir
Covid-19 Vaccination (many platforms)

COVID-19 vaccine will stop pandemic

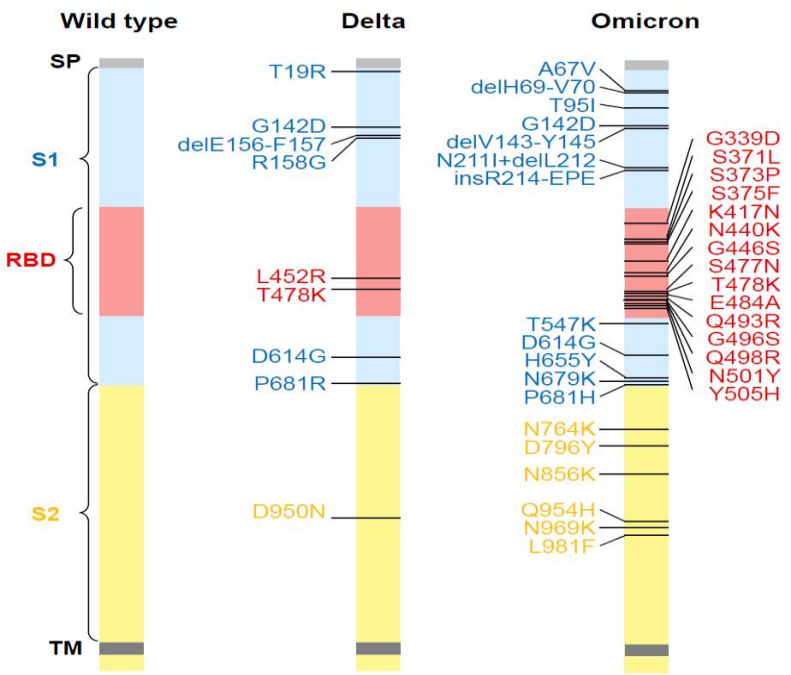
Maintain immunity 80-90%
Natural booster or vac.booster (duration ?)

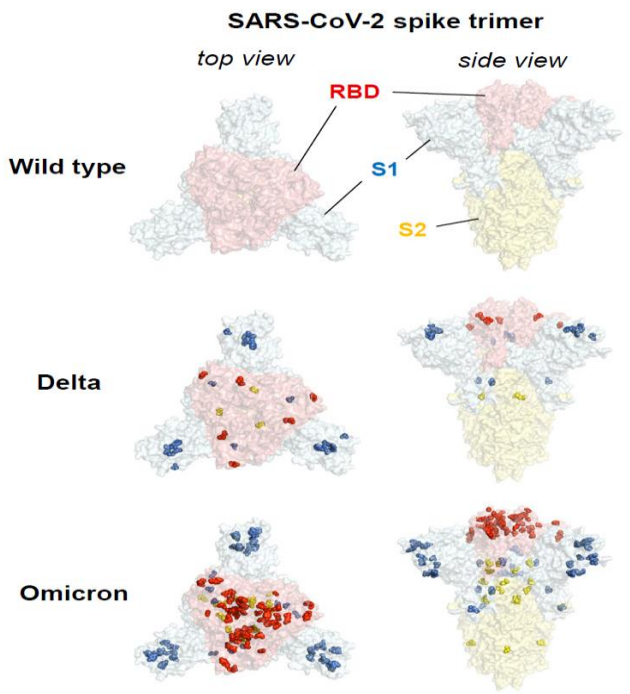
New variant of SAR-CoV 2 VOC
(New vaccine for specific VOC ?)

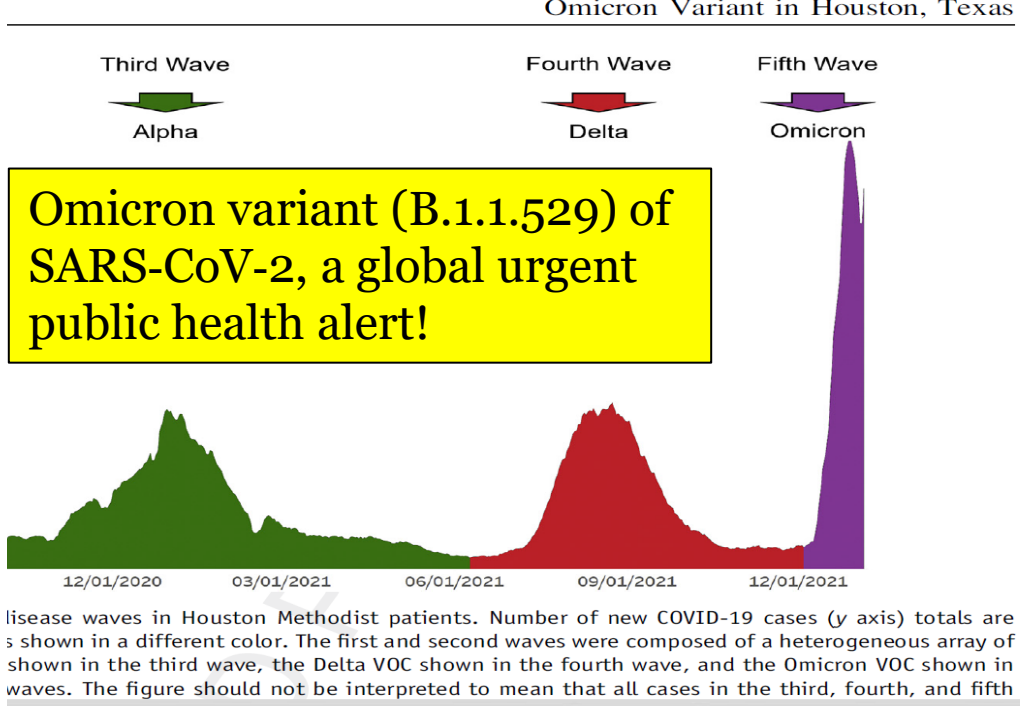
Outbreak in seronegative new area (infant, children)



SARS-CoV-2 is likely to become the fifth endemic common cold virus, causing largely asymptomatic infections ?







Omicron variant (B.1.1.529) of SARS-CoV-2, a global urgent public health alert!

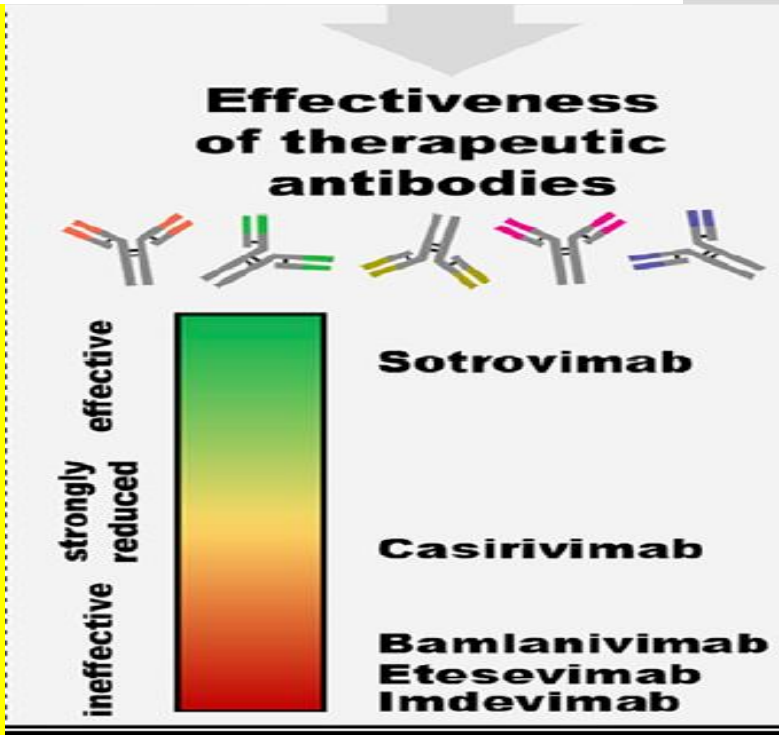
Omicron Variant in Houston, Texas

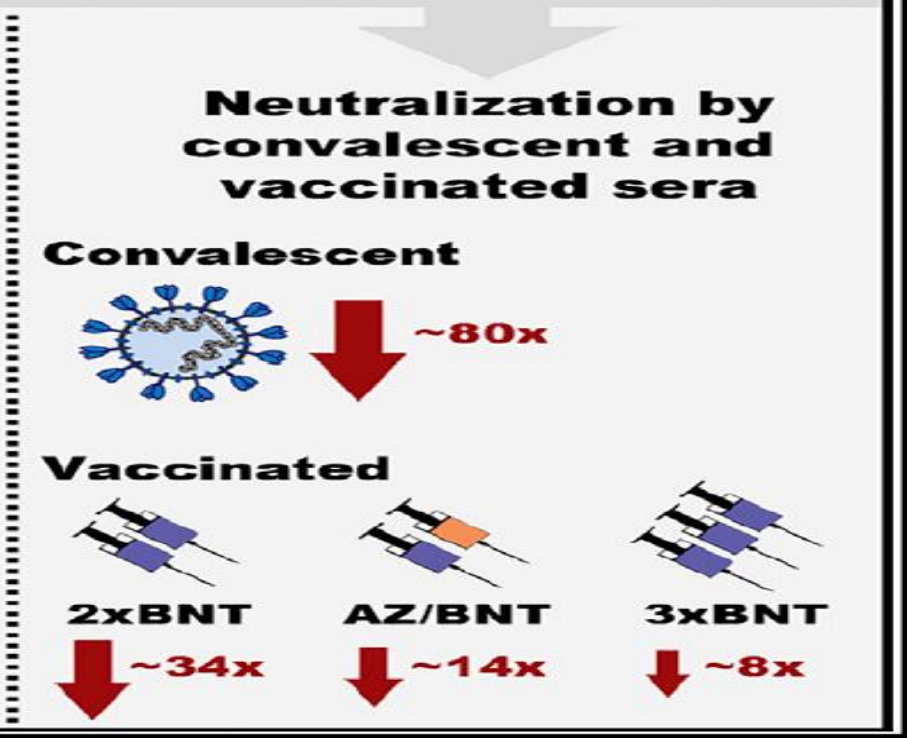
lisease waves in Houston Methodist patients. Number of new COVID-19 cases (*y* axis) totals are s shown in a different color. The first and second waves were composed of a heterogeneous array of shown in the third wave, the Delta VOC shown in the fourth wave, and the Omicron VOC shown in waves. The figure should not be interpreted to mean that all cases in the third, fourth, and fifth

Questions

- Increase in transmissibility or detrimental change in COVID-19 epidemiology
- Decrease in effectiveness of public health and social measures /available diagnostics, vaccines, therapy

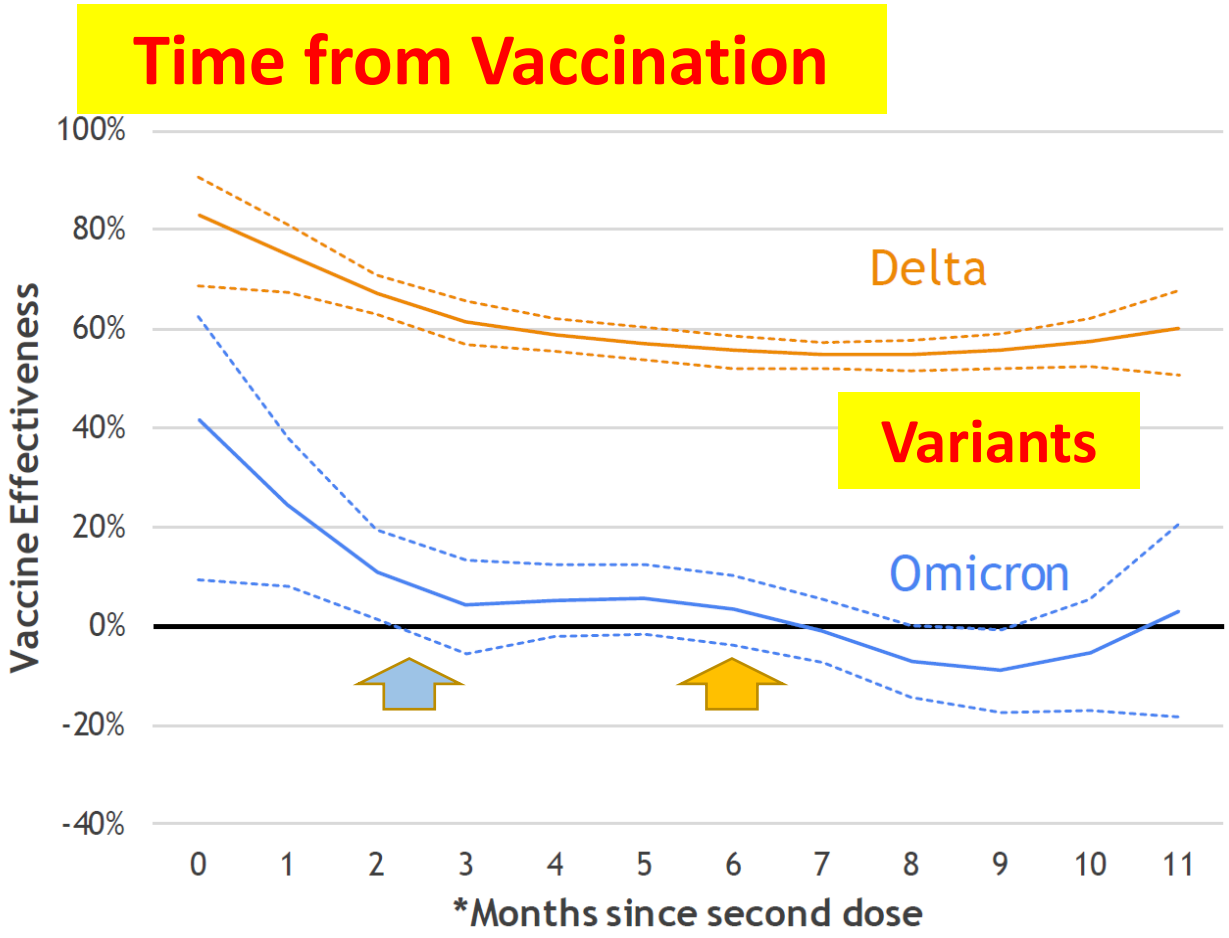
- *increase in virulence or change in clinical disease presentation*





Endpoint: infection | Population: adults

ICATT: Pfizer-BioNTech 2-dose VE against symptomatic infection by variant and time since 2nd dose receipt, adults aged ≥18 years, Dec 10, 2021-Jan 1, 2022



- VE for 2 doses of Pfizer-BioNTech against symptomatic Omicron infection:
  - Starts lower than 2-dose VE against Delta infection
  - No longer significant by 3 months after second dose receipt

VE for Delta
95% CI for Delta
VE for Omicron
95% CI for Omicron

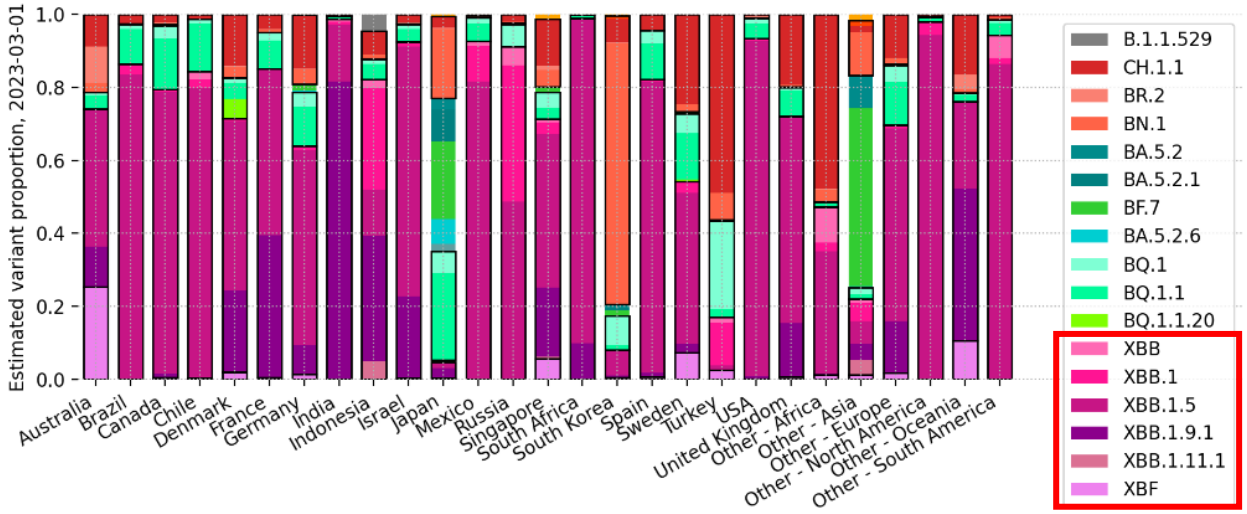
*Vaccination dose dates are collected as month and year. Month 0 represents tests in the same month as 2nd dose (at least 2 weeks after 2nd dose). For all months greater than or equal to 1 the value represents the difference between calendar month of test and calendar month of 2nd dose receipt (at least 2 weeks after 2nd dose).

Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants. JAMA. 2022;327(7):639-651. doi:10.1001/jama.2022.0470

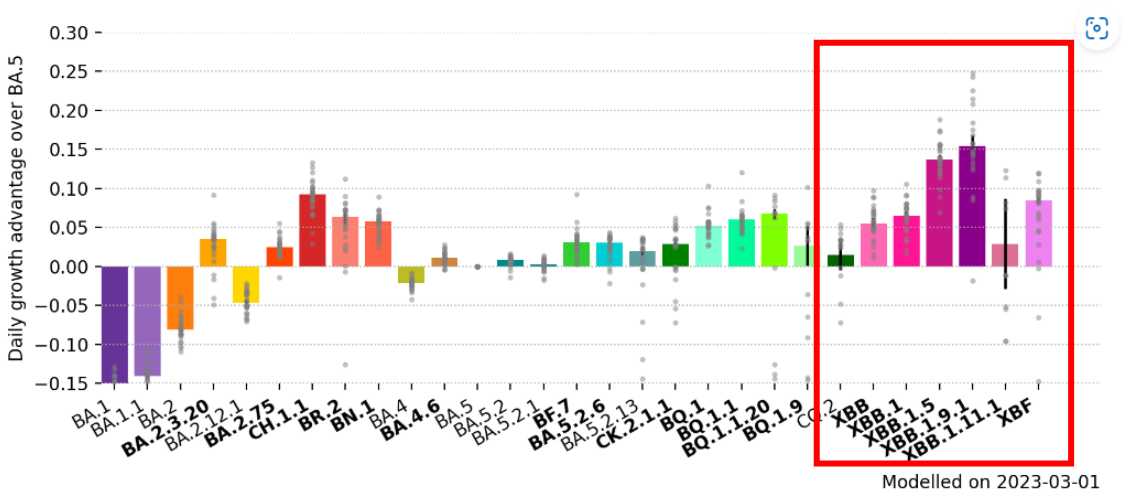
International SARS-CoV-2 genomic surveillance

- The repository uses the **genomicsurveillance** model to estimate daily growth rates of a variety of SARS-CoV-2 lineages in selected countries[1]
- Proportions change slowly as variant fitness equalize out and other BA.5* variants have largely disappeared[1]
- High levels of immunity due to vaccination or from previous infection are creating a selection pressure towards **immune-evading variants**[2]

Global latest estimated SARS-CoV-2 variant proportion[1]



Growth rate of SARS-CoV-2 variants[1]

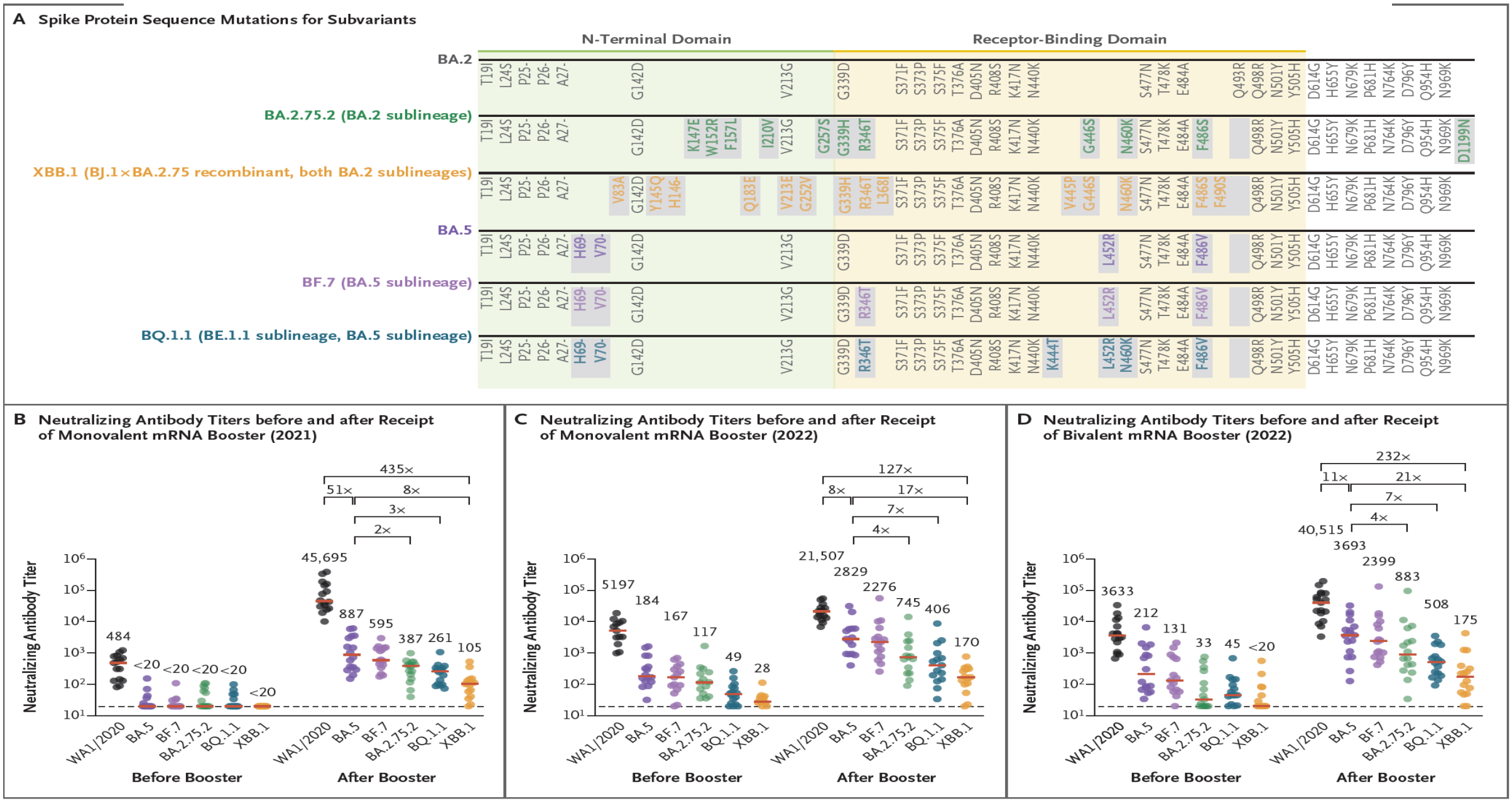


XBB and subvariants are predominant in most regions globally
These subvariants show higher growth rate compared to previous variants[1]

1. Gerstung M. International SARS-CoV-2 genomic surveillance. https://github.com/gerstung-lab/SARS-CoV-2-International . Accessed 07 March 2023.
2. Wong C. Subvariant 'soup' may drive wave. New Sci. 2022;256(3411):11. doi:10.1016/S0262-4079(22)01970-4

Substantial Neutralization Escape by SARS-CoV-2 Omicron Variants BQ.1.1 and XBB.1

Miller J; NEJM 2023



Article

Percentages of Vaccination Coverage Required to Establish Herd Immunity against SARS-CoV-2

Pedro Plans-Rubió [1,2]

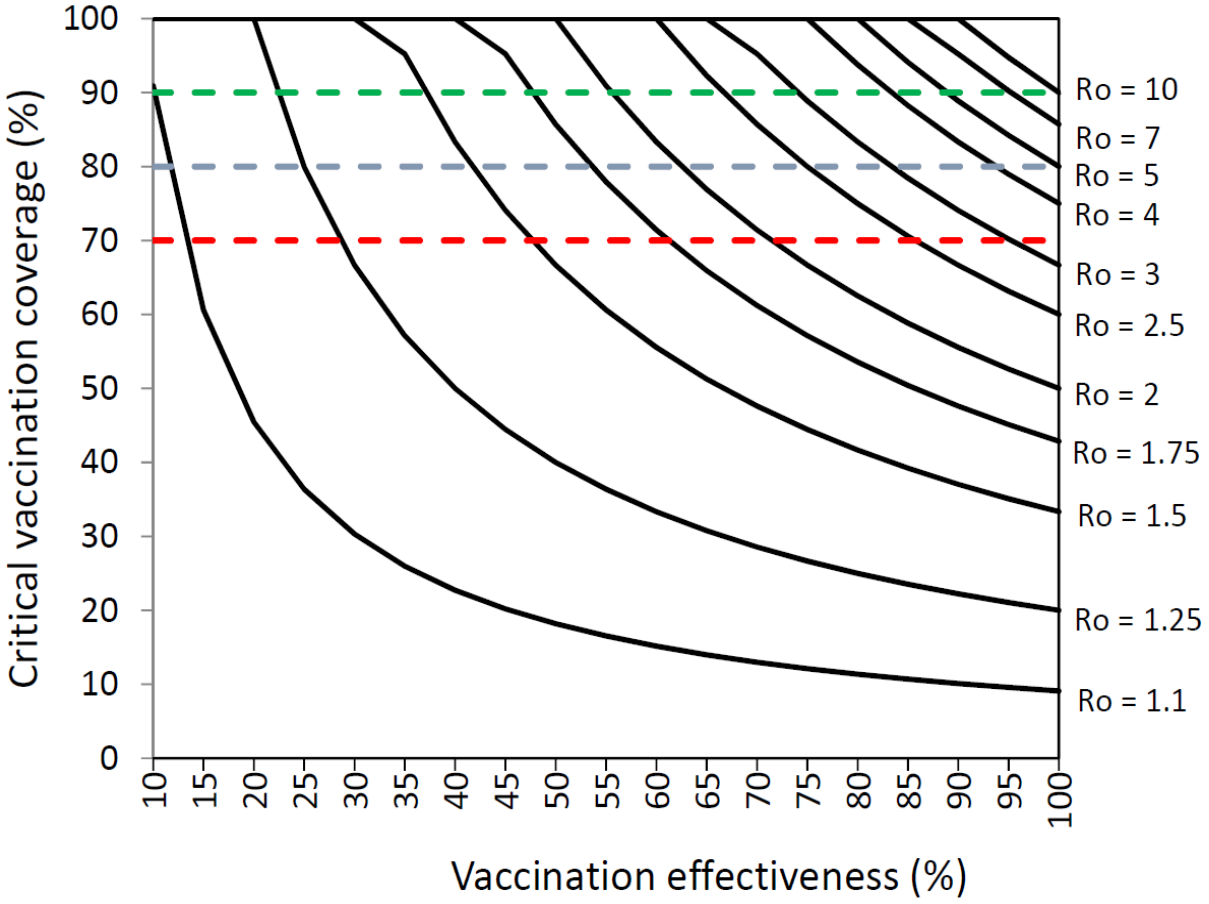


Figure 1. Vaccination coverage (%) required to establish herd immunity against SARS-CoV-2 with different reproductive numbers (Ro) by vaccination effectiveness (%). Objectives of vaccination coverage of 70%, 80%, and 90% are indicated with dashed red, blue, and green lines, respectively.

Two measures should be implemented to establish herd immunity against SARS-CoV-2:

(1) achieve 90% COVID-19 vaccination coverage in all countries worldwide
(2) increase the effectiveness of COVID-19 vaccines in preventing Omicron infection to at least 88%.

Factors reducing COVID-19 vaccination effectiveness
(emergent variants, infections among vaccinated individuals, high risk individuals)

Factors increasing SARS-CoV-2 transmissibility
(close settings)

COVID-19 will continue but the end of the pandemic is near

Christopher J L Murray; lancet: Vol 399 January 29, 2022

New SARS-CoV-2 variants will surely emerge and some may be more severe than omicron. Immunity, whether infection or vaccination derived, will wane, creating opportunities for continued SARS-CoV-2 transmission. *Given seasonality, countries should expect increased potential transmission in winter months.*

The impacts of future SARS-CoV-2 transmission on health, however, will be less because of broad previous exposure to the virus, regularly *adapted vaccines to new antigens or variants, the advent of antivirals, and the knowledge that the vulnerable can protect themselves during future waves* when needed by using high-quality masks and physical distancing.

COVID-19 will become another recurrent disease that health systems and societies will have to manage. The era of extraordinary measures by government and societies to control SARS-CoV-2 transmission will be over. After the omicron wave, COVID-19 will return but the pandemic will not.

Is omicron variant of SARS-CoV-2 coming to an end?

The Innovation (2022), doi: https://doi.org/10.1016/j.xinn.2022.100240.

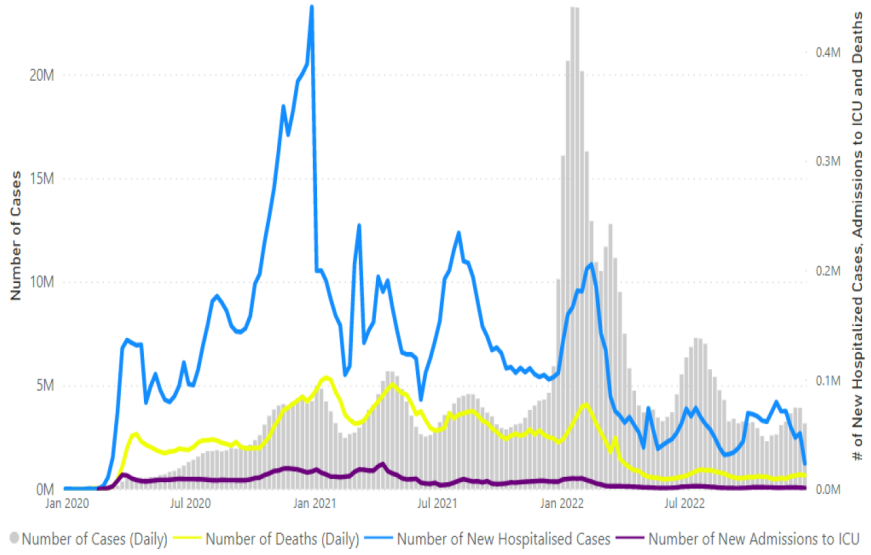
Yingjie Zhao,[1] Jianping Huang, [1,*] Li Zhang,[1,2] Xinbo Lian,[1,2] and Danfeng Wang[1]

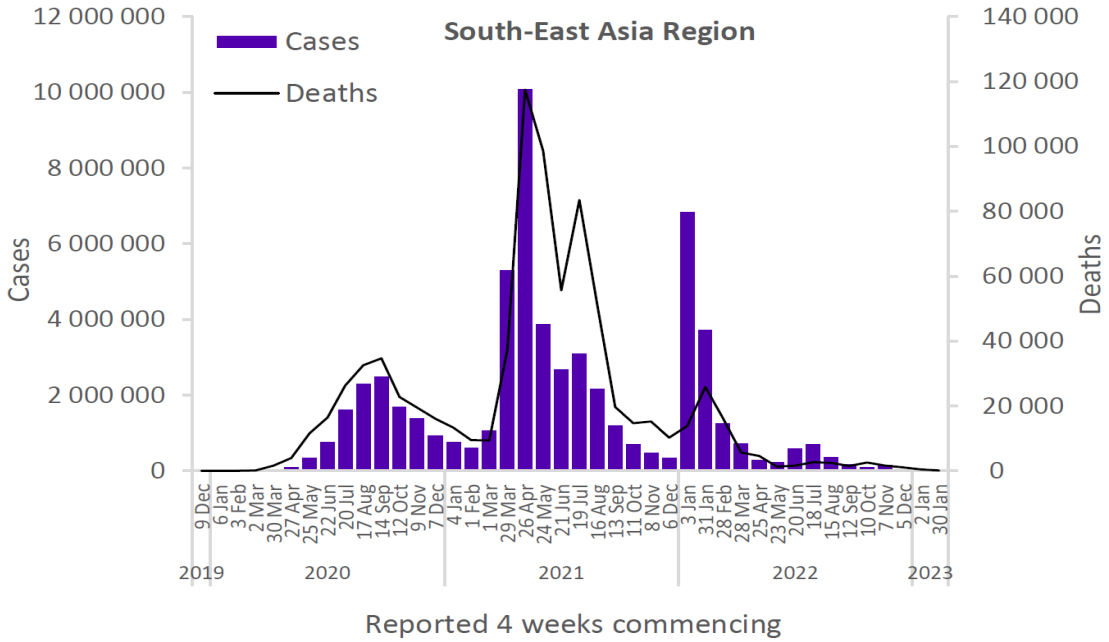
Is Omicron the end of pandemic or start of a new innings?

Swarnali Das [a], Sovan Samanta [a], Jhimli Banerjee [a], Amitava Pal [b], Biplab Giri [a], Suvrendu Sankar Kar [c,**], Sandeep Kumar Dash [a,*]

Travel Medicine and Infectious Disease 48 (2022) 102332

Figure 4. COVID-19 cases, deaths, hospitalizations, and ICU admissions reported weekly to WHO, as of 1 January 2023





Current Covid-19 (Omicron era):

- **Lower disease severity compared to infection due to previous SARS-CoV-2 variants**
- **High levels of population immunity acquired through vaccination and/or natural infection**

During this time, Risk of severe COVID-19 continues to be disproportionately greater in:

- Older age groups
- Residents in care homes for older adults,
- Persons with certain underlying health conditions

Compared to the initial phases of the pandemic, much more is now understood regarding SARS-CoV2 infection

STRATEGIES FOR OMICRON VARIANT / NEW VOC

- ***Interruption of SARS-CoV-2 variant spread:***

  Maintaining present public health prevention measures, including wearing masks, frequent ventilation, keeping physical distance, and washing hands.

  Early diagnosis (accuracy) and timely quarantine

- ***COVID-19 vaccination***

  Improving COVID-19 vaccine coverage:

  - Primary COVID-19 vaccines showed decreased effectiveness against Omicron, it has been shown that the vaccines remain effective in preventing severe diseases, hospitalization, and death.
  - Booster vaccination could undoubtedly help control the Omicron spread and infection

Developing variant-specific vaccines:

Previous study has shown that the vaccine based on the mutant spike would have a *higher level of neutralizing antibodies against mutant viruses, but lower neutralizing antibodies against wild-type SARS-CoV-2*.

Multivalent vaccine candidates

- ***Effective treatment (anticovid-19 agents/anti-inflammatory agents……)***

The allocation of COVID-19 vaccines and antivirals against emerging SARS-CoV-2 variants of concern (VOC)

- **Increased primary vaccination coverage**
- **Additional booster dose for high-risk population or all**
- ***Usage antiviral agents for symptomatic infections***

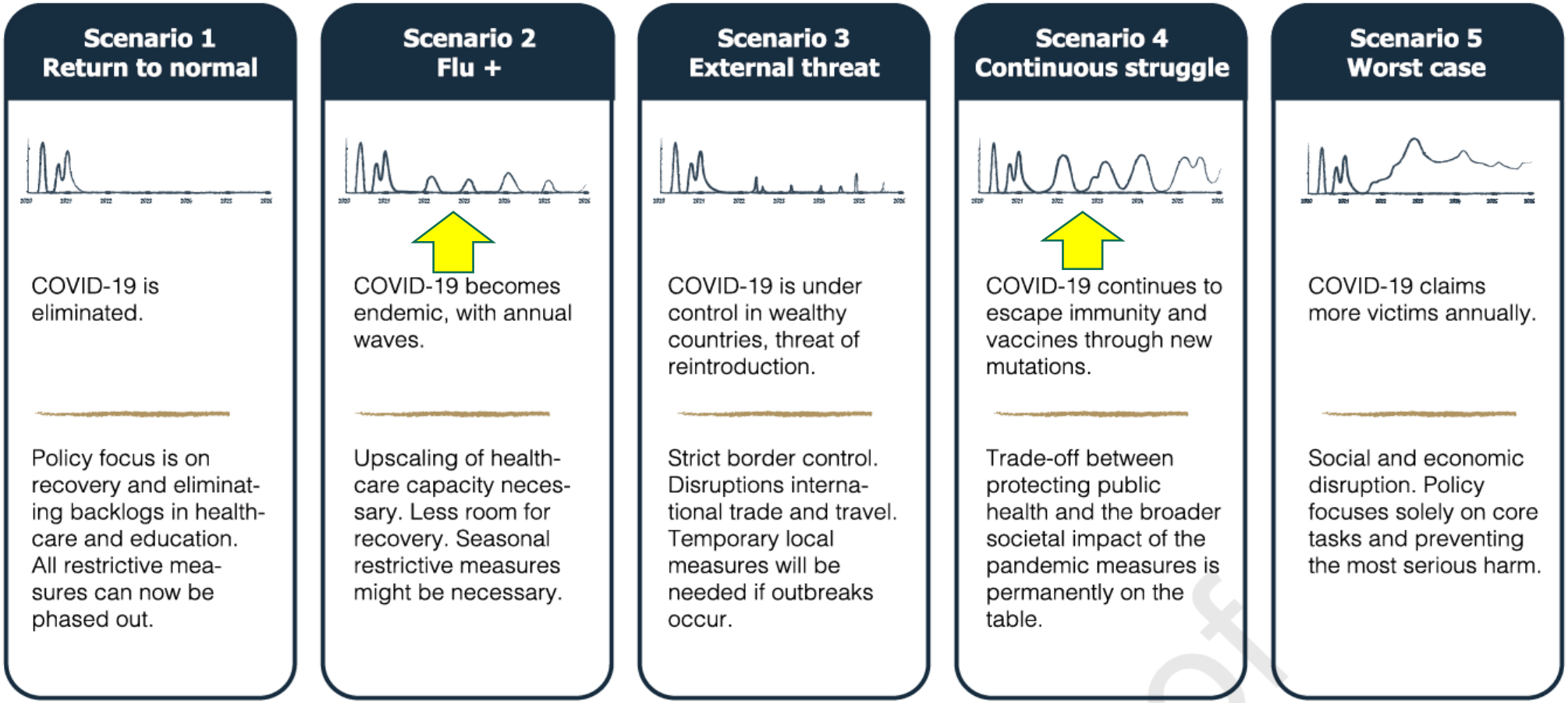
Aims: Reduced spreading of infection, reduced symptomatic infection, reduced hospitalization, reduced death, creating herd immunity, pandemic exit…….

Depend on:

- Types of vaccines and coverage of primary vaccination
- Effectiveness of primary vaccination
- Duration after primary vaccination (waning of nAb after primary vaccination)
- VOC against nAb (by natural infection or vaccination)
- Types of booster dose of vaccines (homologous or heterologous vaccination)
- Effectiveness of an booster dose of vaccine
- Effectiveness of antiviral agents

Kathy Leung;The Lancet Regional Health - Western Pacific 2022;21: 100389

SCENARIOS FOR THE POSSIBLE COURSE OF THE PANDEMIC



Frans Brom J Clin Epidemiol. 2022 (in proved)

Figure: Five exploratory scenarios for the possible course of the pandemic and its societal implications. *The graphs are illustrations visualising the five possible scenarios, not predictions of the course of the pandemic. The x-axis represents time; the y-axis was originally drafted to represent the fatalities, but could also be more broadly interpreted as clinically severe COVID-19 manifestations.*

Reaching the Final Endgame for Constant Waves of COVID-19

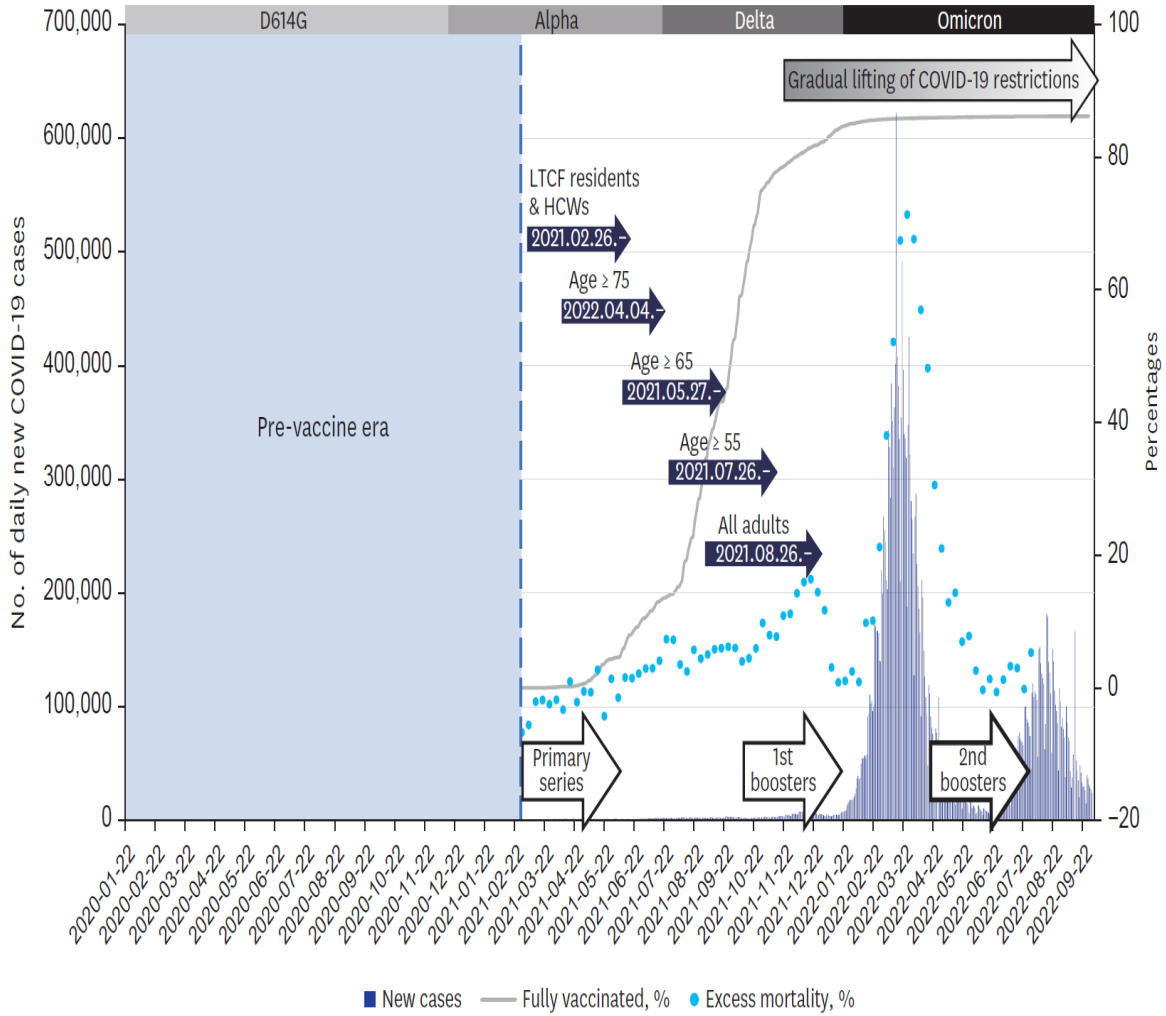


Fig. 2. Timeline of mass vaccination against COVID-19 in Korea. The blue vertical bars represent the number of daily new COVID-19 cases, the light blue dots represent weekly excess mortality (%), the grey curve represents the cumulative percentage of fully vaccinated individuals (i.e., completed primary series vaccination), and the dark blue arrows represent when each group became eligible for COVID-19 vaccines.
COVID-19 = coronavirus disease 2019, LTCF = long-term care facilities, HCWs = healthcare workers.

J Korean Med Sci. 2022 Dec 5;37(47):e351

MASS VACCINATION AND THE MITIGATION OF PANDEMIC WAVES

What's next:

-**Need for additional vaccinations** (target population and time interval between doses)
- Approval process for new COVID-19 vaccines
- **Need multivalent vaccines** that contain several VOC (pan-vaccine)
- Effective communication
- **Preparation for the next pandemic** (strategic, investments in vaccine development….)

Challenges

- **New VOCs** (increased transmission, virulent, resist to ab, diagnosis methods,….)
- **Multi-valent immunity (**vaccine coverage, hesitancy….)
- Supply of vaccines (inequity….)
- **New pan-coronavirus vaccine** (targeting more conserved protein sequences)
- **Roles of non-pharmaceutical intervention**
- **New and better antiviral therapy**
- Control zoonosis and human interaction
- Strong international cooperation among all stakeholders

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Overview:

- **Burden of covid-19 and future directions**

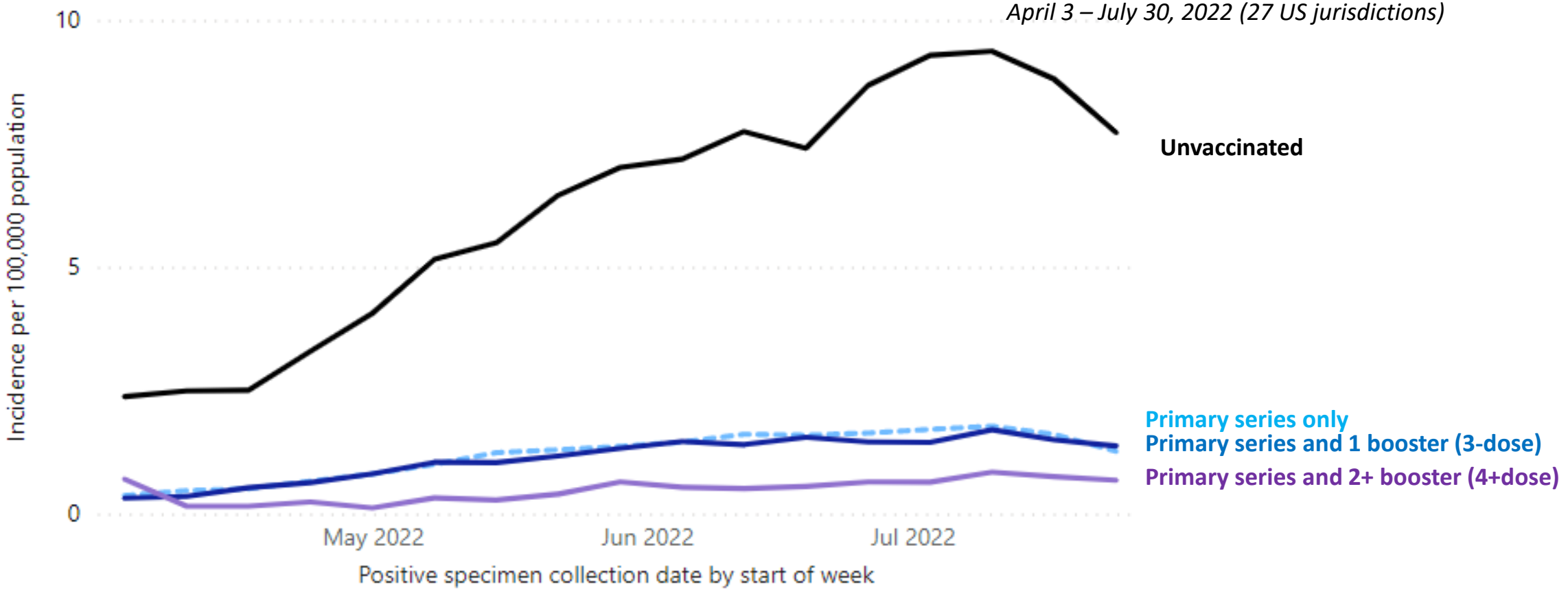
- **Strategies for Covid-19 vaccination:**
  - **Increased coverage of primary vaccination**
  - **Appropriate booster vaccination** *(Target population, types of vaccine, immune response, effectiveness, safety, interval, feasibility and acceptation.)*

Added benefit against COVID-19 related mortality conferred by 2+ doses of mRNA booster vaccination during Omicron period

0 vs 2 vs 3 vs 4 dose

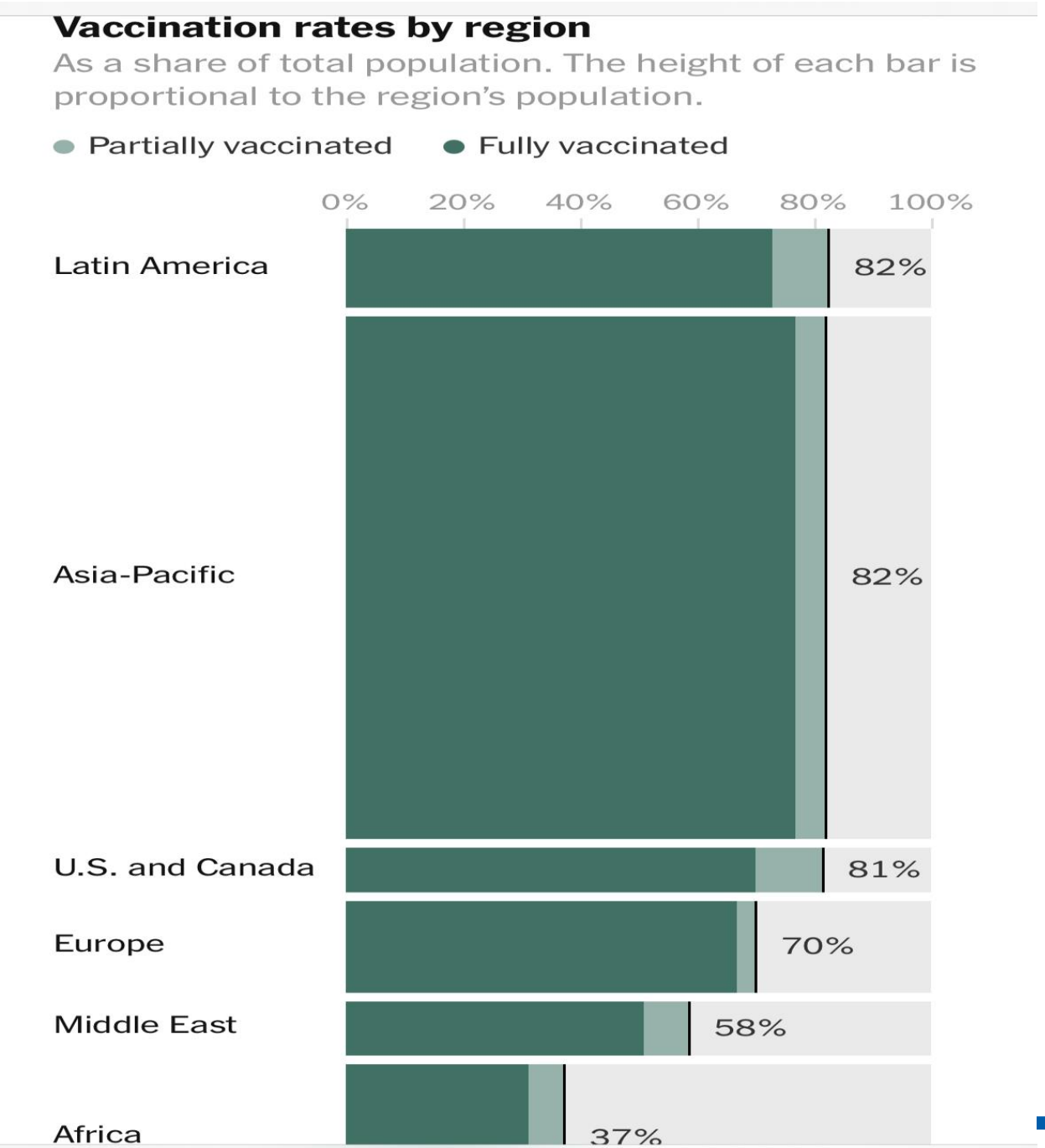
Death rates by vaccination status and receipt of 1st and 2nd booster doses among people ages ≥50 years

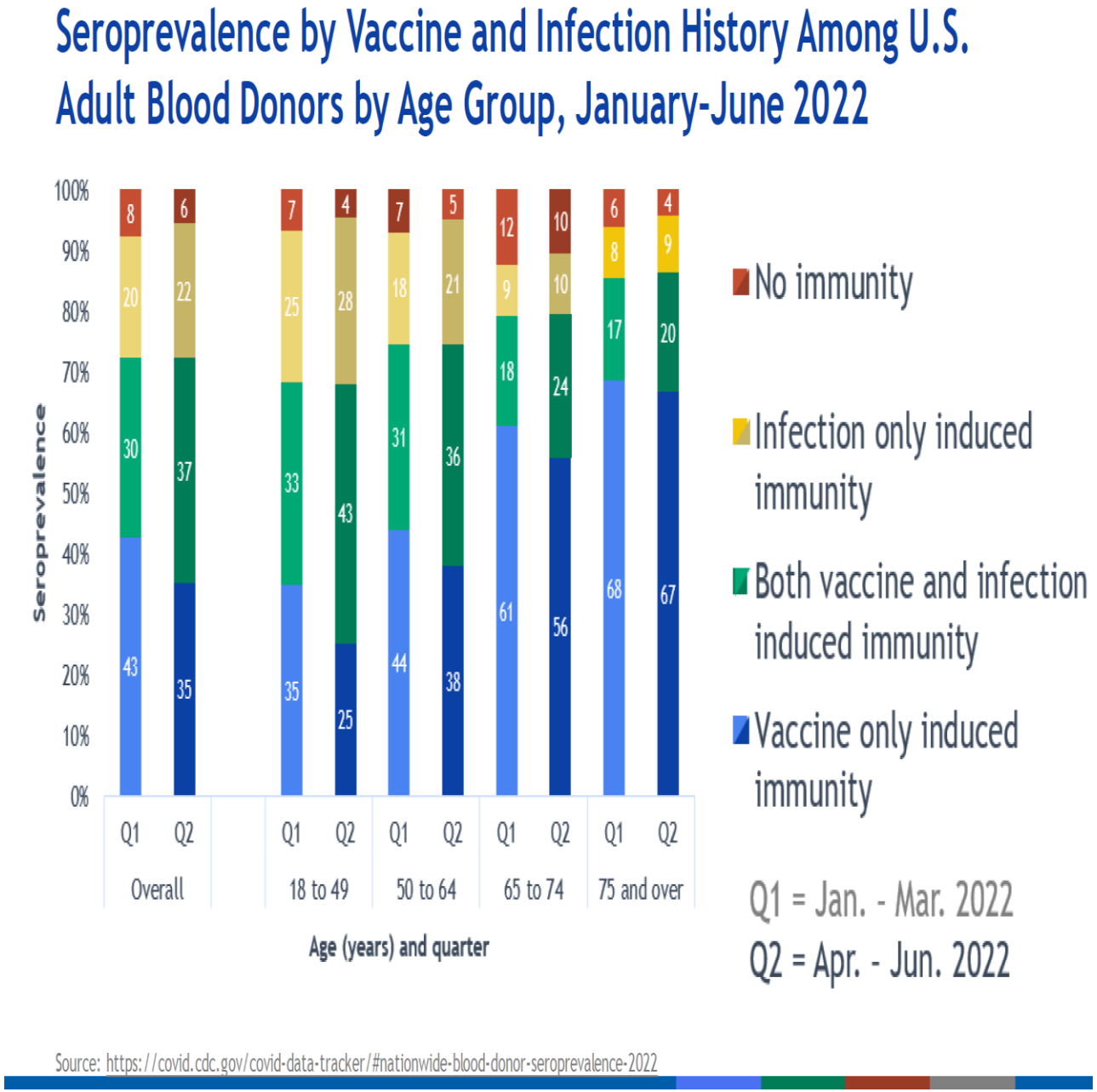
April 3 – July 30, 2022 (27 US jurisdictions)



In July 2022, peoples ages ≥50 years with **≥ 2+ booster doses** had

- **12 times lower risk of dying** from COVID-19, compared to **unvaccinated people** and
- **2 times lower risk of dying** than **people with 1 booster**





Source: https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence-2022

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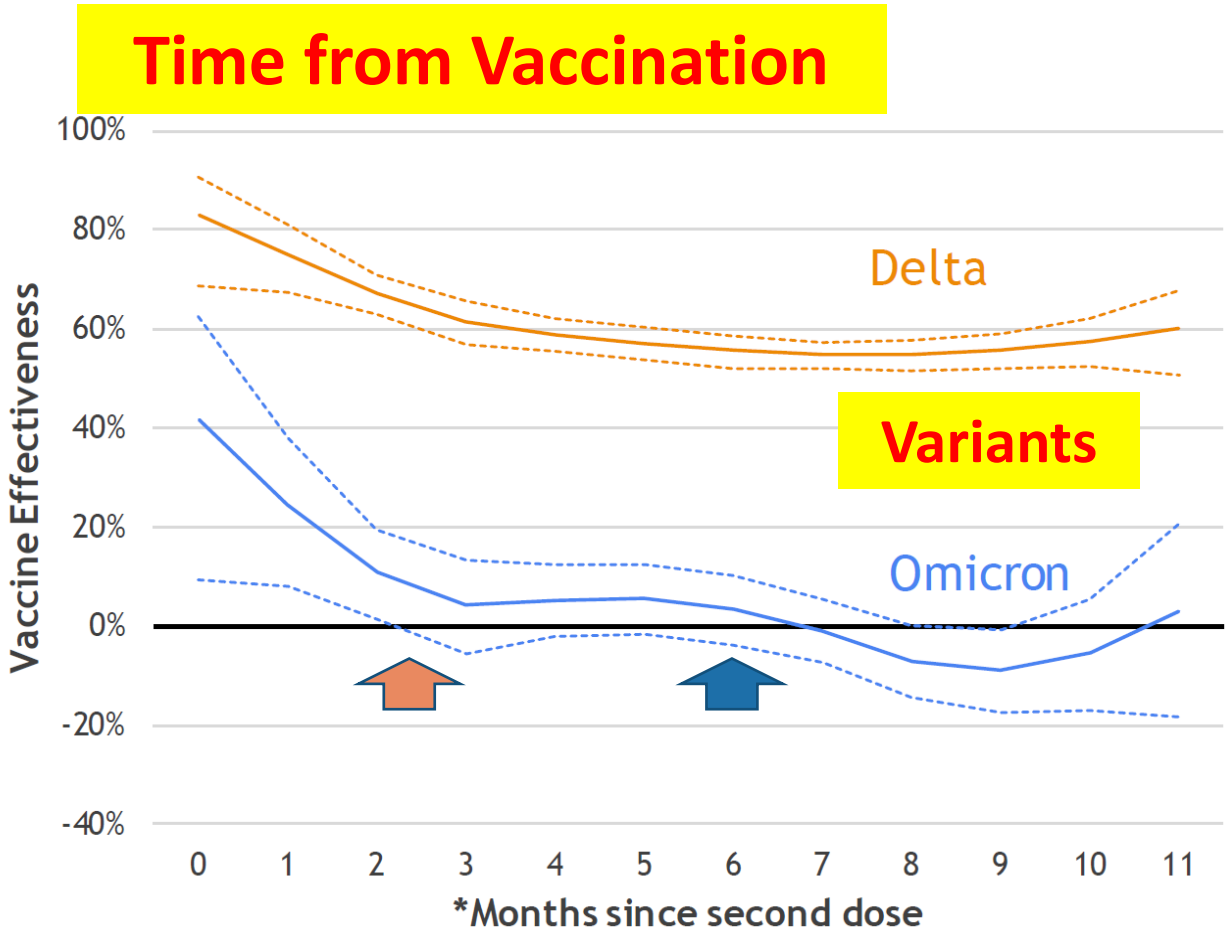

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95% CI for Delta
VE for Omicron
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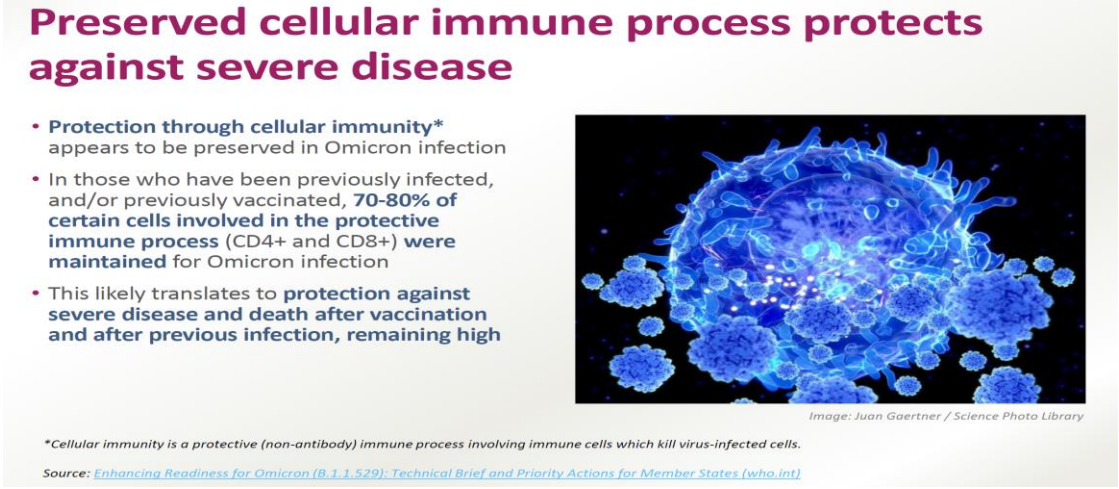
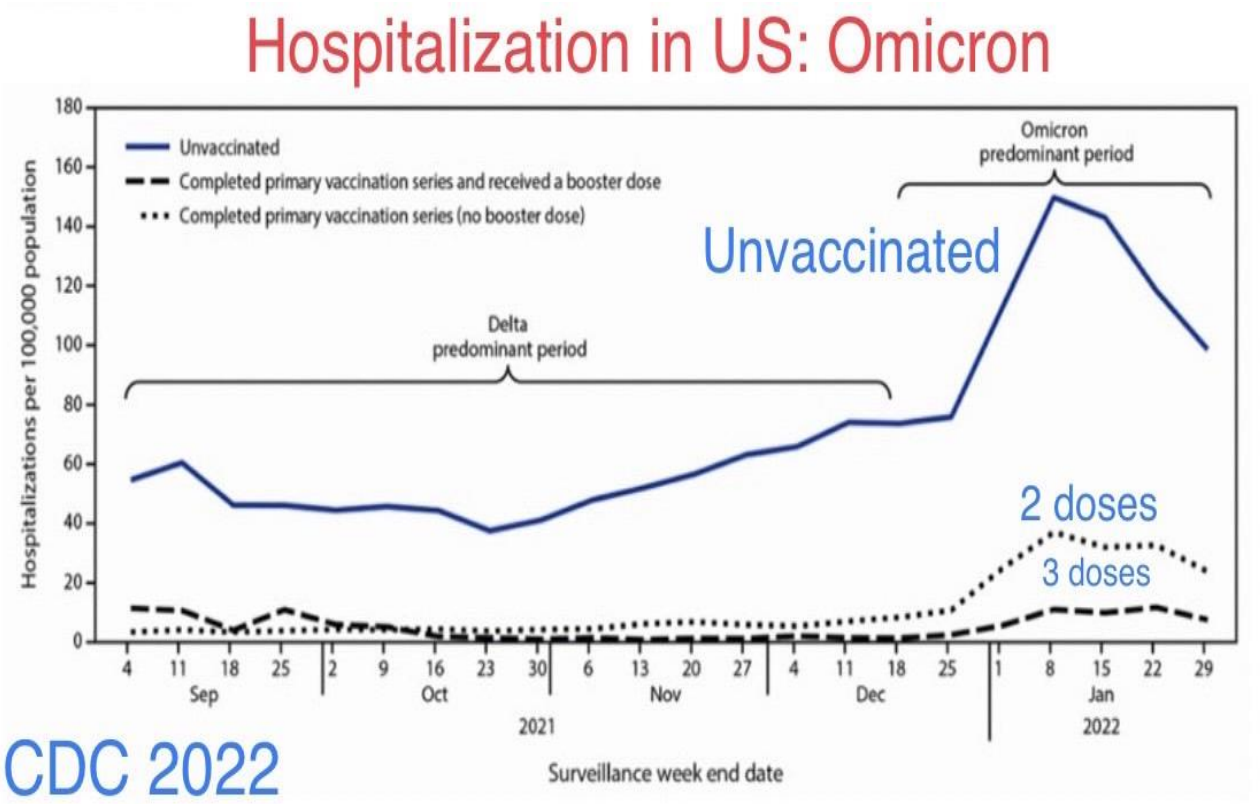
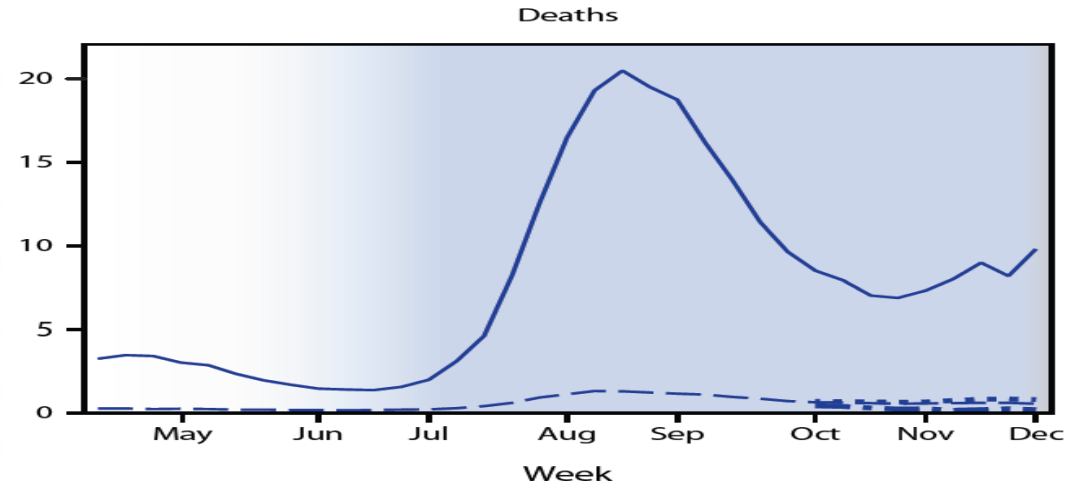
The allocation of COVID-19 vaccines against SARS-CoV-2 variants of concern (VOC)

- **Increased primary vaccination coverage (unvaccinated and naïve people)**

Aims: *Reduced spreading of infection, reduced symptomatic infection, reduced hospitalization, reduced death, creating herd immunity, pandemic exit…….*



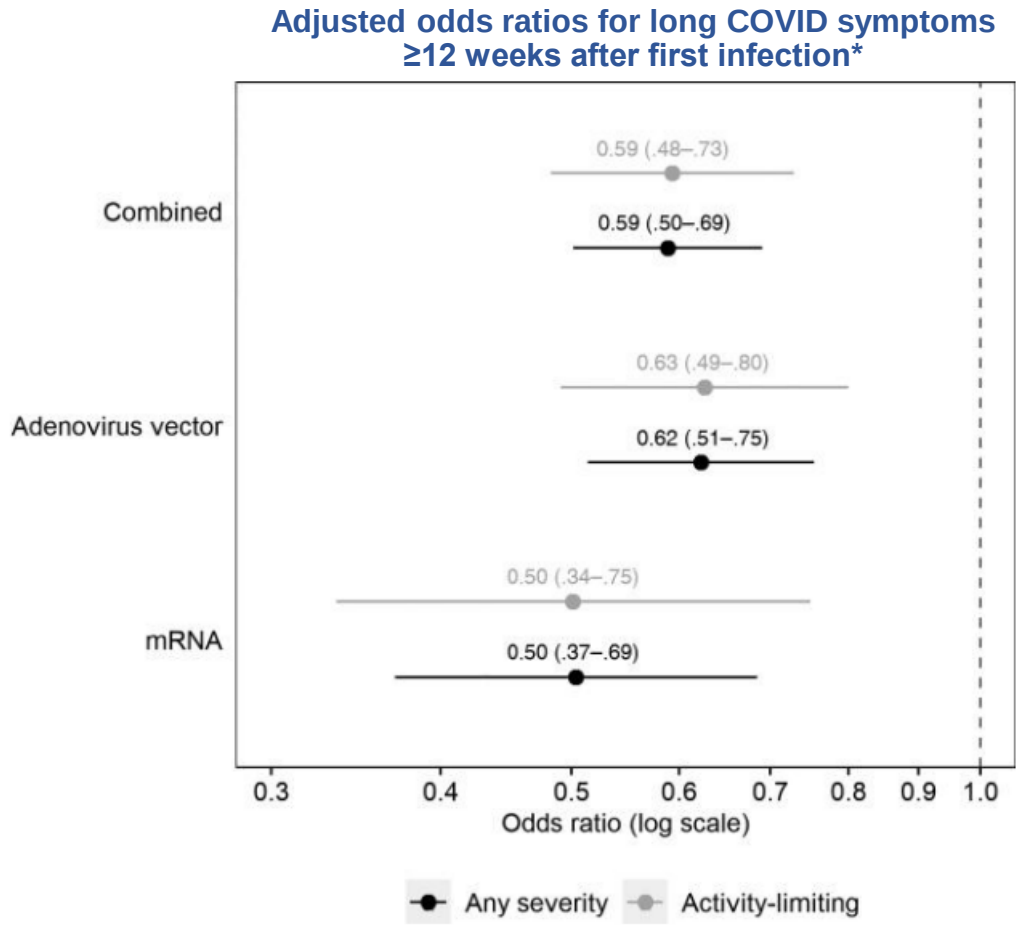




ther SARS-CoV-2 lineages
ARS-CoV-2 B.1.617.2 (Delta) variant
ARS-CoV-2 B.1.1.529 (Omicron) variant

COVID-19 Vaccination Associated with Lower Risk of Long COVID

A community-based, matched cohort study, data from UK COVID-19 Infection Survey (CIS), April 2020 to November 2021



- Participants aged **18-69 years** who tested positive for SARS-CoV-2 by PCR or self-reported between April 2020-November 2021
- **Exposure of interest:** Receipt of at least 2 doses of ChAdOx1 (AstraZenaca), BNT162b2 (Pfizer) or mRNA-1273 (Moderna) ≥14 days before confirmed infection. Data from survey data linked to National Immunisation Management System (NIMS) records

COVID-19 vaccinations (any) was associated with **41%** decrease in the odds of developing long COVID symptoms at least 12 weeks later

mRNA vaccines

50%

(95% CI: 37-69)

Decrease odds of developing long COVID

*Comparing matched study participants who were double-vaccinated or unvaccinated (reference group) before infection. Odds ratios adjusted for sociodemographic characteristics (age, sex, White or non-White ethnicity, country/region of residence, area deprivation quintile group, and self-reported, preexisting health/ disability status) and time from infection to follow-up for long COVID.

Ayoubkhani, et al. *Open Forum Infect Dis*. 2022 Sep; 9(9): ofac464.

Unmet Medical Need in Children Aged 6 Months to <5 Years

- **Severe COVID-19 occurs in children <5 years of age**
  - As of May 2022, 45,000 hospitalizations1(24% require ICU)[1,2] and 475 deaths[3]
  - Roughly 50% of these hospitalizations were likely due to Omicron[4]
  - Burden comparable to influenza –for which children are routinely immunized[5]

- **Severe COVID-19 outcomes are unpredictable and can occur in healthy children**
  - 64% of hospitalizations in children <5 years occur in those without comorbidities[2]

- **COVID-19 can cause additional long-term sequelae in children**
  - 3–6% of children report continued symptoms for >12 weeks[6]

- **Pandemic adversely impacts developmental and psychosocial well-being[7]**

1.Hospitalizations through May 14, 2022. CDC COVID Data Tracker. COVID-NET Laboratory-confirmed COVID-19 hospitalizations.Available from:https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalization-network. May 20, 2022; Counts computed from rates and population size.
2.Marks KJ, Whitaker M, Agathis NT, et al. Hospitalization of Infants and Children Aged 0–4 Years with Laboratory-Confirmed COVID-19 —COVID-NET, 14 States, March 2020–February 2022. MMWR 2022; 71:429-436. doi: http://dx.doi.org/10.15585/mmwr.mm7111e2
3.Deaths through May 19, 2022. CDC COVID Data Tracker. Demographic Trends of COVID-19 cases and deaths in the US reported to CDC. Available from: https://covid.cdc.gov/covid-data-tracker/#demographics
4.Computed by multiplying weekly hospitalization counts from CDC COVID Data Tracker by the biweekly proportion of specimens testing positive for Omicron from CoVariants.org
5.DelahoyMJ, Ujamaa D, Taylor CA, et al. Comparison of Influenza and COVID-19-Associated Hospitalizations among Children < 18 Years Old in the United States-FluSurv-NET (October-April 2017-2021) and COVID-NET (October 2020-September 2021). Clin Infect Dis 2022; May 20:ciac388. doi: 10.1093/cid/ciac388.
6.Office for National Statistics United Kingdom. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 6 May 2022, Table 2 [updated May 6, 2022]. Available from:
https://www.ons.gov.uk/file?uri=%2fpeoplepopulationandcommunity%2fhealthandsocialcare%2fconditionsanddiseases%2fdatasets%2falldatarelatingtoprevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk%2f6may2022/ongoingsymptomsfollowingcovid19220220506accessible.xlsx.
7.Centers for Disease Control and Prevention. COVID-19 Parental Resources Kit –Early Childhood [updated February 28, 2022]. Available from: https://www.cdc.gov/mentalhealth/stress-coping/parental-resources/early-childhood/index.html

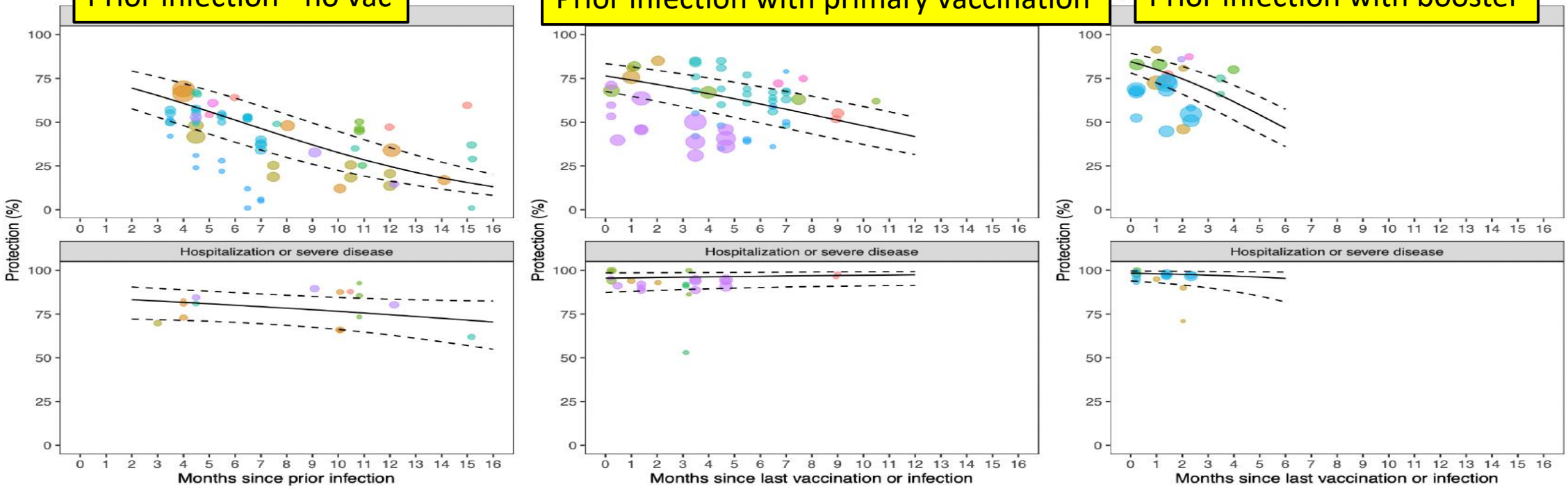
Protective effectiveness of prior SARS-CoV-2 infection and hybrid immunity against Omicron infection and severe disease: a systematic review and meta-regression

Figure 2. Protection against Omicron conferred by prior infection or hybrid immunity compared to immune naive over time

Prior infection –no vac

Prior infection with primary vaccination

Prior infection with booster



This analysis uses a log-odds meta-regression model. Points of the same color represent estimates from the same study. The diameter of points varies with the sample size of the study. Dotted lines represent 95% confidence intervals.

Combination of previous infection and primary vaccination provided better protection against Omicron infection than either one alone.

medRxiv preprint doi: https://doi.org/10.1101/2022.10.02.22280610; this version posted October 24, 2022.

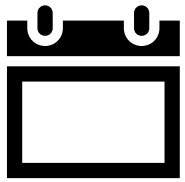
Covid-19: What's Next?

Overview:

- Burden of covid-19 and future directions
- **Strategies for Covid-19 vaccination:**
  - Increased coverage of primary vaccination
  - **Appropriate booster vaccination** *(Target population, types of vaccine, immune response, effectiveness, safety, interval, feasibility and acceptation.)*

Factors that can affect breakthrough infections

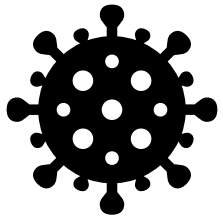
Time from Vaccination



Studies have shown that neutralising antibodies wane six months post vaccination. Although its correlation to vaccine effectiveness has not been thoroughly studied.

Interval 6-12 Mo

Variants



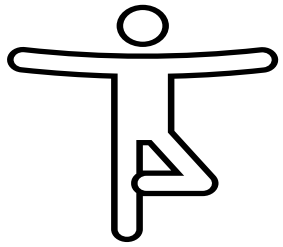
It has been shown that there is decreased sensitivity of neutralizing antibody levels against the variants compared to the wild type. Although RWE showed that the present vaccines confer protection against variants of concern.

Multi-variant vaccine

Vaccine Type

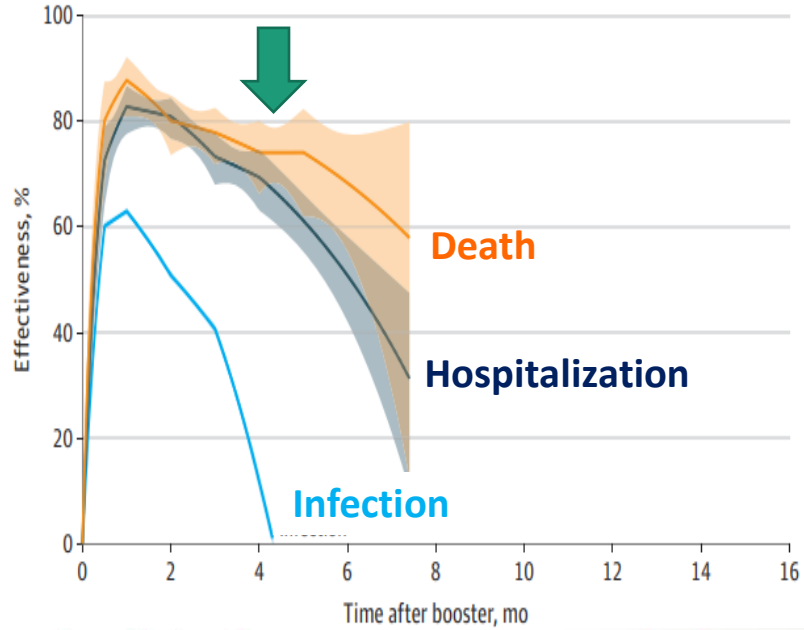
Vaccine efficacy from clinical trial and vaccine effectiveness from real world evidence vary from one vaccine type to another.

Immune System



Immunocompromised individuals might not have the ability to produce adequate antibodies to fight the infection even after vaccination.

Effectiveness of booster vs primary series alone among previously uninfected participants



Preserved cellular immune process protects against severe disease

- **Protection through cellular immunity*** appears to be preserved in Omicron infection
- In those who have been previously infected, and/or previously vaccinated, **70-80% of certain cells involved in the protective immune process** (CD4+ and CD8+) **were maintained** for Omicron infection
- This likely translates to **protection against severe disease and death after vaccination and after previous infection, remaining high**

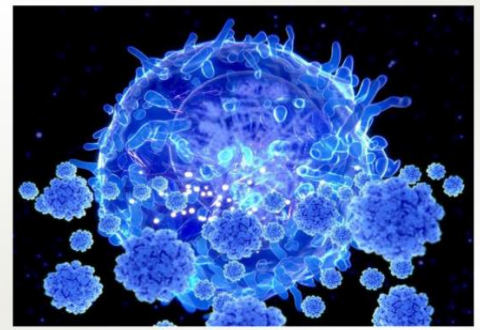


Image: Juan Gaertner / Science Photo Library

*Cellular immunity is a protective (non-antibody) immune process involving immune cells which kill virus-infected cells.

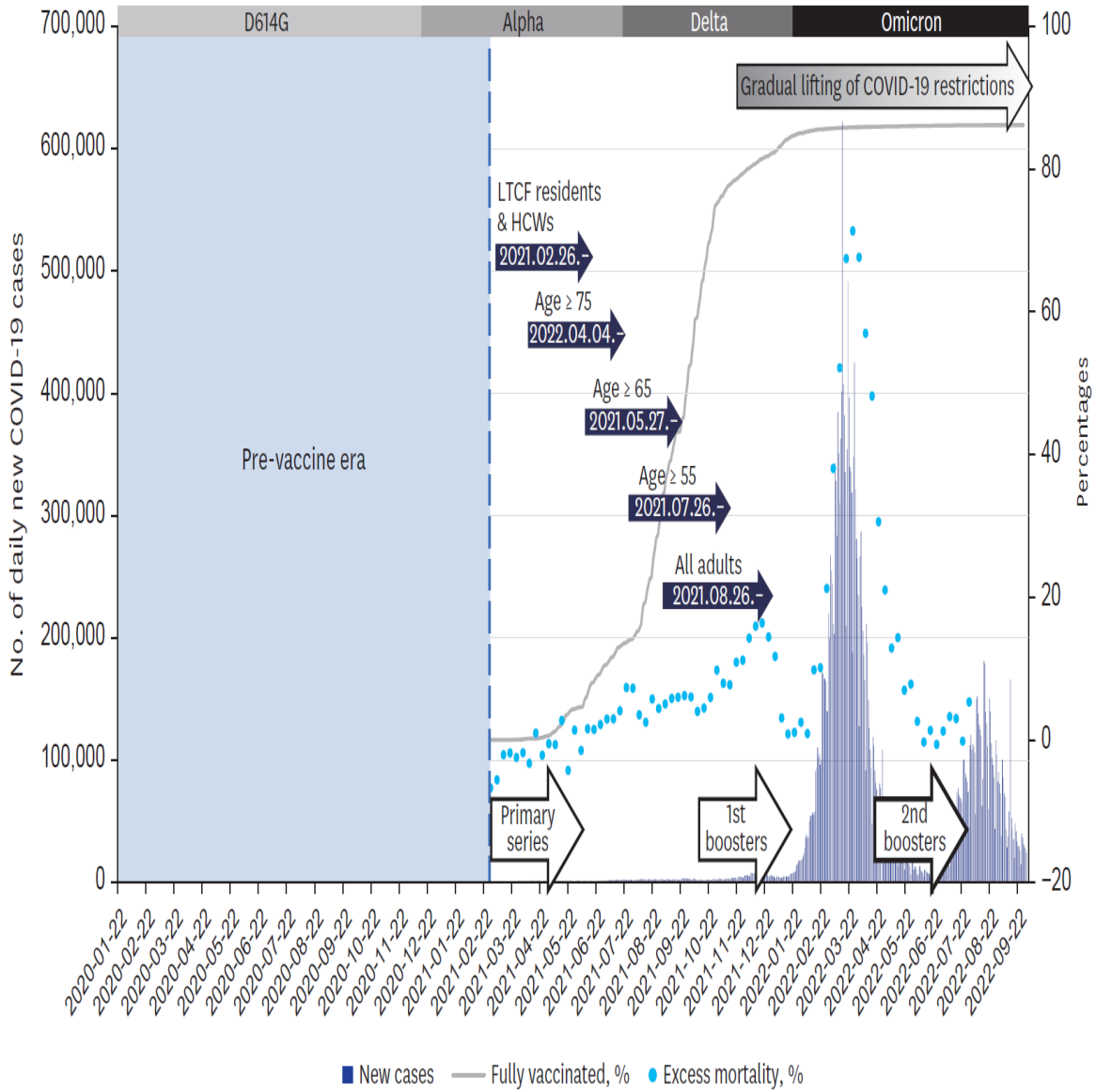
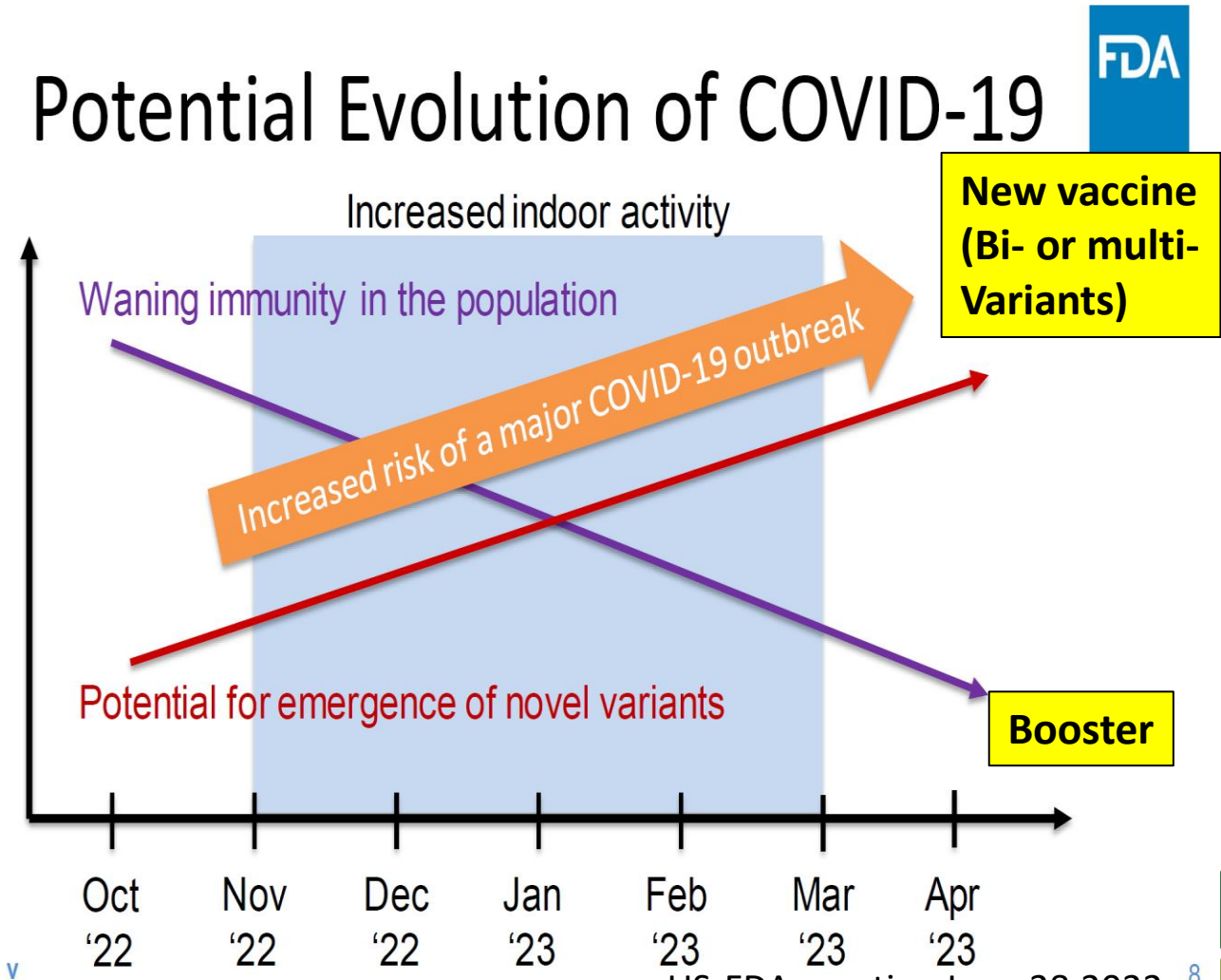


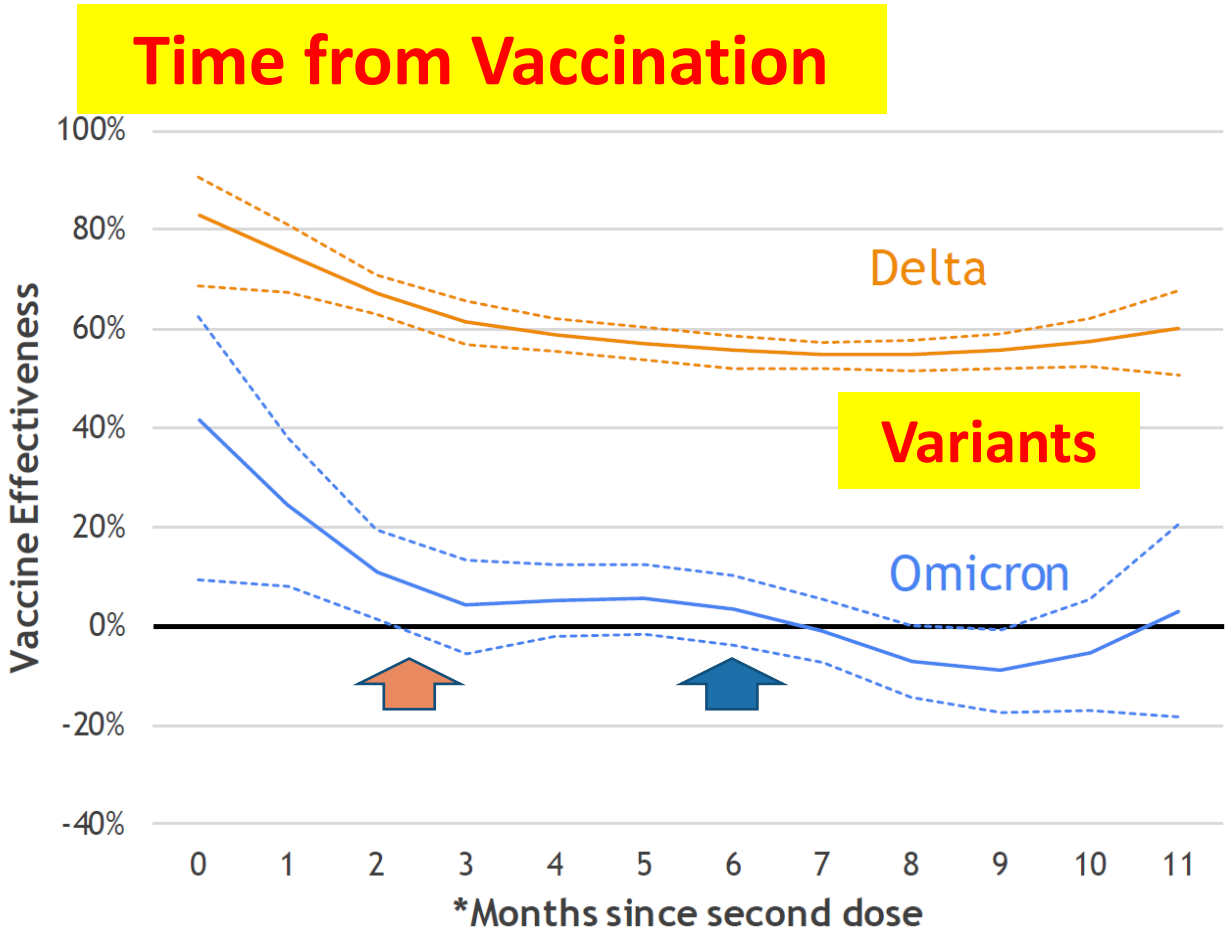
Fig. 2. Timeline of mass vaccination against COVID-19 in Korea. The blue vertical bars represent the number of daily new COVID-19 cases, the light blue dots represent weekly excess mortality (%), the grey curve represents the cumulative percentage of fully vaccinated individuals (i.e., completed primary series vaccination), and the dark blue arrows represent when each group became eligible for COVID-19 vaccines.
COVID-19 = coronavirus disease 2019, LTCF = long-term care facilities, HCWs = healthcare workers.



US-FDA meeting June 28,2022

Endpoint: infection | Population: adults

ICATT: Pfizer-BioNTech 2-dose VE against symptomatic infection by variant and time since 2nd dose receipt, adults aged ≥18 years, Dec 10, 2021-Jan 1, 2022



- VE for 2 doses of Pfizer-BioNTech against symptomatic Omicron infection:
  - Starts lower than 2-dose VE against Delta infection
  - No longer significant by 3 months after second dose receipt

VE for Delta
95% CI for Delta
VE for Omicron
95% CI for Omicron

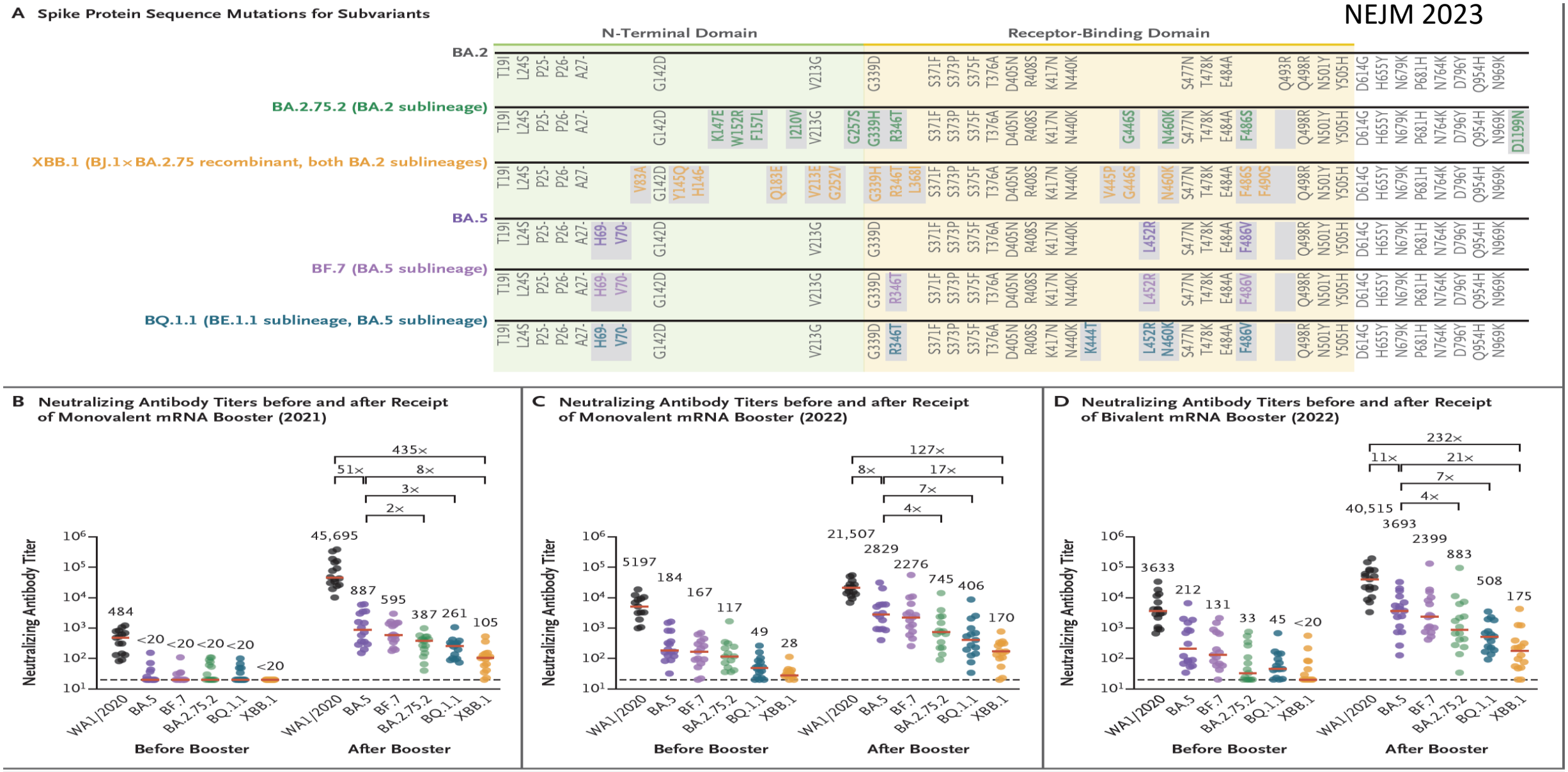
*Vaccination dose dates are collected as month and year. Month 0 represents tests in the same month as 2nd dose (at least 2 weeks after 2nd dose). For all months greater than or equal to 1 the value represents the difference between calendar month of test and calendar month of 2nd dose receipt (at least 2 weeks after 2nd dose).

Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants. JAMA. 2022;327(7):639-651. doi:10.1001/jama.2022.0470

Substantial Neutralization Escape by SARS-CoV-2 Omicron Variants BQ.1.1 and XBB.1

Jessica Miller, B.S.

NEJM 2023



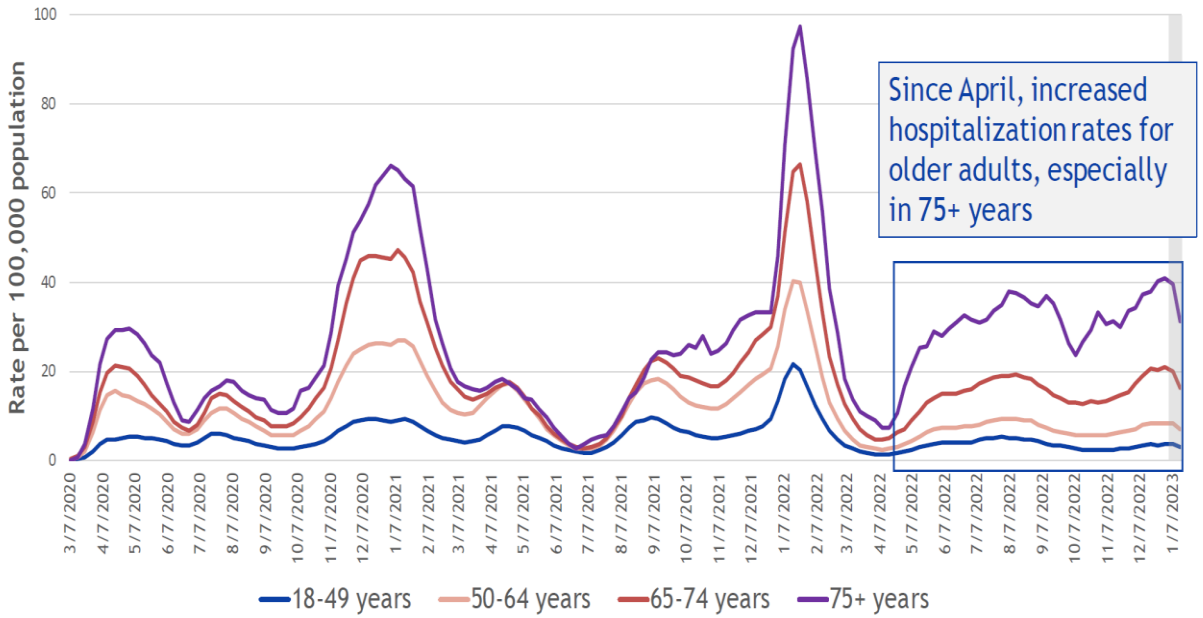
The allocation of COVID-19 vaccines against SARS-CoV-2 variants of concern (VOC)

- **Additional booster dose for high-risk population or all**

Aims: *Reduced spreading of infection, reduced symptomatic infection, reduced hospitalization, reduced death, creating herd immunity, pandemic exit……*

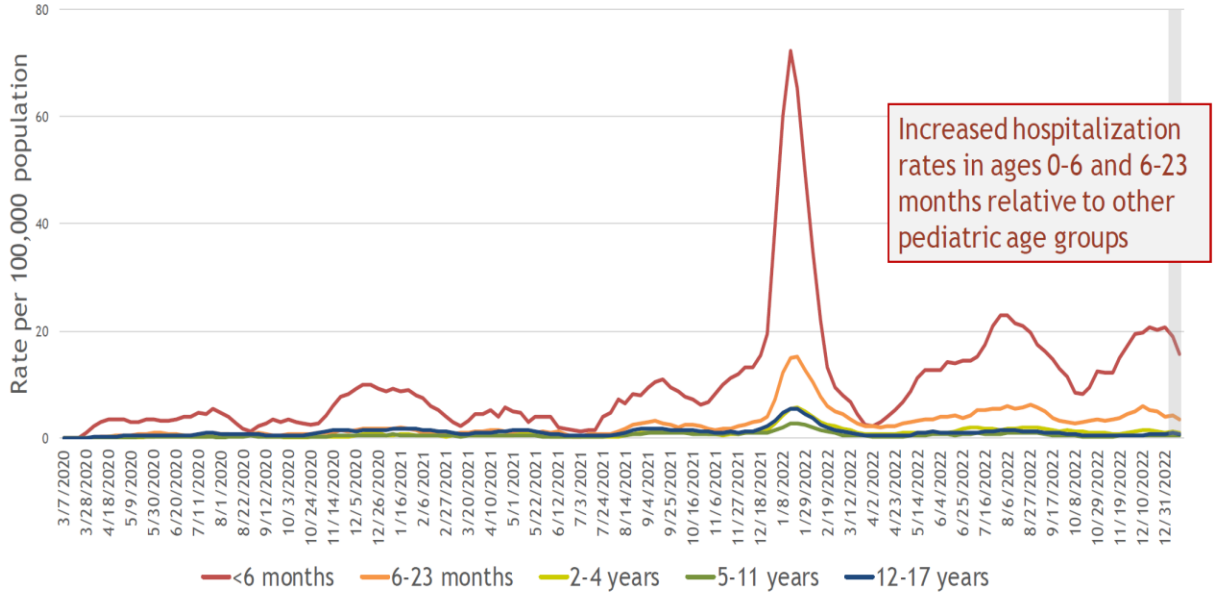
Weekly Trends in COVID-19-Associated Hospitalization Rates (3-Week Moving Average) Among Adults by Age Group

COVID-NET, March 2020 - January 14, 2023



COVID-19-Associated Hospitalization Rates (3-Week Moving Average) in Children by Age Group

COVID-NET, March 2020 - January 14, 2023



Source: COVID-NET; https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html Accessed Jan 20, 2022. Grey shaded area denotes the most recent 2 weeks where reporting is <95% complete .

Bi-valant booster vaccines to address Omicron

Moderna

- Extensive evaluation of 3 monovalent and 4 bivalent investigational variant vaccines in past year
  - >7,000 individuals boosted across all variant vaccine candidates
- Bivalent vaccine candidates include:

Wuhan strain plus Omicron strain

BA.1 Omicron-containing vaccine (mRNA-1273.214)

25 µg Original SARS-CoV-2 + 25 µg Omicron Variant (BA.1)

BA.4/BA.5 Omicron-containing vaccine (mRNA-1273.222)

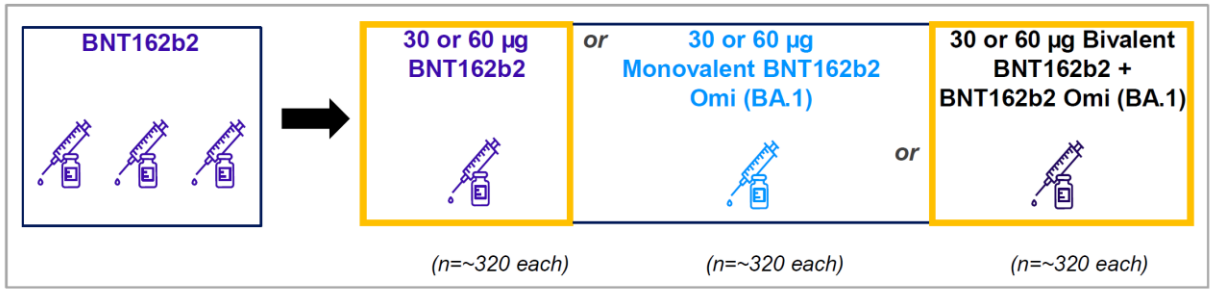
25 µg Original SARS-CoV-2 + 25 µg Omicron Variant (BA.4/BA.5)

Pfizer

Modified Vaccine	Age Group	Vaccine Regimen	Clinical Data	Preclinical Data
Omicron BA.1 *monovalent*	18-55y		✓	✓
			✓	✓
Omicron BA.1 *bivalent*	>55y		✓	✓
Omicron BA.4/5 *bivalent*	12-55y, >55y		Study Ongoing	✓

Clinical Study to Evaluate Monovalent and Bivalent Omicron BA.1-modified Vaccine Candidates in Vaccine-experienced Participants
>55y Participants

C4591031 Substudy E Evaluates Safety & Immunogenicity in ~1920 participants >55 Years



Dose 4 administered a median of 6.3 months (4.7, 12.9) from Dose 3

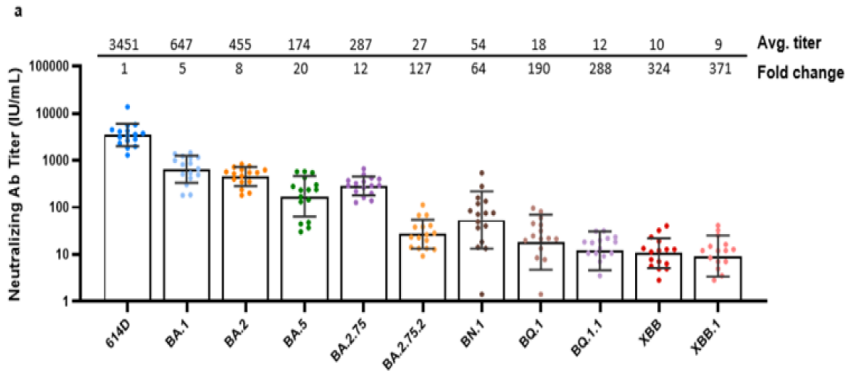
Monovalent BNT162b2 Omi (BA.1) 60 µg (N~330), bivalent BNT162b2 + BNT162b2 Omi (BA.1) 30 µg (N~180) and 60 µg (N~480) also being evaluated in participants 18-55 years of age

ACIP Meeting – 1 Sep - Dr. J Miller & Dr. K Swanson presentation https://www.cdc.gov/vaccines/acip/meetings/slides-2022-09-01-02.html

Neutralization Activity of Monovalent Booster Sera (2021) and Bivalent Booster (2022) Sera Against Omicron Lineages

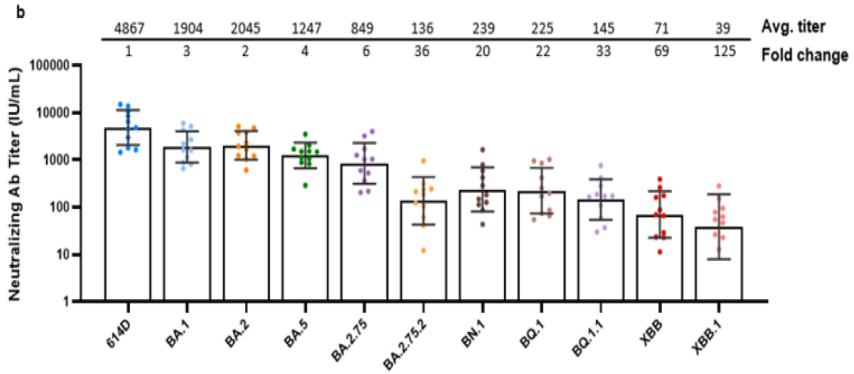
Monovalent Booster

3 monovalent doses in total,
sera collected 2-6 weeks after last dose



Bivalent Booster

3 monovalent doses + 1 bivalent dose in total,
sera collected 2-7 weeks after last dose



Jiang et al. MedRxiv preprint (Jan 9, 2023): https://www.biorxiv.org/content/10.1101/2023.01.08.523127v1
Another recent paper with XBB.1.5: Qu et al. MedRxiv preprint (Jan 17, 2023): https://www.biorxiv.org/content/10.1101/2023.01.16.524244v1

Both of the bivalent mRNA vaccines have been demonstrated to produce improved neutralizing antibody responses to the BA.5, BQ.1.1, and XBB variants as compared to the original vaccines (encoding S protein from the original strain of SARS-CoV-2) while maintaining excellent neutralizing capability against the original strain.

Monovalent vaccine is a vaccine with one strain or component of a virus ***(Wuhan). : Primary /booster vaccine***

Bivalent vaccine is a vaccine with two strains or components of a virus.
(Wuhan and Omicron- BA1 and Wuhan and Omicron- BA4,5): Booster vaccine

Only 2 mRNA vaccines - available (next- protein....)

Are bivalent vaccines (mRNA vac) more effective than monovalent (mRNA vac)?

Initial clinical trials for the updated boosters have shown that bivalent COVID-19 boosters:

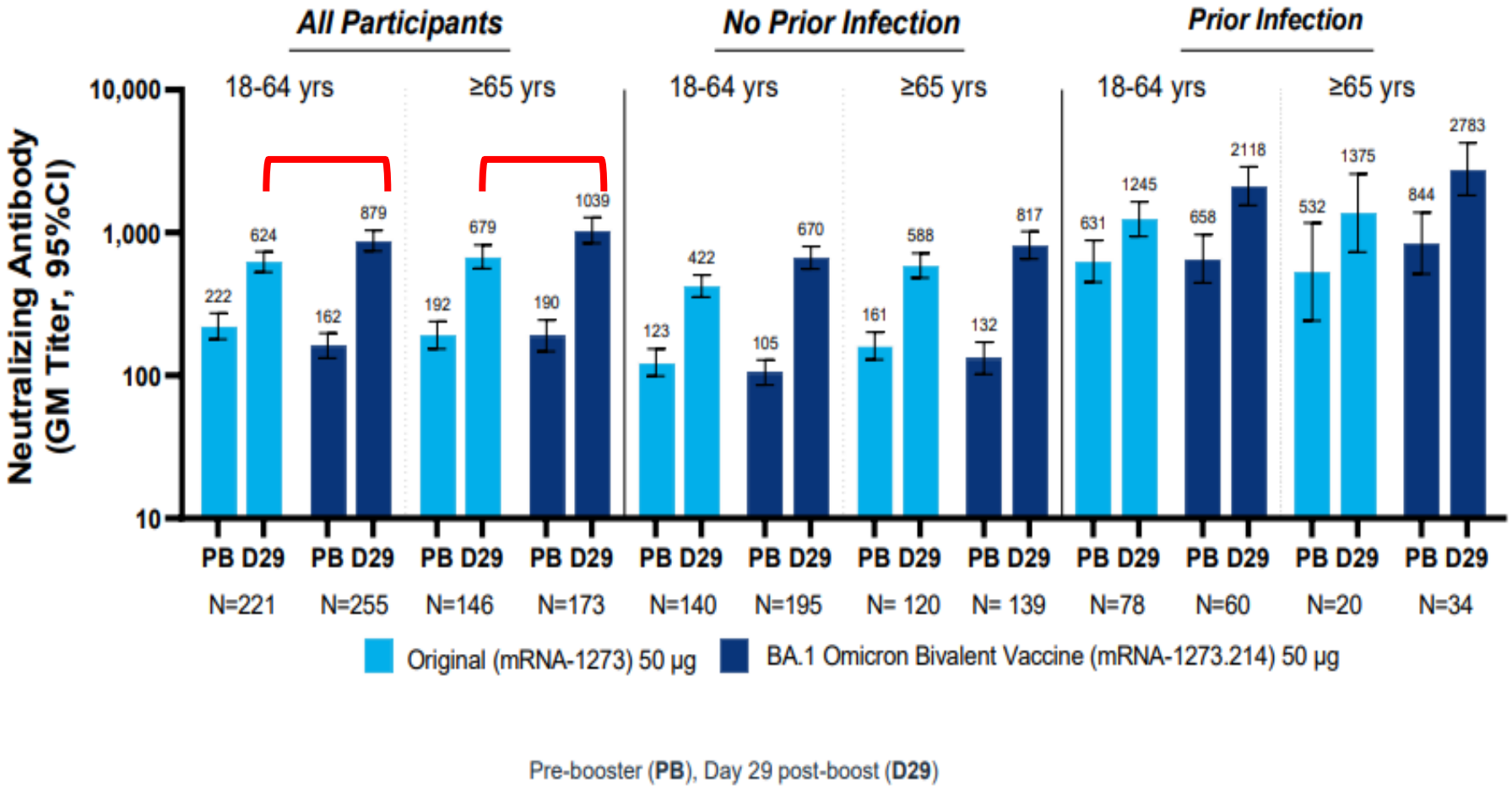
Provide broader protection against COVID-19 illness than monovalent boosters

Lengthen the period of protection from severe illness/death, especially from the omicron variant.

4th Dose (2nd Booster) with mRNA-1273.214 Resulted in Higher nAb Titers against Omicron BA.4/BA.5 Across Age Groups, Including ≥65-Year-old, than mRNA-1273

- Extensive evaluation of 3 monovalent and 4 bivalent investigational variant vaccines in past year
  - >7,000 individuals boosted across all variant vaccine candidates
- Bivalent vaccine candidates include:

Beta-containing vaccine (mRNA-1273.211)	25 µg Original SARS-CoV-2	+	25 µg Beta Variant (B.1.351)
BA.1 Omicron-containing vaccine (mRNA-1273.214)	25 µg Original SARS-CoV-2	+	25 µg Omicron Variant (BA.1)
BA.4/BA.5 Omicron-containing vaccine (mRNA-1273.222)	25 µg Original SARS-CoV-2	+	25 µg Omicron Variant (BA.4/BA.5)



Effectiveness of Bivalent mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection — Increasing Community Access to Testing Program, United States, September–November 2022

Bi-valent booster (Wuhan and Omicron BA4,5)

TABLE 2. Absolute vaccine effectiveness against symptomatic SARS-CoV-2 infection for a single bivalent mRNA COVID-19 booster dose received after 2, 3, or 4 doses of monovalent vaccine compared with no doses, by age group and number of monovalent COVID-19 vaccine doses — Increasing Community Access to Testing program, United States, September–November 2022

	Absolute VE (95% CI), by no. of monovalent doses received before the bivalent vaccine dose			
Age group, yrs	2 doses	3 doses	4 doses*	≥2 doses
18–49	41 (31–49)	43 (39–46)	NA	43 (39–46)
50–64	50 (35–61)	25 (17–33)	28 (20–34)	28 (22–33)
≥65	32 (9–49)	19 (8–29)	23 (15–30)	22 (15–29)

Abbreviations: NA = not applicable; VE = vaccine effectiveness.

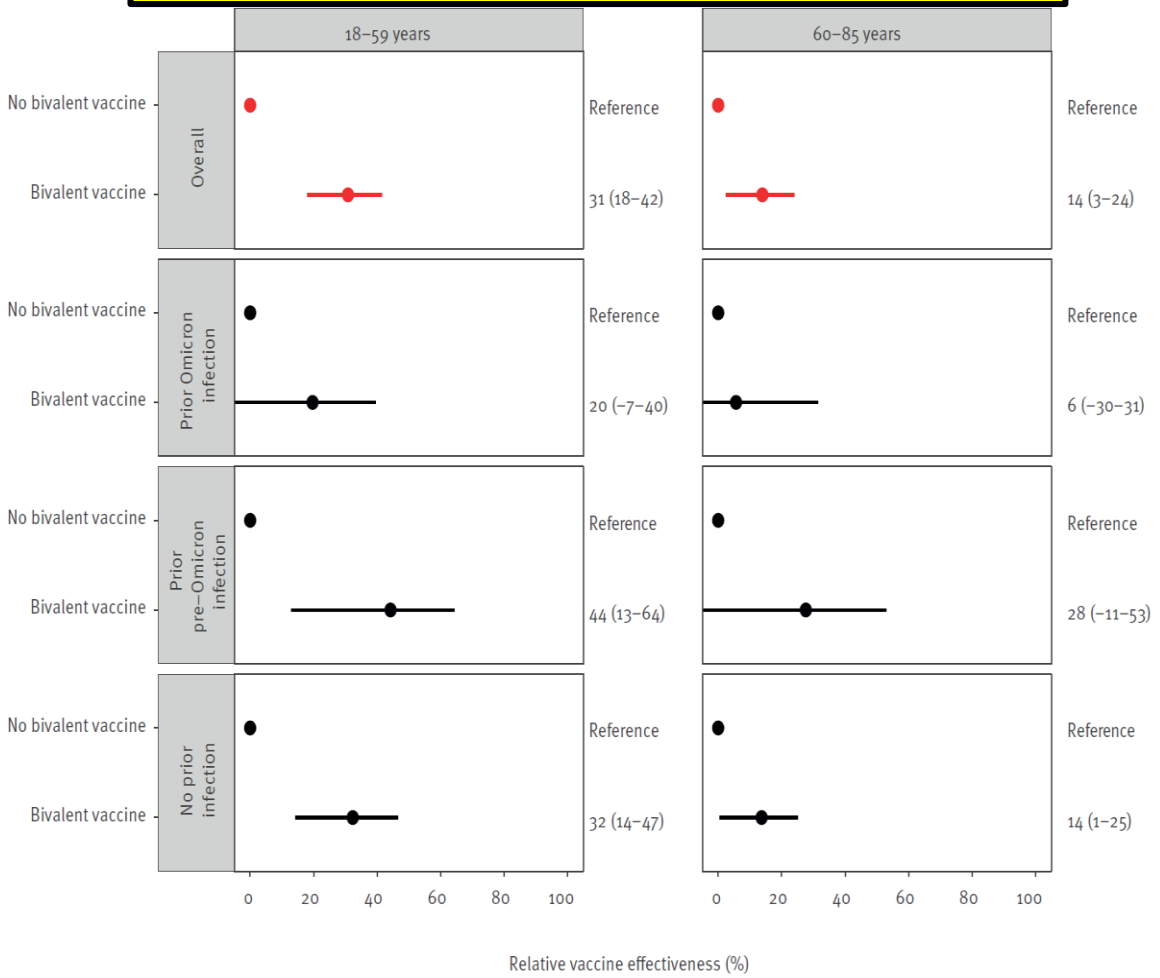
* Persons aged <50 years without moderate or severe immunocompromise were not eligible for a fourth monovalent (second booster) dose.

Effectiveness of bivalent mRNA booster vaccination against SARS-CoV-2 Omicron infection, the Netherlands, September to December 2022

FIGURE 2

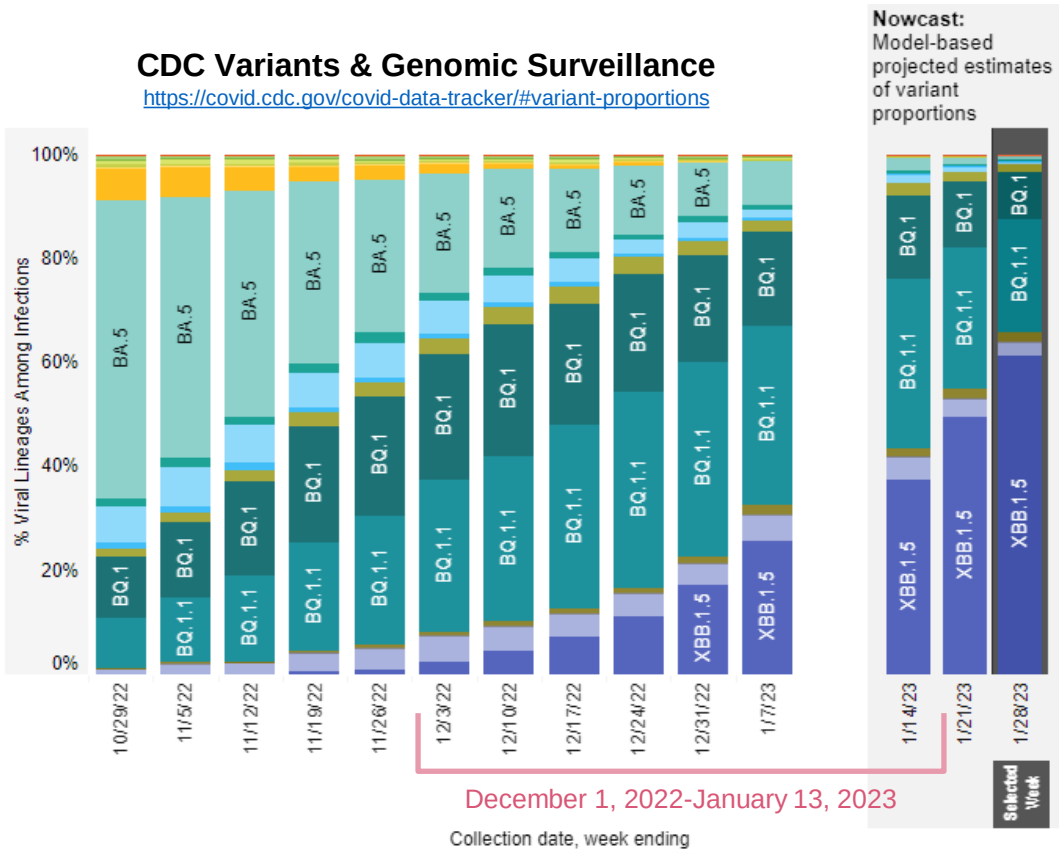
Relative vaccine effectiveness[a] and 95% confidence interval of bivalent COVID-19 vaccine overall and stratified by infection history and by age group, the Netherlands, 26 September 2022–19 December 2022 (n = 32,542)

Bi-valent booster (Wuhan and Omicron BA 1)



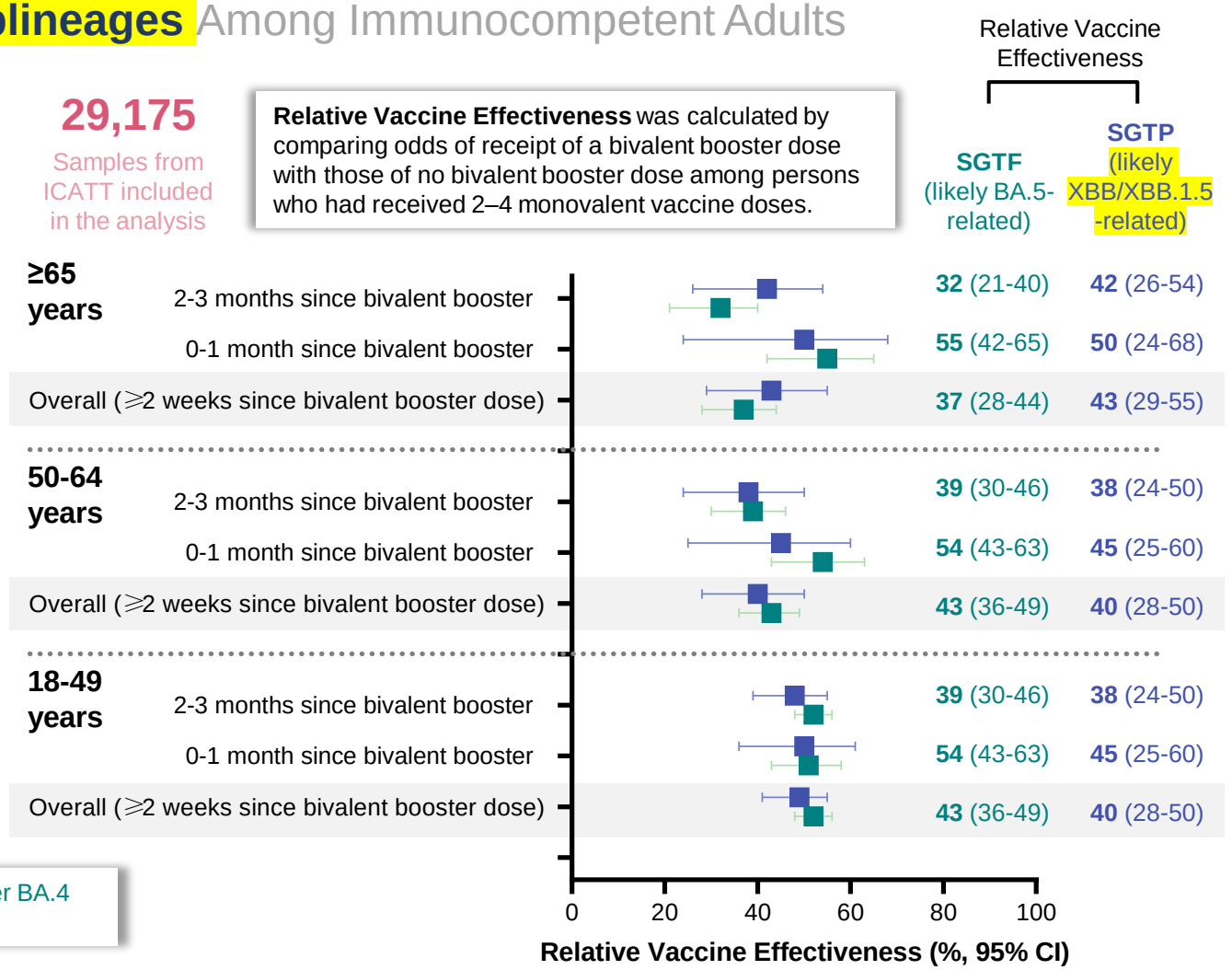
Early Estimates of Bivalent BA.4/5 mRNA Booster Effectiveness Against Symptomatic SARS-CoV-2 Infection in the US

Omicron BA.5– and XBB/XBB.1.5–Related Sublineages Among Immunocompetent Adults



29,175
Samples from ICATT included in the analysis

Relative Vaccine Effectiveness was calculated by comparing odds of receipt of a bivalent booster dose with those of no bivalent booster dose among persons who had received 2–4 monovalent vaccine doses.



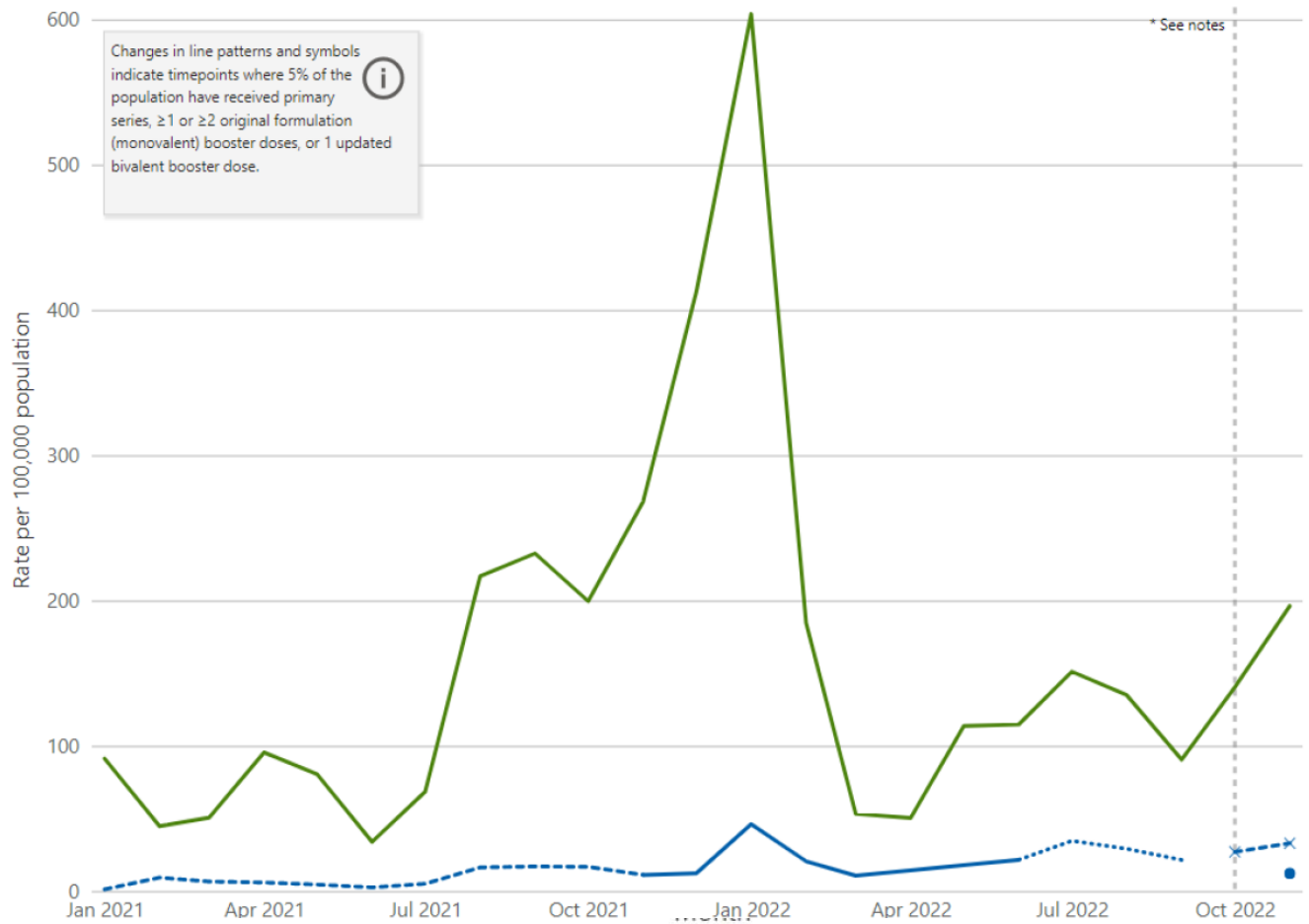
Circulating SARS-CoV-2 variants were classified by **SGTF** (BQ.1.1, BQ.1, BF.7, and other BA.4 and BA.5 sublineages) and **SGTP** (XBB.1.5, XBB, BN.1, and other BA.2 sublineages).

40% of patients has at least 1 underlying disease including diabetes

SGTF: Reduction or failure of spike gene (S-gene) amplification in real-time reverse transcription–polymerase chain reaction; SGTP: S-gene target presence; ICATT: Increased Community Access To Testing program;

Link-Gelles R et al. MMWR Morb Mortal Wkly Rep. ePub: 25 January 2023. DOI: http://dx.doi.org/10.15585/mmwr.mm7205e1

Age-Adjusted Rates of COVID-19-Associated Hospitalization by Vaccination Status and Receipt of Booster Dose in Adults Ages ≥18 Years COVID-NET, January 2021–November 2022



In November 2022, adults ages ≥18 years who received a **bivalent booster** had **16X lower risk of hospitalization for** COVID-19 compared to **unvaccinated people** and **3X lower risk of hospitalization** compared to those vaccinated **without a bivalent booster**

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination Accessed Jan. 20, 2022

Vaccine Effectiveness of Bivalent BA.4/5 COVID-19 Vaccine Against Hospitalization Among Older Adults Aged ≥65 Years

Test-negative, case-control study

Sept 1, 2022
Bivalent BA.4/BA.5 COVID-19 mRNA vaccines were recommended by ACIP.
Pfizer ≥ 12 years
Moderna ≥ 18 years

Sept 8, 2022

Study Period

1168 immunocompetent **adults aged ≥65 years** admitted for COVID-19-like illness in the IVY Network (**22** hospitals in **18** states)

Predominance of Omicron variant BA.4/BA.5 and their sublineages

Nov 30, 2022

Absolute Vaccine Effectiveness (aVE)

The odds of **receiving a bivalent booster dose** (after 2, 3, or 4 monovalent doses) versus the odds of **being unvaccinated** (zero doses of any COVID-19 vaccine) among hospitalized SARS-CoV-2 cases and control patients

Relative Vaccine Effectiveness (rVE)

The odds of **receiving a bivalent booster dose** (after 2, 3, or 4 monovalent doses) versus the odds of **not receiving a bivalent booster dose** (but receiving 2, 3, or 4 monovalent doses) among hospitalized SARS-CoV-2 cases and control patients

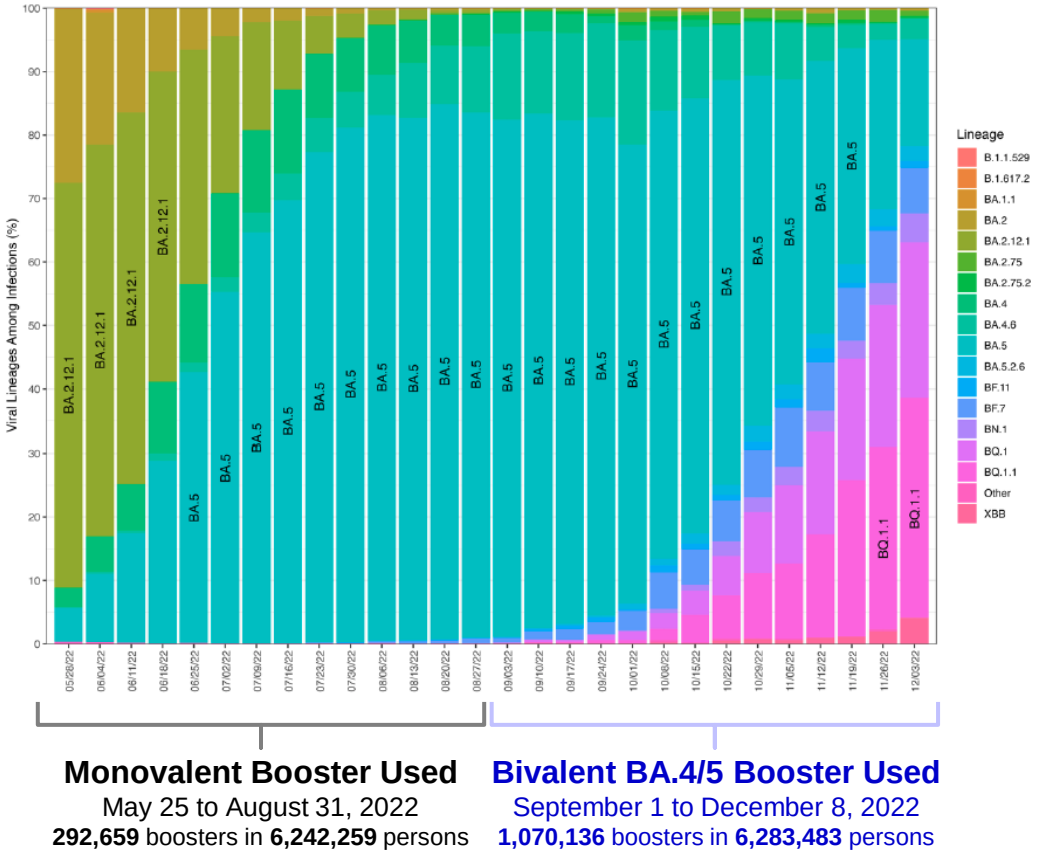
Effectiveness against laboratory confirmed **COVID-19–associated hospitalization**

aVE	rVE		
	≥2 mo post last monovalent	**6-11 mo** post last monovalent	**≥11 mo** post last monovalent
84%	**73%**	**78%**	**83%**
(95% CI: 64-93)	(95% CI: 52-85)	(95% CI: 57-89)	(95% CI: 63-92)

Image: Flaticon.com; Surie D, et al. MMWR Morb Mortal Wkly Rep. ePub: 16 December 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm715152e2

Effectiveness of Bivalent BA.4/5 Booster vs Monovalent Booster Against Severe Outcomes Caused by Omicron

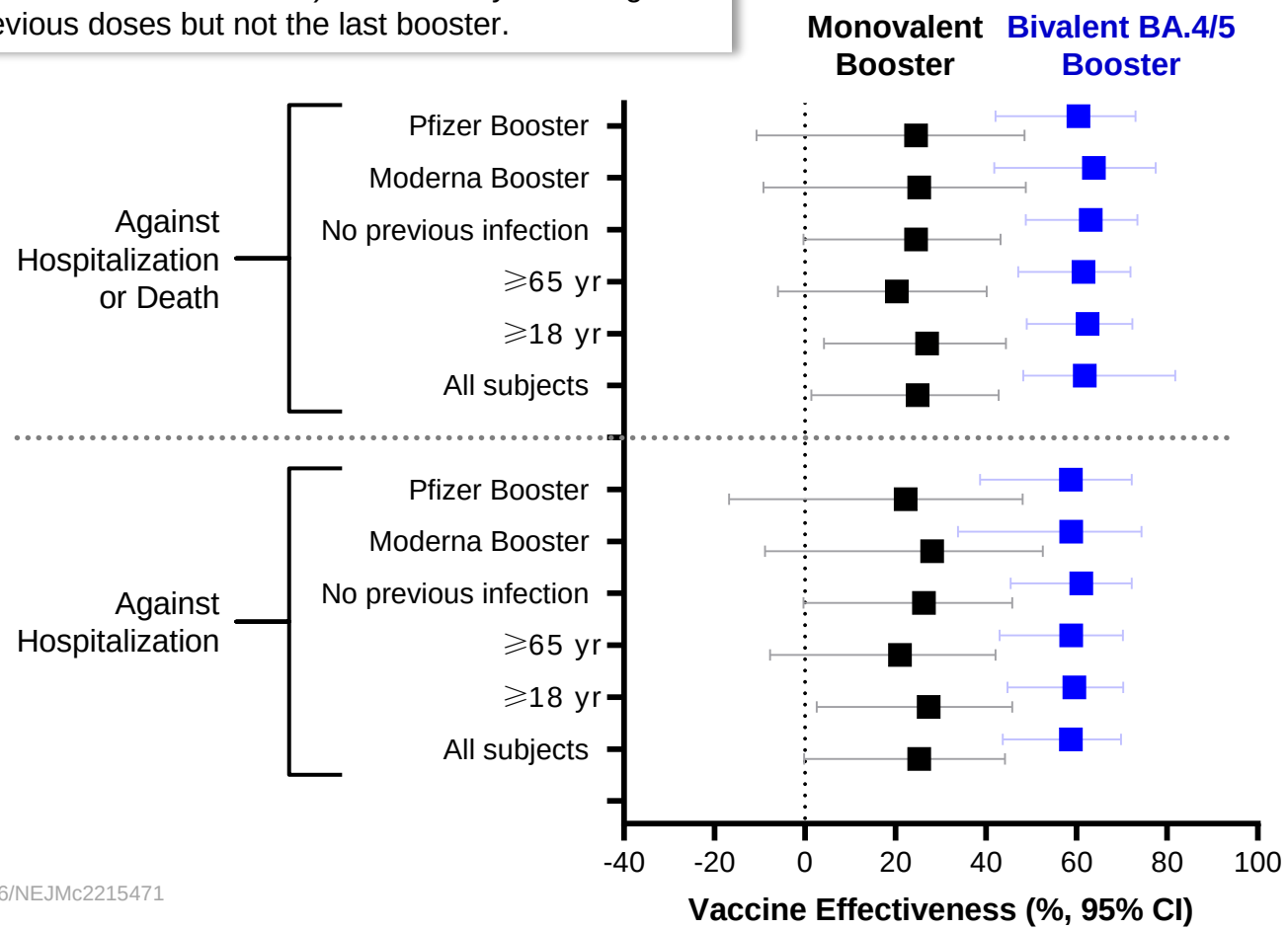
Variant Proportions in the State of North Carolina During the Study



Monovalent Booster Used
May 25 to August 31, 2022
292,659 boosters in **6,242,259** persons

Bivalent BA.4/5 Booster Used
September 1 to December 8, 2022
1,070,136 boosters in **6,283,483** persons

Vaccine effectiveness in this study indicates **the additional benefit** of receiving the last booster (**monovalent** or **bivalent**) dose vs only receiving previous doses but not the last booster.



Lin D-Y et al. Effectiveness of bivalent boosters against severe omicron infection. N Engl J Med.2023 DOI: 10.1056/NEJMc2215471

BI-valent mRNA covid-19 vaccines:

Effectiveness of bivalent mRNA booster vaccines in the U.S. in preventing:

(1) symptomatic SARS-CoV-2 infection during circulation of BA.4/BA.5 and their sublineages (Link-Gelles et al. 2022);

(2) COVID-19-associated emergency department or urgent care encounters and hospitalizations among immunocompetent adults (Tenforde et al. 2022)

(3) COVID-19-associated hospitalization among immunocompetent adults aged ≥65 years (Surie et al. 2022).

Additionally, observational data suggest that bivalent mRNA booster vaccination provides additional protection against symptomatic infection, emergency department/urgent care visits, and hospitalization.

Simplification of vaccine composition should reduce complexity, decrease vaccine administration errors

Covid-19 vaccines should be

1) Use of the same vaccine strain composition for primary series and booster doses,
2) Simplification of the COVID-19 immunization schedules: primary vaccination, annual/seasoning
3) Routine periodic strain selection procedures.

COVID-19 Cumulative Cases and Deaths per 100,000 Population by Age Group, United States, January 2, 2022 - January 18, 2023 (Omicron Variant Period)

Age group	COVID-19 Cases per 100,000 Population	COVID-19 Deaths per 100,000 Population
0 - 1 years	12,165.8	3.8
2 - 4 years	7,879.8	0.8
5 - 11 years	9,814.9	0.6
12 - 17 years	10,918.4	0.9
18 - 49 years	13,960.2	7.2
50 - 64 years	11,684.0	44.3
65 - 74 years	10,173.5	129.7
75+ years	11,758.9	510.5

Source: https://covid.cdc.gov/covid-data-tracker/#demographicsovertime Accessed Jan 24, 2023

Risk of Severe COVID-19 Illness

- Unvaccinated people at higher risk of severe illness compared with vaccinated people
- Most (75%) vaccinated people with severe COVID-19 illness have multiple risk factors:
  - Older age (most ≥65 years, but with risk increasing with age)
  - Underlying medical conditions (with risk increasing with number of underlying conditions)
    - Immunosuppression
    - Diabetes mellitus
    - Chronic kidney disease
    - Chronic lung disease
    - Chronic cardiovascular disease
    - Chronic neurologic disease
- Antiviral drugs can help reduce risk of severe illness in people at higher risk, regardless of vaccination status

Yek et al. MMWR 2022;71:19-25. https://www.cdc.gov/mmwr/volumes/71/wr/mm7101a4.htm; Taylor et al. MMWR 2022;71:466-473: http://dx.doi.org/10.15585/mmwr.mm7112e2 and unpublished COVID-NET data, as described here; Malden et al. MMWR 2022; 71(25);830-833: https://www.cdc.gov/mmwr/volumes/71/wr/mm7125e2.htm ; Gold et al. MMWR 2022; 71(25);825-829: https://www.cdc.gov/mmwr/volumes/71/wr/mm7125e1.htm ; Najjar-Debbiny et al. CID 2022;, ciac443, https://doi.org/10.1093/cid/ciac443 Dryden-Peterson et al. medRxiv 2022.06.14.22276393; https://doi.org/10.1101/2022.06.14.22276393

Comparing immunogenicity and efficacy of two different mRNA-based COVID-19 vaccines as a fourth dose; six-month follow-up, Israel, 27 December 2021 to 24 July 2022

Barda N; Eurosurveillance 29 September 2022

700 HCW who received three doses of the Comirnaty vaccine at least 4 months prior, were not previously infected with Covid-19 , and had anti-RBD IgG < 700 BAU 3 months prior, were assigned to receive either the Comirnaty vaccine or the Spikevax vaccine and Control gr.- HCW received only 3 doses)

Results

Immunogenicity:

6 months, IgG levels following Spikevax and Comirnaty doses were 1.58-fold and 1.16-fold (95% CI: 0.98–1.37) higher than baseline, respectively, and Nab titres were 1.04-fold and 0.75-fold the baseline, respectively.

Efficacy:

By the end of the study, 70/120 (58.3%) and 89/154 (57.8%) of the Spikevax and Comirnaty vaccine recipients, respectively, contracted SARS-CoV-2, and 7/108 (6.5%) and 14/140 (10.0%), respectively, had substantial disease, though none required hospitalisation or medical attendance.

VE against infection over the entire study period, compared with controls vaccinated with three doses at least 4 months prior, was similar and not statistically significant in both vaccine groups

FIGURE

Estimated geometric mean titres (with 95% confidence interval) of (A) IgG and (B) neutralising antibodies, at baseline and 180 days post-vaccination, according to the vaccine received, Israel, 29 December 2021–6 January 2022 (n = 274)

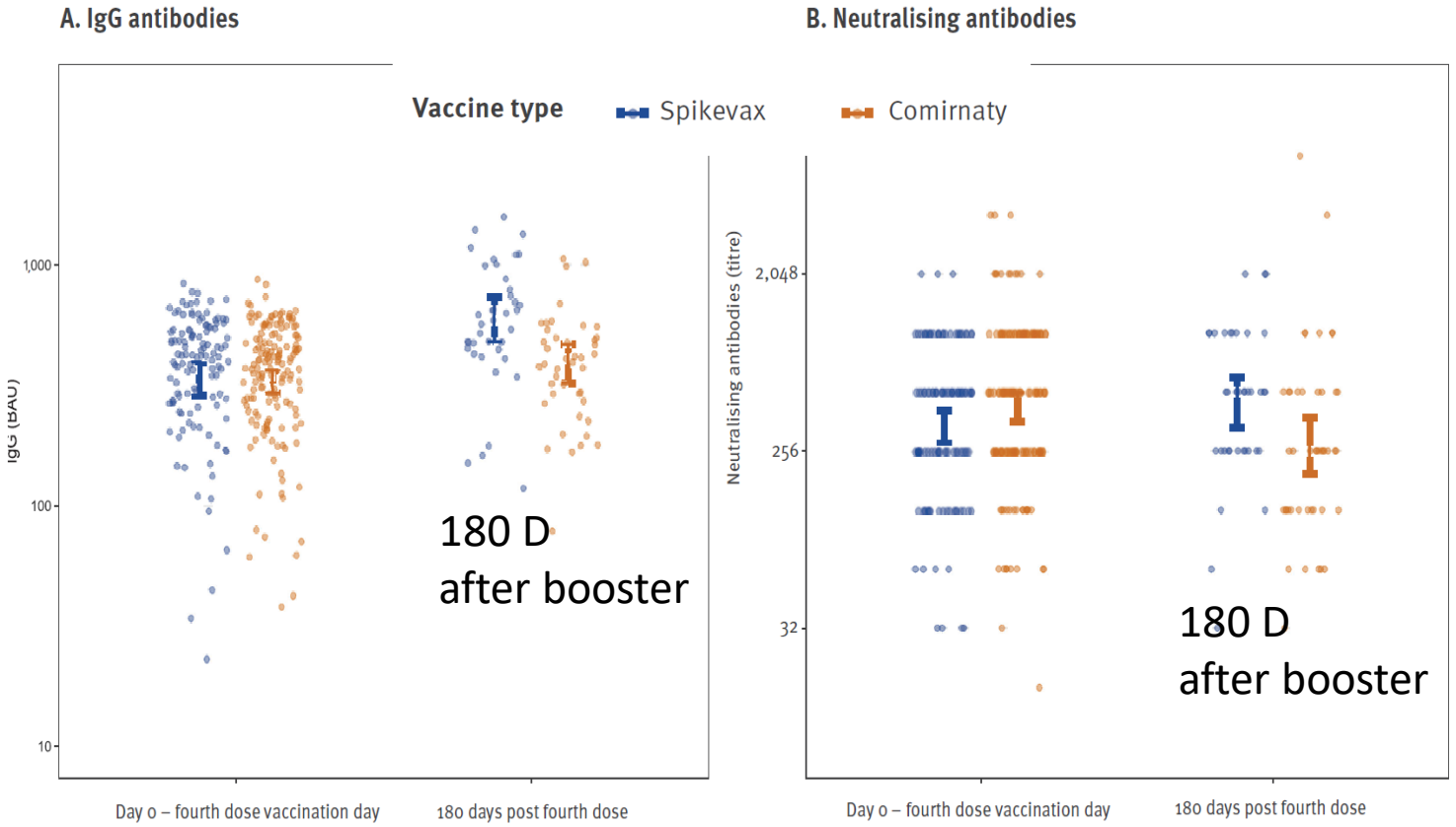


TABLE 3. Relative vaccine effectiveness of a single bivalent mRNA COVID-19 booster dose against symptomatic SARS-CoV-2 infection* received after 2, 3, or 4 monovalent vaccine doses, by age group, number of monovalent COVID-19 vaccine doses received, and interval since last monovalent dose — Increasing Community Access to Testing program, United States, September–November 2022

Age group, yrs/mos since receipt of most recent monovalent dose	Relative VE (95% CI), by no. of monovalent doses received†			
	2 doses	3 doses	4 doses§	≥2 doses
18–49				
2–3	45 (31–56)	24 (14–33)	NA	30 (22–37)
4–5	47 (35–57)	41 (35–47)	NA	43 (38–48)
6–7	42 (30–52)	47 (42–52)	NA	46 (41–50)
≥8	53 (45–60)	58 (56–61)	NA	56 (53–58)
50–64				
2–3	—	15 (–4–31)	33 (24–41)	31 (24–38)
4–5	44 (18–62)	31 (18–42)	36 (29–43)	36 (30–41)
6–7	46 (22–62)	36 (25–45)	40 (32–47)	38 (32–43)
≥8	61 (49–70)	51 (45–55)	NA	48 (45–51)
≥65				
2–3	—	—	32 (23–40)	28 (19–35)
4–5	—	21 (1–36)	36 (29–42)	33 (27–39)
6–7	—	14 (–6–30)	40 (33–46)	36 (29–41)
≥8	45 (27–58)	42 (35–48)	NA	43 (39–46)

Abbreviations: NA = not applicable; VE = vaccine effectiveness.

* VE estimates with 95% CIs >50 percentage points are not shown because of imprecision.

† Total number of monovalent doses received for persons who did and did not receive a bivalent booster dose.

Protection against severe COVID-19 after second booster dose of adapted bivalent (original/Omicron BA.4-5) mRNA vaccine in persons ≥ 60 years, by time since infection, Italy, 12 September to 11 December 2022

www.eurosurveillance published on 23 Feb 2023

TABLE 2

Effectiveness against severe COVID-19 of a second booster dose of the bivalent (original/BA.4–5) mRNA vaccine relative to a first booster dose of an mRNA vaccine received ≥ 120 days earlier, by time since prior infection, Italy, 12 September–11 December 2022 (n = 11,190,209)

Time since prior infection	First booster dose since ≥ 120 days (reference)		Bivalent second booster dose (original/BA.4–5)		rVE	
	n events	Rate per 100,000 PD	n events	Rate per 100,000 PD	%	95% CI
Primary analysis						
No prior infection	18,594	2.60	413	1.54	59.4	55.1 to 63.3
≥ 40 weeks	433	1.93	17	0.93	61.6	37.5 to 76.3
27–39 weeks	494	1.37	26	0.76	61.7	43.1 to 74.2
17–26 weeks	507	0.52	18	0.73	10.0	−44.0 to 43.8
Sensitivity analysis[a]						
No prior infection	13,879	1.94	308	1.15	61.5	56.7 to 65.8
≥ 40 weeks	322	1.43	13	0.71	61.6	33.1 to 78.0
27–39 weeks	353	0.98	17	0.50	65.8	44.3 to 79.0
17–26 weeks	366	0.38	14	0.57	8.5	−56.1 to 46.4

For maximum effectiveness, individuals who recently had COVID-19 may consider delaying any COVID-19 vaccination, including the updated booster dose, by 3-6 months from the start of their symptoms or positive test.
Individuals previously infected with a pre-Omicron variant of SARS-CoV-2 retain substantial protection against the Omicron variant for **at least 6 months in the absence of vaccination**. **(CID 2022:75 (15 December)**

Although some scientific uncertainty remains as to the duration of protection against symptomatic disease, hospitalization, and death across all age ranges, it appears clear **from multiple clinical studies that additional boosters restore protection against COVID-19.**

Although the beneficial effect associated with a **reduction in hospitalization and death is most apparent in older individuals,** younger individuals appear to also benefit with a reduction in symptomatic disease and health care utilization (Link-Gelles et al. 2022, Tenforde et al. 2022, Surie et al. 2022).

Though perhaps not identical, this pattern of response is analogous to that observed with annual influenza vaccination, a well-accepted intervention in individuals 6 months of age and older that on an average year provides a 10% to 60% in reduction of influenza-like illness (CDC 2022, Treanor 2016, Minozzi et al. 2022).

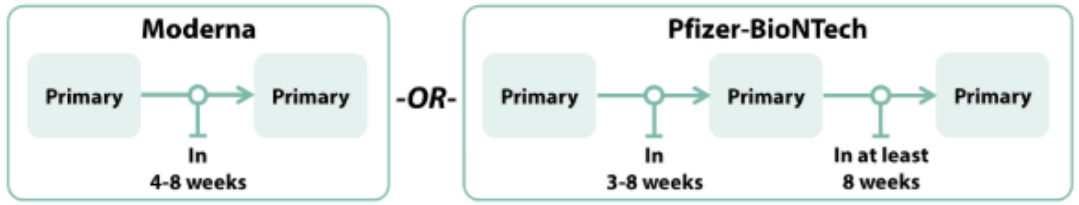
Administration of an updated vaccine on an annual basis also appears to be reasonable (Townsend et al. 2023). As such, an annual frequency may provide a reasonable and practical starting point to implement COVID-19 vaccine composition evaluation and recommendations in the U.S.

US-FDA ACIP meeting 26 Jan 2023

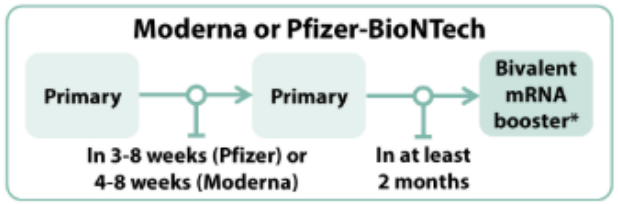
COVID-19 vaccination guidance-US

COVID-19 Vaccination Schedule Infographic for People who are NOT Moderately or Severely Immunocompromised

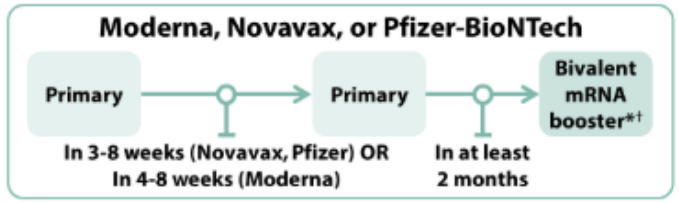
People ages 6 months through 4 years



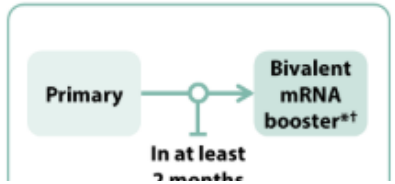
People ages 5 through 11 years



People ages 12 years and older

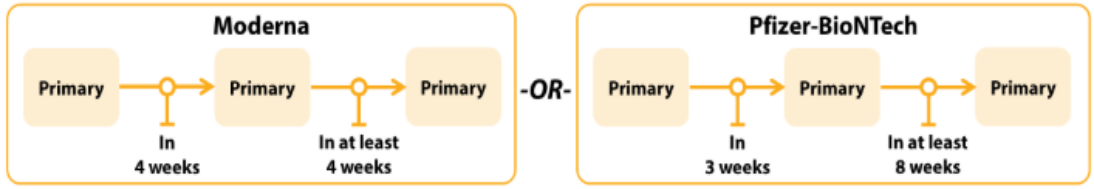


People ages 18 years and older who previously received Janssen primary series dose‡

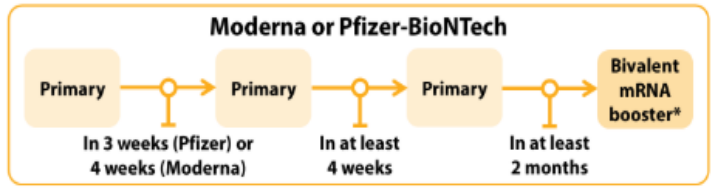


COVID-19 Vaccination Schedule Infographic for People who are Moderately or Severely Immunocompromised

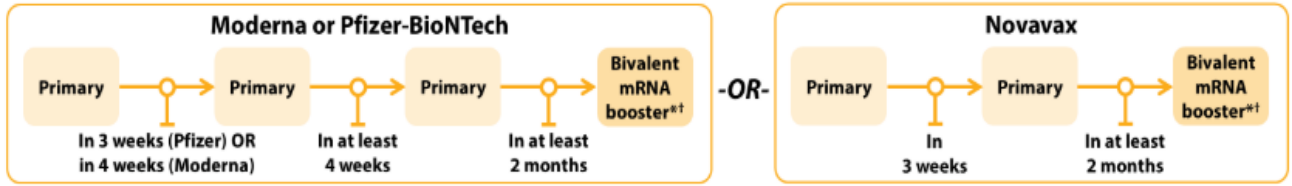
People ages 6 months through 4 years



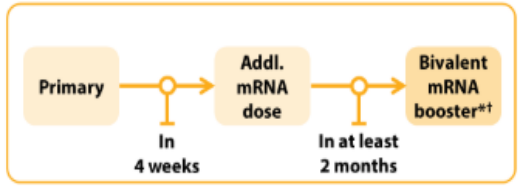
People ages 5 through 11 years



People ages 12 years and older



People ages 18 years and older who previously received Janssen primary series dose‡



***The bivalent booster dose is administered at least 2 months after completion of the primary series.**
For people who previously received a monovalent booster dose(s), the bivalent booster dose is administered at least 2 months after the last monovalent booster dose.

erim COVID-19 Immunization Schedule (Updated 10/21/2022)

COVID-19 vaccination guidance-UK (Seasonal Autumn booster)

Guidance

A guide to the COVID-19 autumn booster

Updated 28 September 2022

Applies to England

Contents

People aged 50 years and older, residents in care homes for older people, those aged 5 years and over in a clinical risk group and health and social care staff will be offered a booster of coronavirus (COVID-19) vaccine this autumn.

Appointments will be available from the National Booking Service shortly.

- ▶ Residents and staff in older adult care homes
- ▶ Frontline health and social care workers
- ▶ People aged 50 and over
- ▶ People aged 5-49 in a clinical risk group
- ▶ Household of immunosuppressed people
- ▶ Unpaid carers aged 16-49

Which vaccine will you be offered?

You will be given a booster dose of a vaccine made by Pfizer or Moderna. You may be offered an updated combination version of these booster vaccines – the combination vaccines include a half-dose of the previous vaccine combined with a half-dose of a vaccine against the Omicron variant. For a very small number of people another vaccine product may be advised by your doctor.

Both the previous and the combination vaccines boost protection very well, although the combination vaccines produce slightly higher levels of antibody against some strains of Omicron.

As we cannot predict which variants of COVID-19 will be circulating this winter, the Joint Committee on Vaccination and Immunisation (JCVI) have concluded that both types of vaccine can be used in adults, and that no one should delay vaccination to receive combination vaccines. So you will be offered the right vaccine for you at the right time.

Both mRNA vaccines in original and updated bivalent versions will be offered as an Autumn booster

การบริหารจัดการวัคซีนโควิด 19

1. เห็นชอบ หลักการให้วัคซีนโควิด 19 ชนิด Pfizer (Bivalent) ดังนี้

1.1 การให้วัคซีน : แนะนำให้ใช้วัคซีน Pfizer (Bivalent) เป็นวัคซีนเข็มกระตุ้น

1.2 กลุ่มเป้าหมาย : เจ้าหน้าที่ด่านหน้า อาสาสมัครสาธารณสุข และกลุ่มเสี่ยงต่อโรครุนแรง (608)
ทั้งนี้ประชาชนทั่วไป สามารถรับวัคซีนได้เช่นกัน ภายใต้การบริหารจัดการของพื้นที่

1.3 ระยะเวลาที่ได้รับ โดยมีหลักการเดียวกับการให้วัคซีน Pfizer (Monovalent)

1.3.1 แนะนำให้ฉีดวัคซีน Pfizer (Bivalent) เข็มกระตุ้น ในผู้ที่มีประวัติได้รับวัคซีนโควิด 19 มาแล้วอย่างน้อย 2 เข็ม โดยมีระยะห่างจากวัคซีนเข็มสุดท้าย 4 - 6 เดือน

1.3.2 กรณีเคยติดเชื้อโควิดมาก่อน แนะนำให้ฉีดวัคซีน Pfizer (Bivalent) ห่างจากการติดเชื้ออย่างน้อย 3 เดือน

1.3.3 กรณีผู้ที่ได้รับวัคซีน Pfizer (Bivalent) มาก่อน สามารถรับ LAAB ได้ หลังจากได้รับวัคซีนอย่างน้อย 2 สัปดาห์ สำหรับกรณีที่ได้รับ LAAB มาก่อน สามารถรับวัคซีน Pfizer (Bivalent) เมื่อใดก็ได้

1.3.4 กรณีอื่น ๆ ให้พิจารณาตามความเสี่ยงและดุลพินิจของแพทย์ผู้ให้การรักษา โดยคำนึงถึงประโยชน์ ความเสมอภาค และความเป็นไปได้ เป็นสำคัญ

2. เห็นชอบ หลักการให้วัคซีนโควิด 19 ประจำปี

2.1 แนะนำหลักการให้วัคซีนโควิด 19 ประจำปี อย่างน้อยปีละ 1 ครั้ง

2.2 มอบหมายให้คณะทำงานทบทวนข้อมูล Bivalent Covid 19 Vaccine ฯ พิจารณาหลักการให้วัคซีนโควิด 19 ประจำปี ทั้งนี้ขอให้ปรับหน้าที่และอำนาจของคณะทำงานฯ ดังกล่าว ให้สามารถให้คำแนะนำทางวิชาการในการให้วัคซีนโควิด 19

The Rates of Rare Adverse Events Remain Low for mRNA Vaccines Compared With Other Vaccine Platforms

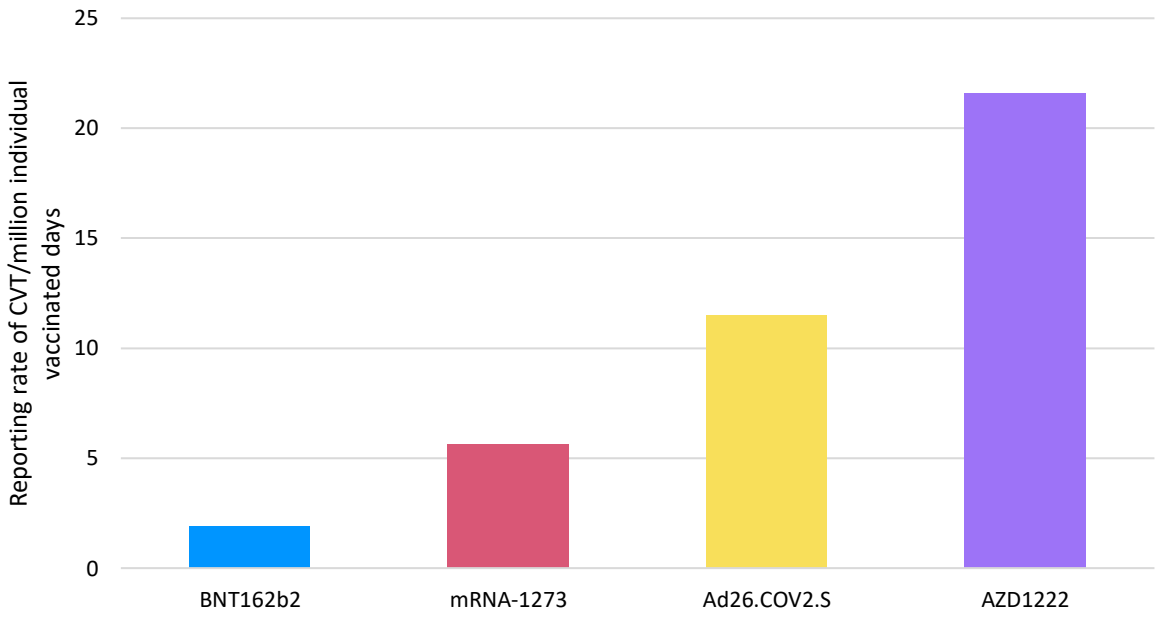
Cerebral venous thrombosis has a decreased reporting rate in BNT162b2 compared to **non-replicating viral vector vaccines** (AZD1222 and Ad26.COV2.S) per million individuals[1,2]

Myocarditis has only been reported in **3.5 cases per million** second doses of mRNA vaccine administered, mainly affecting **males between 18 to 29 years** of age[3]

Guillain-Barré Syndrome occurs at a higher rate after vaccination with **Ad26.COV2.S, at 20.2 cases per million** doses administered, while there is **no increased risk** associated with **mRNA vaccines[3]**

The rates of anaphylaxis after BNT162b2 or mRNA-1273 vaccination currently present minimal concern due to a decrease in cases[4]

CVT was more prevalent in inactivated vaccines compared with mRNA vaccines[1]



CVT: Cerebral venous thrombosis.

1. Abbattista M, et al. *J Thromb Haemost.* 2021;19(10):2554-2558. 2. Fiolet T, et al. *Clin Microbiol Infect*. 2022;28(2):202-221. 3. Rosenblum HG, et al. *MMWR Morb Mortal Wkly Rep.* 2021;70(32):1094-1099. 4. Shimabukuro TT, et al. *JAMA*. 2021;325(11):1101-1102.

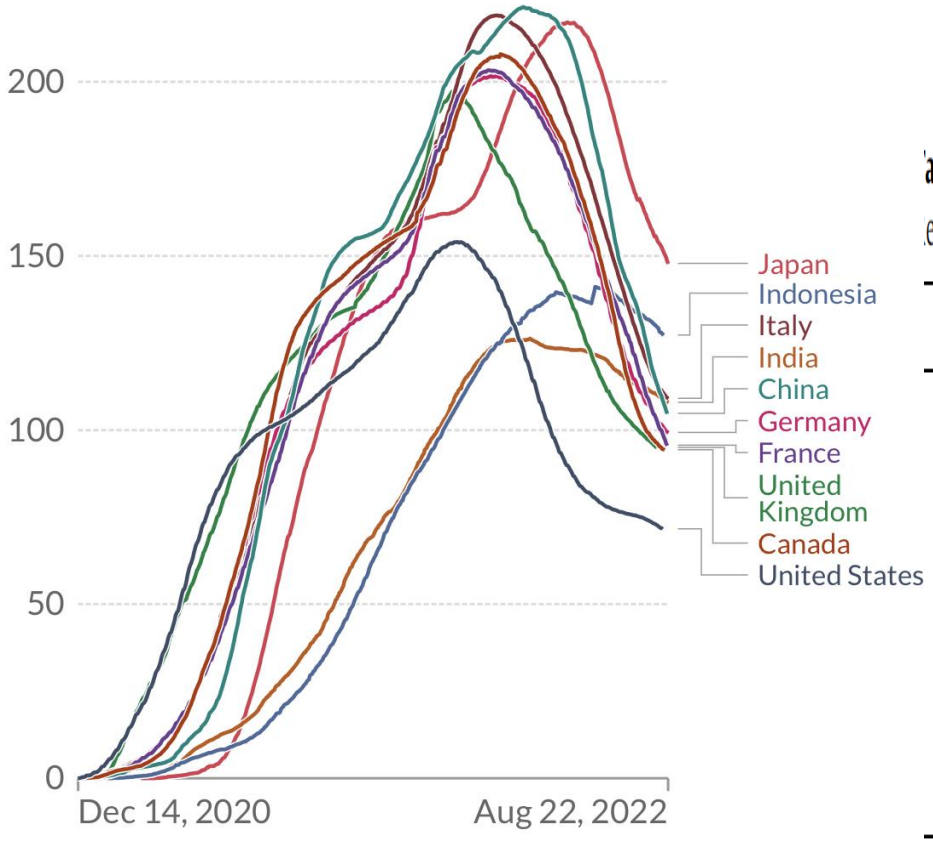
How many COVID-19 vaccine doses were administered in the previous 12 months?

Our World in Data

Per 100 people in the population. The value shown for each date is the total number of vaccine doses administered in the 12 months preceding that date. All doses, including boosters, are counted individually.

LINEAR LOG

Add country



Source: Official data collated by Our World in Data

CC BY

Dec 14, 2020 Aug 22, 2022

Vaccine 41 (2023) 136–144

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Misinformation and COVID-19 vaccine hesitancy

Tara Zimmerman [a,*], Kristina Shiroma [b], Kenneth R. Fleischmann [b], Bo Xie [b], Chenyan Jia [c], Nitin Verma [b], Min Kyung Lee [b]

[a] Texas Woman's University, Denton, TX, USA
[b] University of Texas at Austin, Austin, TX, USA
[c] Stanford University, Stanford, CA, USA

Table 1

Reasons for not getting the COVID-19 vaccine.

Category	Description	Number of Responses	%
Unforeseen future effects*	Worries about unforeseen problems for adults and/or children	355	49
Fear of commercial profiteering*	Belief that vaccines are promoted by authorities and corporations to advance their financial interests	92	13
Doubting effectiveness*	Mistrust of vaccine benefit due to a perceived lack of safety, effectiveness, and/or protectiveness	87	12
Preference for natural immunity*	Belief that natural exposure achieves safer and longer lasting immunity	26	4
Health/scheduling barriers	Difficulty getting the vaccine logistically or due to specific health problems	96	13
Personal freedom	Resistance to governmental mandates, religious beliefs, or conspiracy-related theories	156	22
COVID-19 denial	The disease is overblown, non-threatening, or a hoax	41	6

VAX scale vaccine attitude.

Strategies of Covid-19 vaccination to address Omicron or another VOCs

Primary covid-19 vaccination:

Primary covid-19 vaccination (2 or 3 doses of vaccine with definite interval) for unvaccinated persons age **18 years and over with or without prior covid-19 infection**

Booster covid-19 vaccination:

Annually one update bi-valent booster dose (mono-valent ?) of covid-19 vaccine for persons who had **previously completed primary covid-19 vaccination** with or without booster dose / prior covid-19 infection and:

1. **Healthy persons age 65 years and over (or 50 years and over ?)**
2. **Persons age 18 years and over at higher risk of severe COVID-19**
3. More targeted offer to protect those persons at higher risk of severe COVID-19.
   - **Health-care workers and social care workers**
   - Residents in a care home for older adults and staff working in care homes for older adults
   - All adults aged 50 years and over
   - All adults who are household contacts of people with immunosuppression
4. All persons age ≥ 18 years and over

NOTE:

- Administer a single booster dose at least 6 months (4 months ?) after the last vaccine dose.
- Covid-19 can be administration simultaneously with influenza vaccine
- Persons with a recent SARS-CoV-2 infection may consider delaying a primary series or booster dose by 6 months (3 months ?) from symptom onset or positive test (if infection was asymptomatic).
- Extra-booster dose may need for person who has severe immunosuppression

Reaching the Final Endgame for Constant Waves of COVID-19

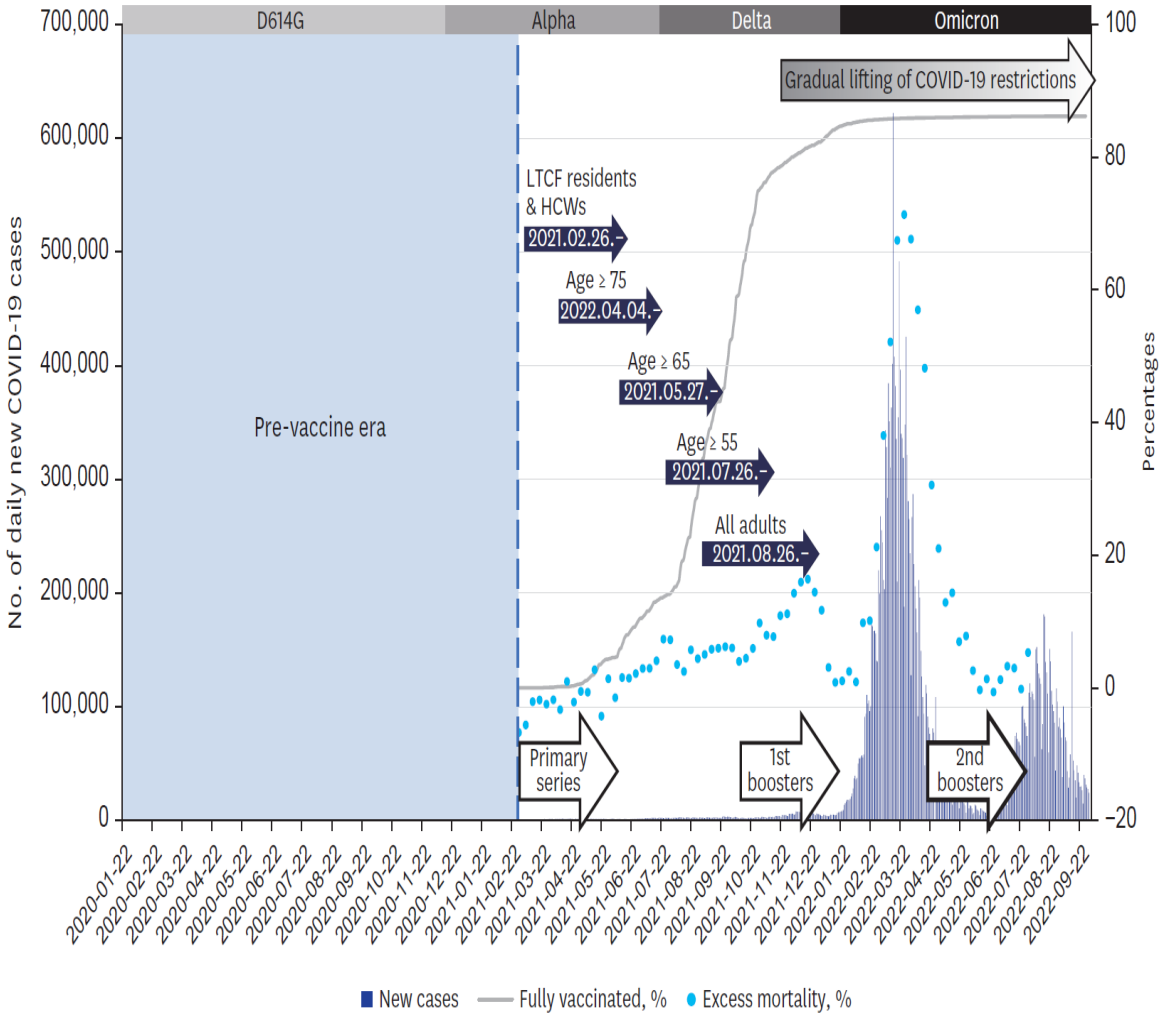


Fig. 2. Timeline of mass vaccination against COVID-19 in Korea. The blue vertical bars represent the number of daily new COVID-19 cases, the light blue dots represent weekly excess mortality (%), the grey curve represents the cumulative percentage of fully vaccinated individuals (i.e., completed primary series vaccination), and the dark blue arrows represent when each group became eligible for COVID-19 vaccines.
COVID-19 = coronavirus disease 2019, LTCF = long-term care facilities, HCWs = healthcare workers.

J Korean Med Sci. 2022 Dec 5;37(47):e351

MASS VACCINATION AND THE MITIGATION OF PANDEMIC WAVES

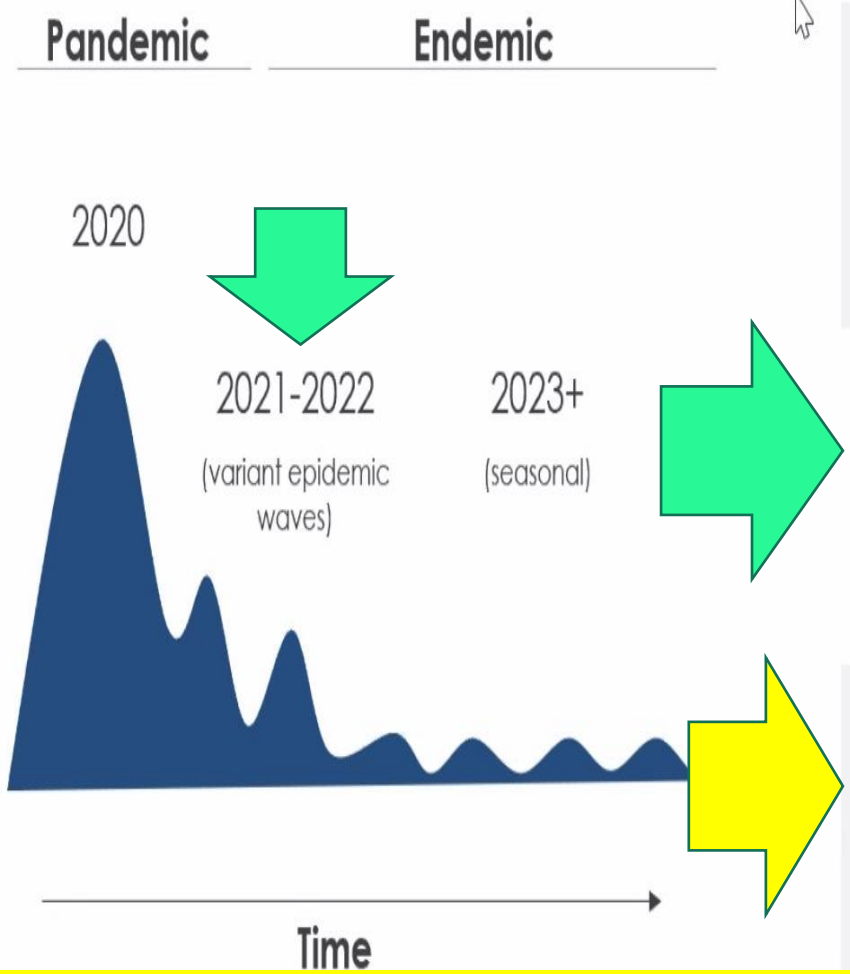
What's next:

-**Need for additional vaccinations** (target population and time interval between doses)
- Approval process for new COVID-19 vaccines
- **Need multivalent vaccines** that contain several VOC (pan-vaccine)
- Effective communication
- **Preparation for the next pandemic** (strategic, investments in vaccine development….)

Challenges

- **New VOCs** (increased transmission, virulent, resist to ab, diagnosis methods,….)
- **Multi-valent immunity (**vaccine coverage, hesitancy….)
- Supply of vaccines (inequity….)
- **New pan-coronavirus vaccine** (targeting more conserved protein sequences)
- **Roles of non-pharmaceutical intervention**
- **New and better antiviral therapy**
- Control zoonosis and human interaction
- Strong international cooperation among all stakeholders

Post-pandemic immunity after immunization and natural infection will maintain endemic COVID-19 Immunity to human coronaviruses (natural infection): < 1 year



Stage	Focus for vaccines
Pandemic *Initial waves*	• Heavy focus on protecting high-risk populations • Mostly ancestral virus vaccine
Variant epidemics *Reinfection waves*	• Focus to suppressing transmission of variants • Speed & adaptability are critical
Endemic *Seasonal*	• Multi-valent approaches with broadest immunity • Focus on toddlers and seasonal protection against waning immunity in high-risk (e.g., 65+)

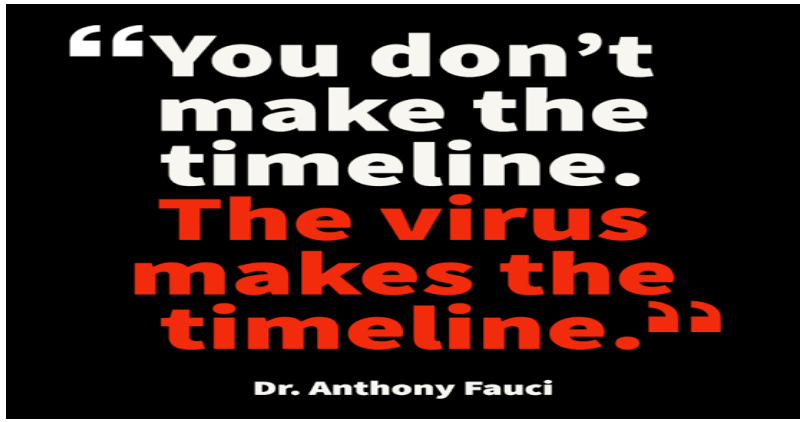
Non-pharmacologic interventions: non-restriction?
Effective treatment: Rem, Paxlovid, Mulnuperavir
Covid-19 Vaccination (many platforms)

COVID-19 vaccine will stop pandemic

Maintain immunity 80-90%
Natural booster or vac.booster (duration ?)

New variant of SAR-CoV 2 VOC
(New vaccine for specific VOC ?)

Outbreak in seronegative new area (infant, children)



Thank you

Chula ID Weekend 2023

Infectious Diseases Hot Issues in Pandemic Era

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