

COVID-19: What's Next?



COVID-19 PREVENTION
Let's all do our part to prevent the spread of COVID-19

MySejahtera
Install, register and track in via the MySejahtera app.

Social Distancing
Keep a physical distance of at least 1 meter from others.

Wash Hands
Practice good personal hygiene and wash your hands often.

Wear Mask
Wear a face mask when in public places.

Avoid the SCs
Avoid close conversation, crowded spaces and crowded places.

Check Temperature
Monitor your temperature and see a doctor if you are sick.

Stay at Home
Go out only when you have an important reason to leave the house.

Stop Fake News
Be responsible and do not share news and information about Covid-19 that has not been verified.

For any inquiries regarding COVID-19, please contact: **CRISIS PREPAREDNESS AND RESPONSE CENTRE (CPRC)**
Hotline: 03-8881 0200 | 03-8881 0600 | 03-8881 0700 | Website: www.moh.gov.my | Email: cprc@moh.gov.my



ศ.นพ. อีระพงษ์ ตันทวีเชียร MD., FRCP(Edin)
อาจารย์หน่วยโรคติดเชื้อ ภาควิชาอายุรศาสตร์
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
หัวหน้า Tropical Medicine Cluster, Health Supercluster,
จุฬาลงกรณ์มหาวิทยาลัย
ผู้ช่วยผู้อำนวยการและรักษาการหัวหน้าฝ่ายวิจัยและบริการคลินิก
สถานเสาวภา สภากาชาดไทย

Disclosure

Prof. Terapong Tantawichien: has received support for

Travel for International Conference (Sanofi)

Lectureships (GlaxoSmithKline, Pfizer, MSD, Takeda, Siam Pharm, Sanofi, Biovalys, Biogenetec).

Advisory board for pneumococcal vaccine (MSD), zoster vaccine (GSK), dengue vaccines (Sanofi, MSD, Takeda), influenza vaccine (Sanofi), COVID-19 vaccine (Pfizer)

Prof. Terapong Tantawichien: has received research funds from

MPH, Thailand (shorten rabies PET) 2019-2020

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) 2021-2023

Jansen (E.coli vaccine 2023-2025

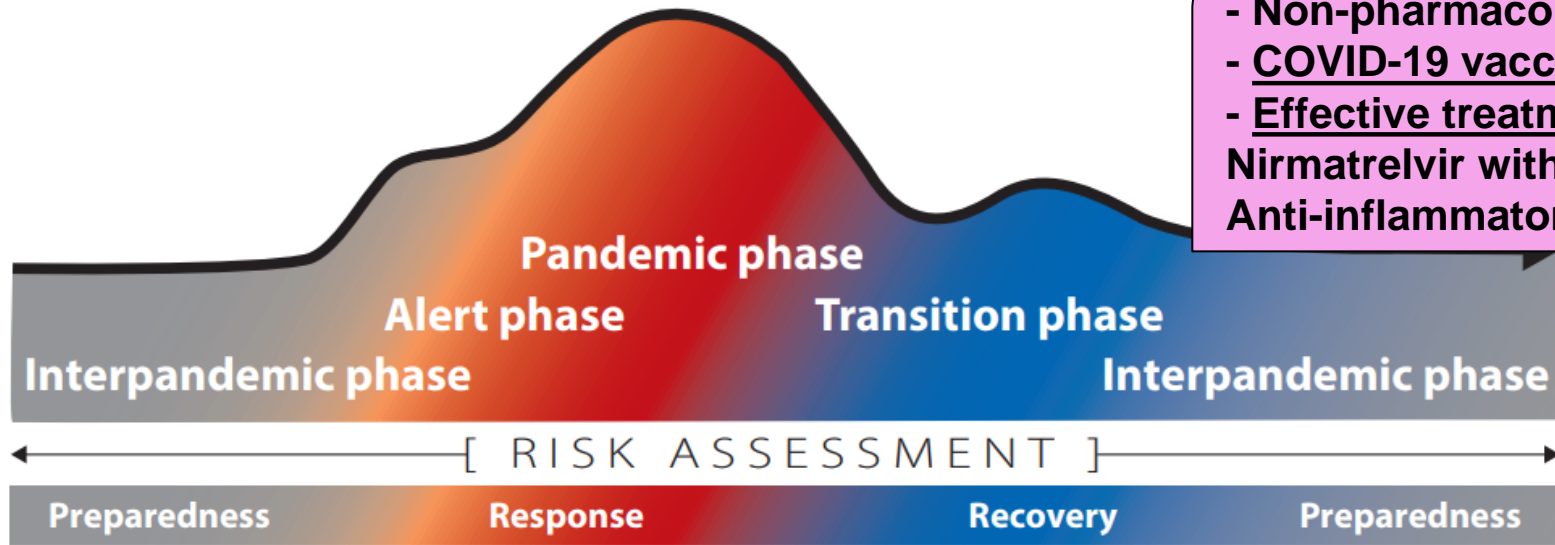
Chula-Cov (COVID-19 vaccine) 2023-2024

Covid-19: What's Next?

Overview:

- **End and Burden of Covid-19**
- **Strategies for Prevention and Control of Covid-19**

Flattening COVID-19 pandemic



- Non-pharmacologic interventions
- COVID-19 vaccination (many platforms)
- Effective treatment: Remdesivir, Nirmatrelvir with Ritonavir, Molnuperavir, Anti-inflammatory

The higher the population immunity and vaccination rate, the lower the number of hospitalizations and deaths²

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

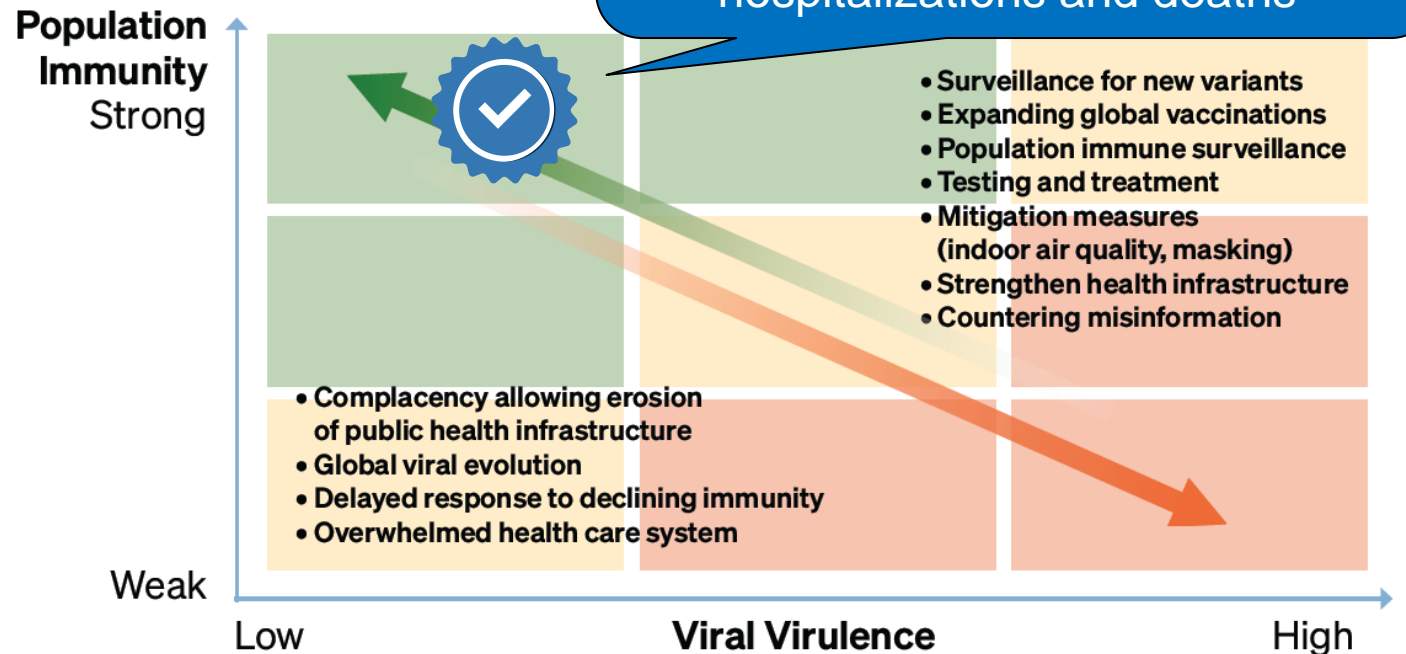
Herd immunity threshold = $1 - 1/R_0$

COVID-19 $R_0 = 2-3 = 60\%$

Delta 5-7

Omicron 8 (80–90%)

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

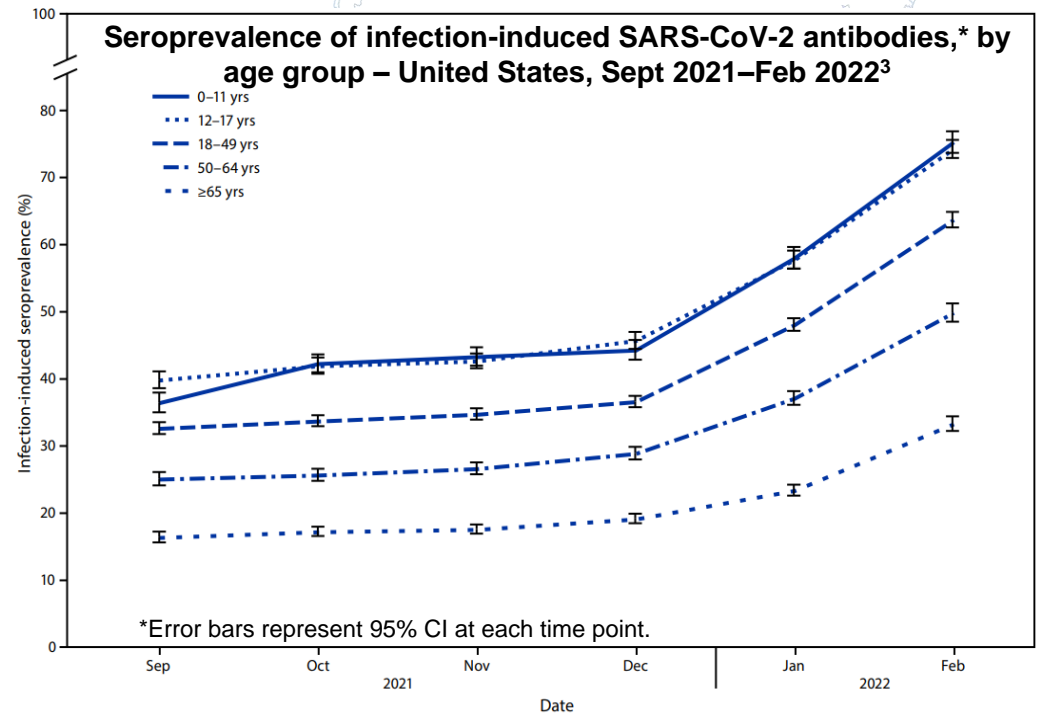
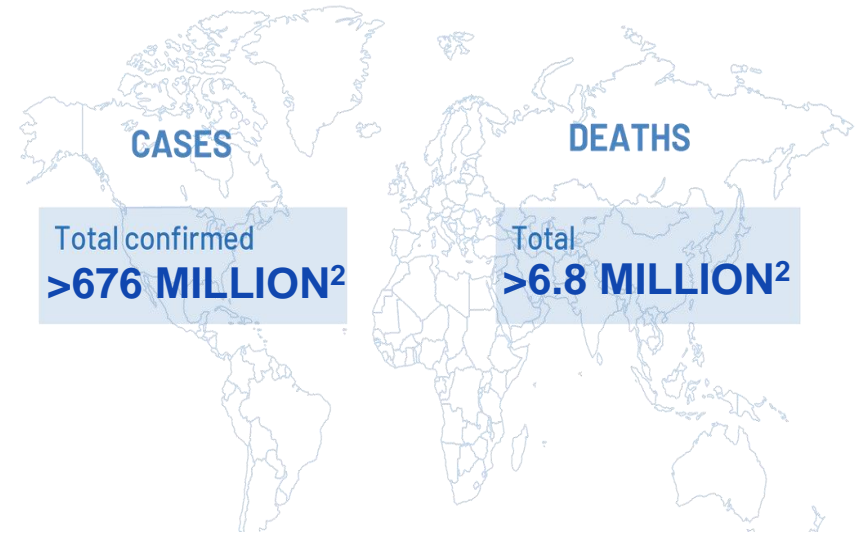
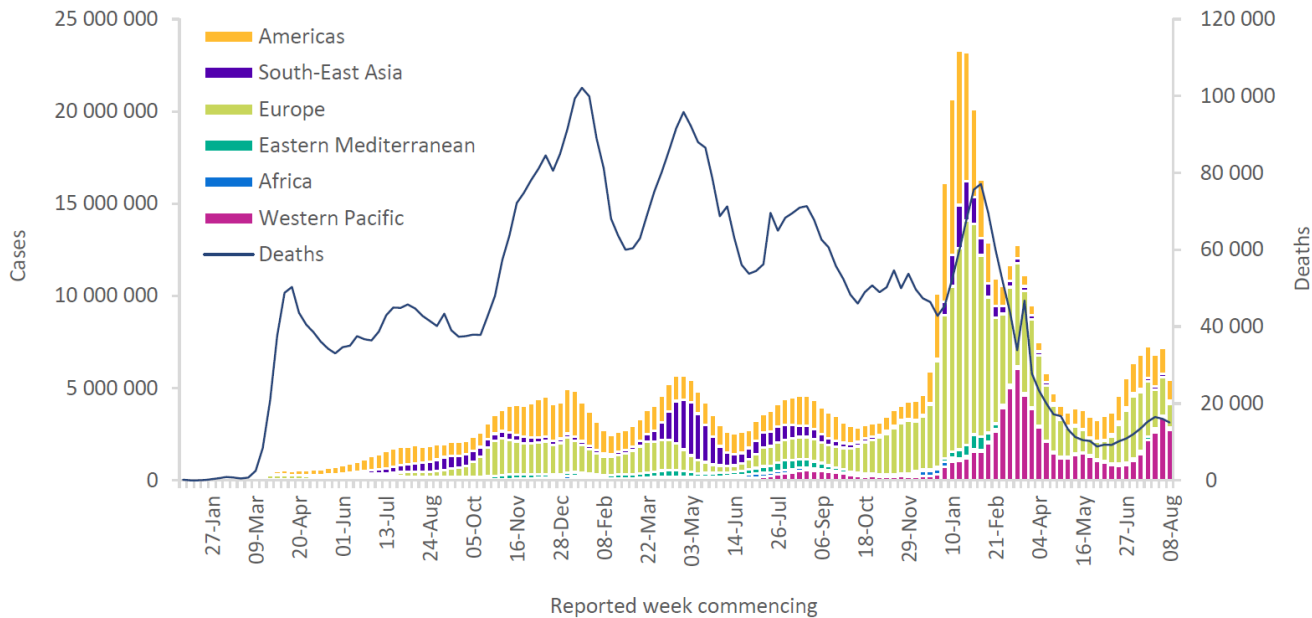


COVID-19, coronavirus disease 2019; R0, basic reproduction number.

1. Pandemic Influenza_Risk Management_Interim Guidance_Jun 2013 WHO Available at: https://www.icao.int/APAC/Meetings/2014%20CAPSCAAP7/Pandemic%20Influenza_Risk%20Management_Interim%20Guidance_Jun%202013%20WHO.pdf Accessed February 2024. 2. Getting to and Sustaining the Next Normal A Roadmap for Living with COVID, March 2022. Available at: <https://rockefellerfoundation.org/wp-content/uploads/2022/03/Getting-to-and-Sustaining-the-Next-Normal-A-Roadmap-for-Living-with-Covid-Report-Final.pdf>. Accessed February 2024.

The COVID-19 pandemic remains unpredictable and continues to evolve, with the ongoing burden of disease impacting governments, populations, healthcare systems, and economies¹

COVID-19 cases reported weekly by WHO Region, and global deaths as of 14 August 2022²



COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

1. Williams BA, et al. *NPJ Vaccines*. 2023;8(1):178. 2. World Health Organization Weekly Update August 2022. Available at: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-COVID-19---17-august-2022> Accessed February 2024. 3. Clarke KEN, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(17):606-609.

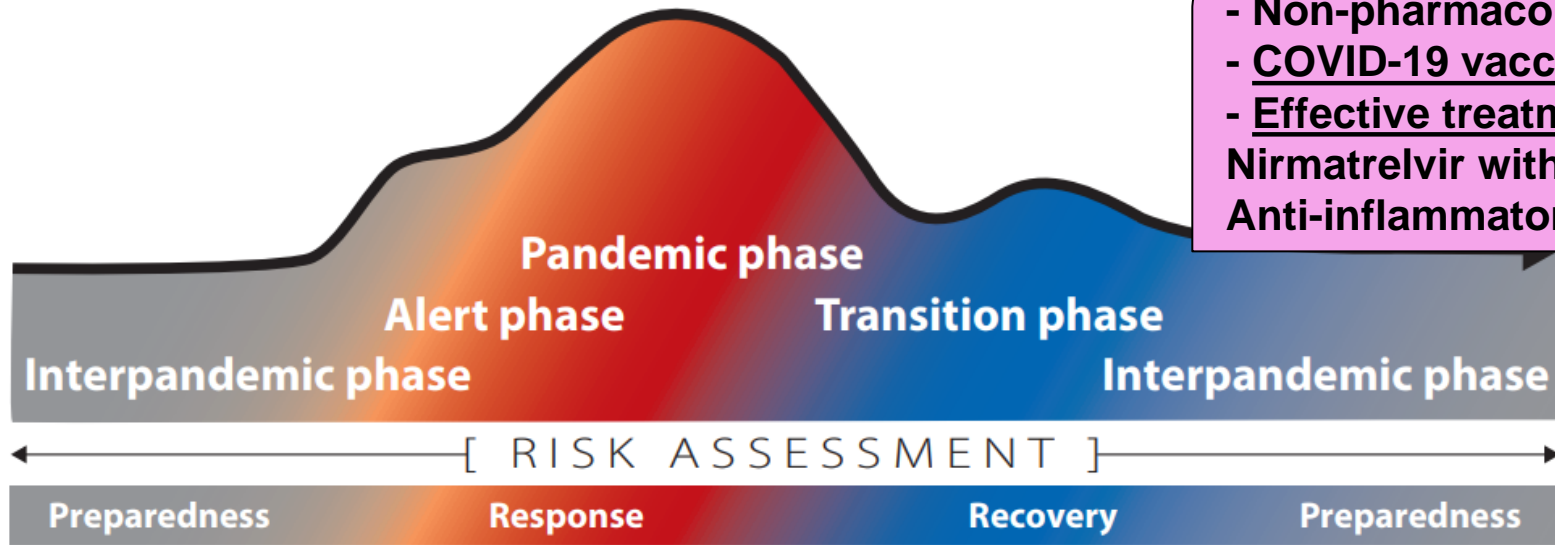
Global death burden of major 20th and 21st century pandemics and of seasonal influenza

Pandemic (global_ population, billions)	Proportion of global population dying (%)	Age distribution of deaths				Life expectancy at birth (years)	Relative magnitude ^a
		<20 (%)	20–40 (%)	40–65 (%)	>65 (%)		
1918–20 (1.8)	1–6 or more	30	40	25	5	38	100–1000
1957–9 (2.9)	0.02–0.05	50	10	5	35	50	1.5–4
1968–70 (3.5)	0.03–0.12	10	5	20	65	56	1.5–4
2009–11 (6.8)	0.003–0.01	30	30	20	20	66	1–3
COVID-19 (7.8)							
Due to infection	0.06–0.12	<<1	5	20	75	73	1.5–4
Excess deaths	0.1–0.28	?	?	?	?	73	2–10
Seasonal flu (7.5) ^b	0.015–0.03	10	10	20	60	73	1 (reference)

^aBased on proportion of person- years lost.

^bCounting a total of 3 seasons, for a fair comparison against pandemic circles.

Flattening COVID-19 pandemic



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- COVID-19 vaccination (many platforms)
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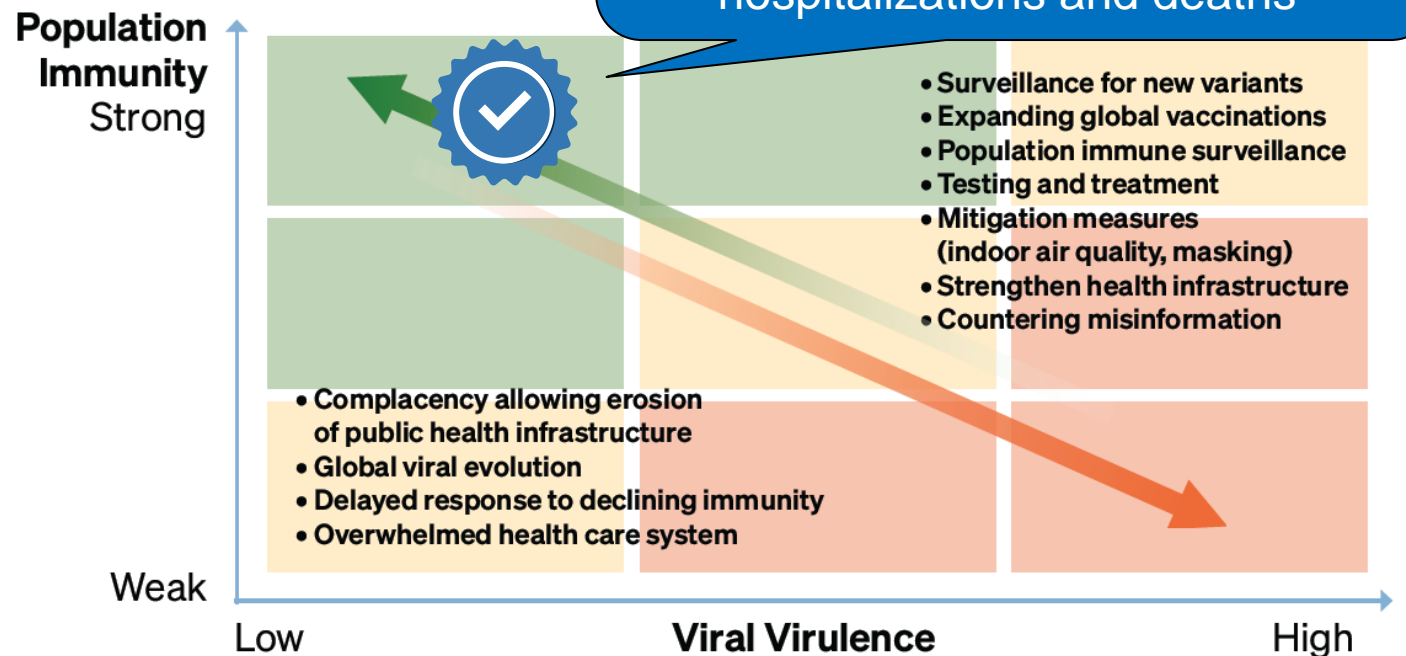
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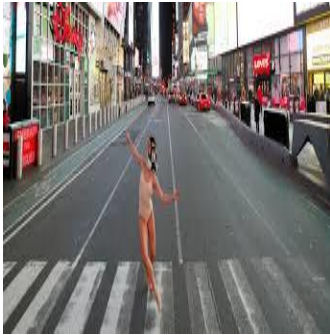
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COVID-19, coronavirus disease 2019; R0, basic reproduction number.

1. Pandemic Influenza_Risk Management_Interim Guidance_Jun 2013 WHO Available at: https://www.icao.int/APAC/Meetings/2014%20CAPSCAAP7/Pandemic%20Influenza_Risk%20Management_Interim%20Guidance_Jun%202013%20WHO.pdf Accessed February 2024. 2. Getting to and Sustaining the Next Normal A Roadmap for Living with COVID, March 2022. Available at: <https://rockefellerfoundation.org/wp-content/uploads/2022/03/Getting-to-and-Sustaining-the-Next-Normal-A-Roadmap-for-Living-with-Covid-Report-Final.pdf>. Accessed February 2024.

Lockdown Period¹



- **Proactive surveillance** via large scale PCR-testing and digital real-time contact tracing
- **Medical care management** to protect high-risk individuals
- **Travel restrictions** across national and international borders
- **Physical distancing, mask wearing and handwashing**
- Re-implementation of **regional lockdowns** in cases of endemic outbreak

Effects of Global Lockdown²

About 265 million people will face acute food insecurity.



Worldwide recession, with 40-60 million people in extreme poverty.



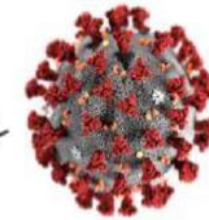
Lack of access to education, (1,184,126,508) 67.6% of students affected



Effects of the Global Lockdown

Telehealth might become the new normal

Covid-19



100-120 million tourism jobs affected and \$1.2 trillion lost by the tourism sector globally



Increase in mental health challenge and post-traumatic stress disorder



31 million new cases of gender-based violence.



90% reduction in air pollution



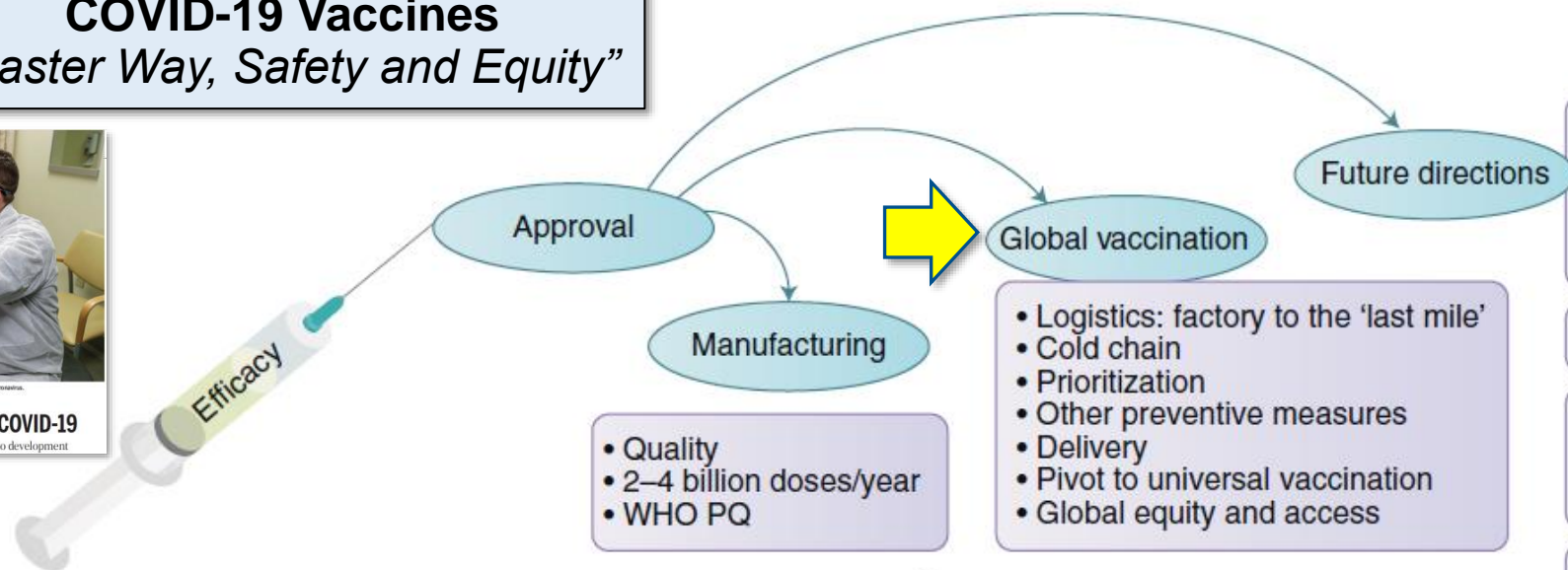
COVID-19 Herd Immunity in the Absence of a Vaccine: An Irresponsible Approach

Reasons why a strategy that aims to reach herd immunity against COVID-19 in the absence of a vaccine is largely irresponsible:

- It results in a **large loss of life**, more severe disease, and long-term harm
- It results in ***endemic disease, not the absence of disease, with ongoing harm***
- ***Protecting large vulnerable groups becomes nearly impossible***, as they cannot safely participate in society where disease is endemic
- **Reinfection undermines immunity**, especially because the disease can be more severe in subsequent infections
- Containing the virus has been successful in dozens of countries, while ***attempting herd immunity has failed with a high cost***. (suppressing the disease gives time for development of treatments and vaccines)
- ***Various uncertainties associated with a novel virus***

The next steps for a COVID-19 vaccine¹

COVID-19 Vaccines
“Faster Way, Safety and Equity”



- Quality
- 2–4 billion doses/year
- WHO PQ

- Logistics: factory to the 'last mile'
- Cold chain
- Prioritization
- Other preventive measures
- Delivery
- Pivot to universal vaccination
- Global equity and access

- Optimizations
- Durability?
- Dose?
- Schedule?
- Boosters?

Correlates of protection?

- Effectiveness
- Real-world evidence,
- Herd immunity?

Safety—long term?

- Surveillance
- New COVID-19 mutants
- COVID-2X?

Overcoming hesitancy

12 Vaccines in Phase III (and beyond)

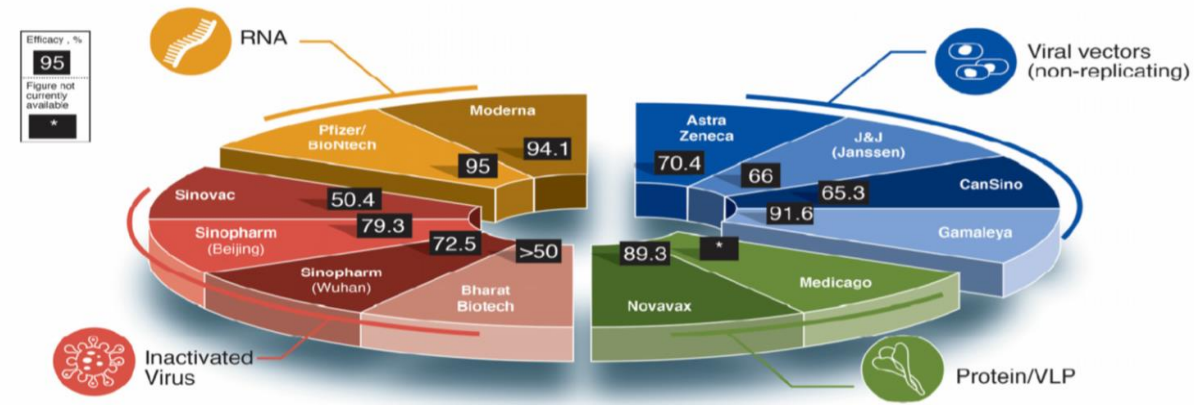
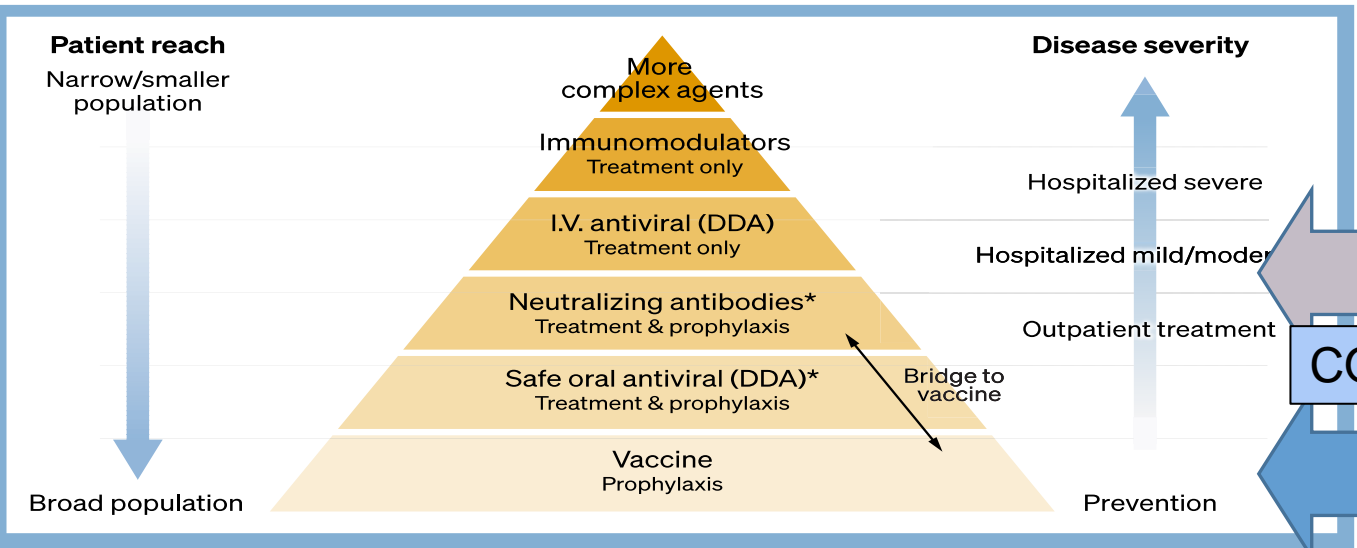
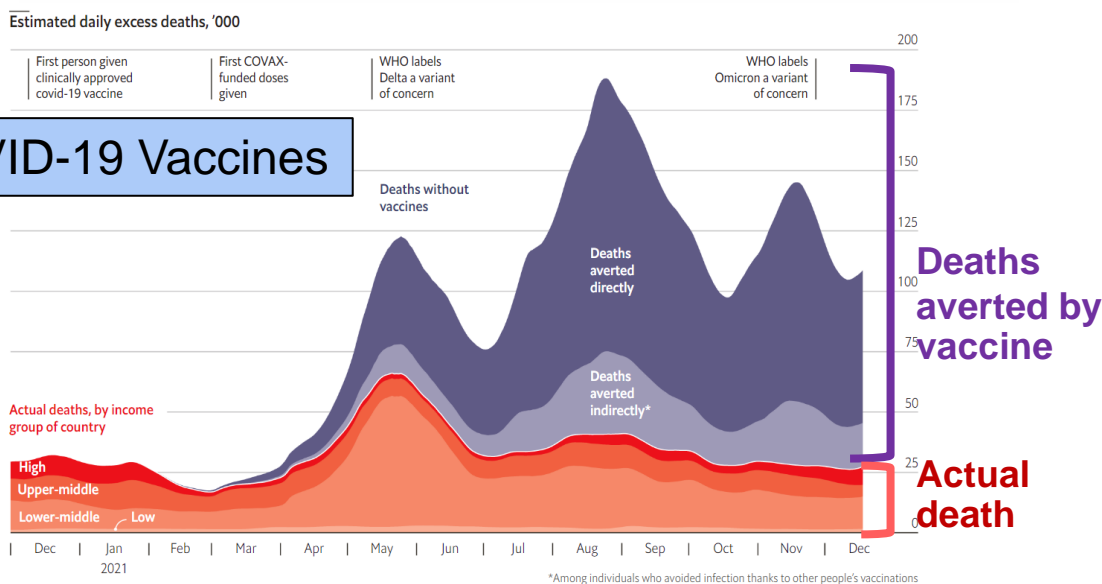


Figure 1. The twelve SARS-CoV-2 vaccine candidates reaching/announcing Phase III clinical trials by mid-November 2020. Shown in pie-chart configuration are the companies responsible for the development of the vaccines as well as their reported efficacy in Phase III trials. *, efficacy not yet available. Due to variability in reporting criteria for cases of COVID-19, efficacy results may not be directly comparable.

COVID-19, coronavirus disease 2019; WHO PQ, World Health Organization prequalification; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
 1. Kim JH, et al. *Nat Med.* 2021;27(2):205-211. 2. Cohen J. *Science.* 2020;368(6486):14-16. 3.. Funk CD, et al. *Viruses.* 2021;13(3):418.

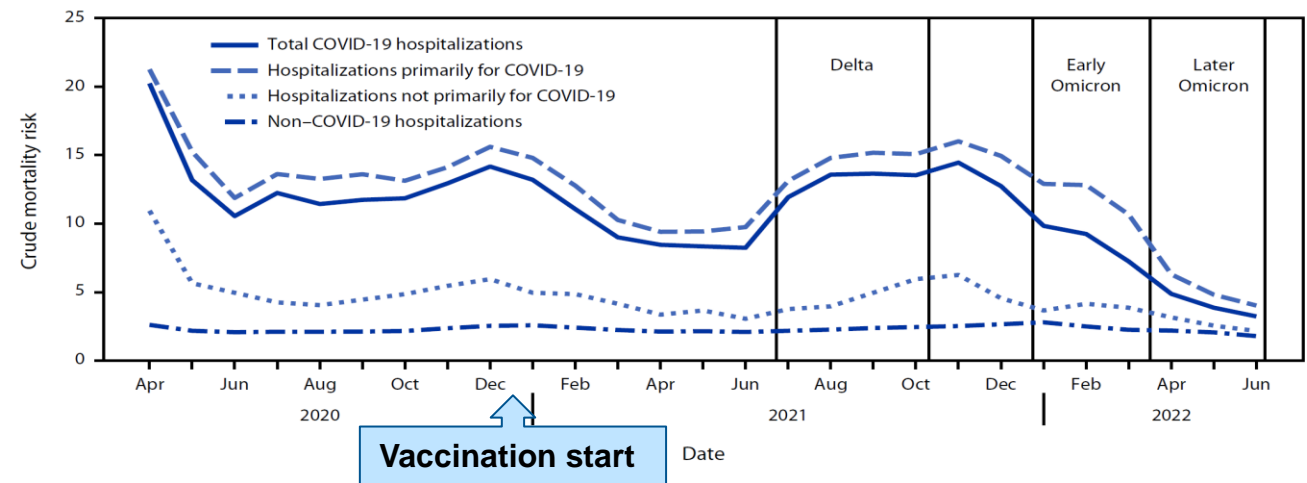


Vaccines are powerful tools



The global COVID-19 death toll would be more than double by now without vaccines. Tens of millions of lives were saved globally last year from COVID-19 vaccines

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¶

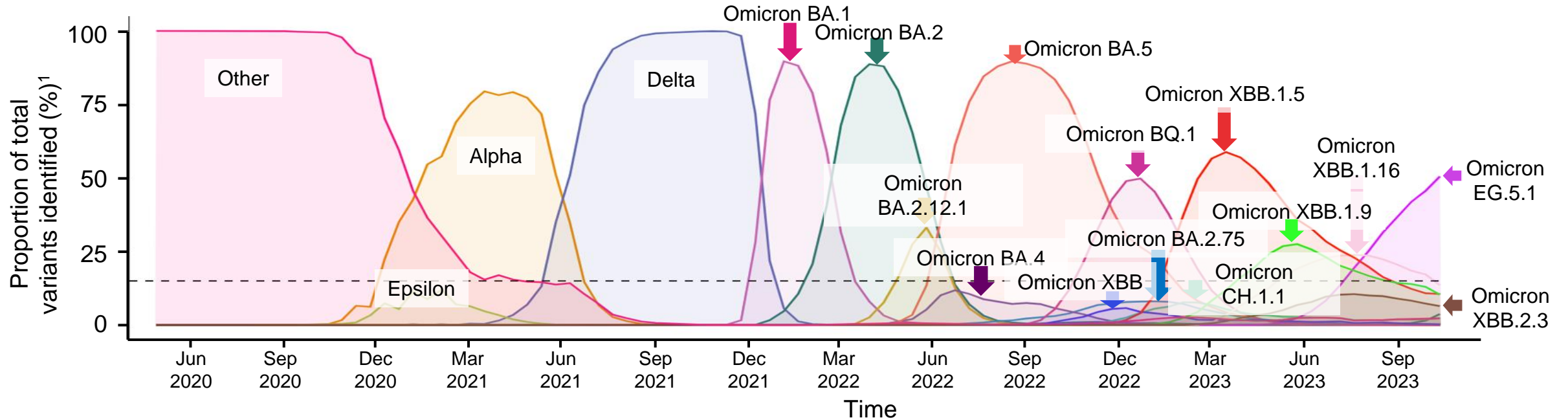


Based on official reported COVID-19 deaths, a mathematical modelling estimated that **vaccinations prevented 19.8 million deaths from COVID-19**, representing a **global reduction of 63% in total deaths** during the first year of COVID-19 vaccination⁴

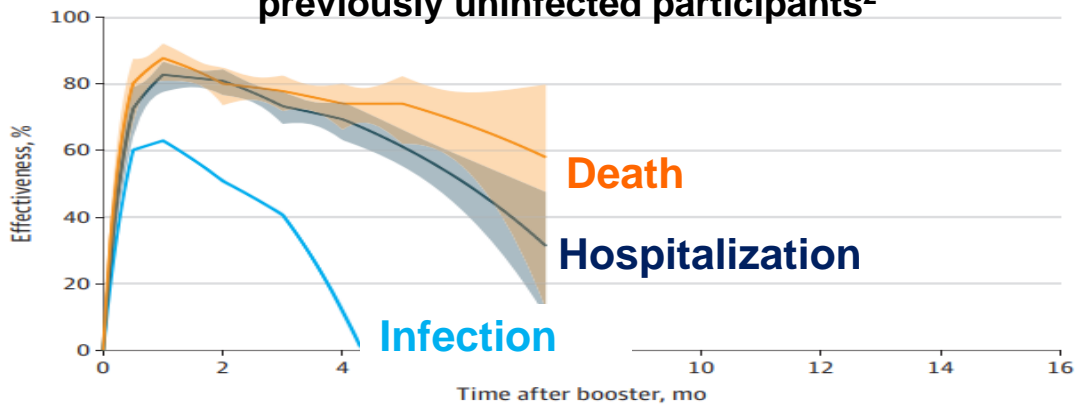
COVID-19, coronavirus disease 2019; DDA, direct acting antiviral.

1. Getting to and Sustaining the Next Normal A Roadmap for Living with COVID, March 2022. Available at: <https://rockefellerfoundation.org/wp-content/uploads/2022/03/Getting-to-and-Sustaining-the-Next-Normal-A-Roadmap-for-Living-with-Covid-Report-Final.pdf>. Accessed February 2024. 2. Adjei S, et al. *MMWR Morb Mortal Wkly Rep.* 2022;71(37):1182-1189. 3. Figure adapted from the Economist. Available at: <https://www.economist.com/graphic-detail/2022/07/07/covid-19-vaccines-saved-an-estimated-20m-lives-during-their-first-year>. Accessed February 2024. 4. Watson OJ, et al. *Lancet Infect Dis.* 2022 Sep;22(9):1293-1302.

Rapid Evolution of SARS-CoV-2 Variants



Effectiveness of booster vs primary series alone among previously uninfected participants²



Vaccination or infection do not always guarantee effective immune responses; and durability and adequacy to prevent from newer variants and prevent serious clinical outcomes carries substantial uncertainty.

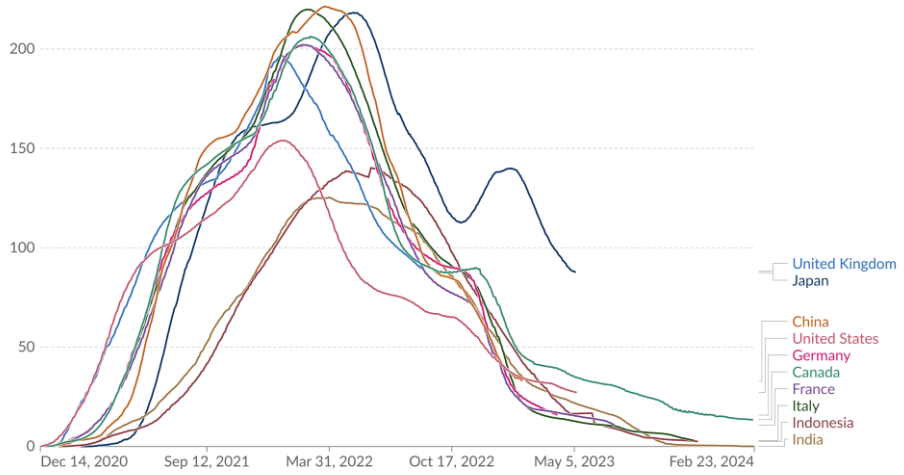
Vaccine effectiveness (VE) against severe disease continues to be higher and more sustained over time than VE against infection

The booster dose provides significant additional protection against infection and severe disease in all ages

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

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.

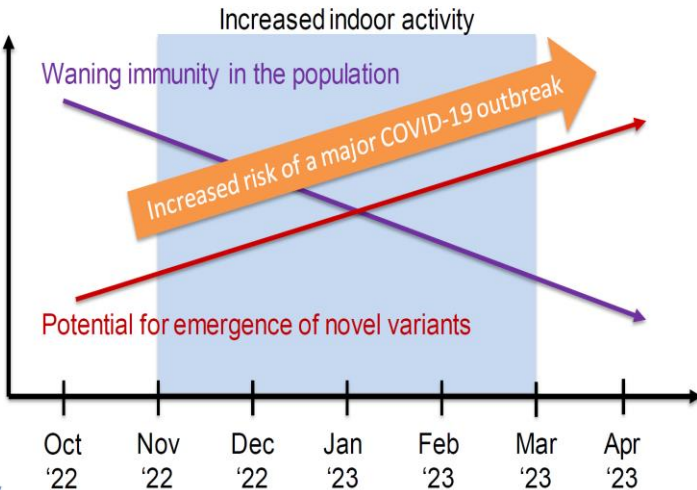
Our World in Data



Data source: Official data collated by Our World in Data

CC BY

Potential Evolution of COVID-19



www.fda.gov

8

Misinformation and COVID-19 Vaccine Hesitancy³

Reasons for not getting the COVID-19 vaccine

Category	Description	Number of responses	%
Unforeseen future effects ^a	Worries about unforeseen problems for adults and/or children	355	49
Fear of commercial profiteering ^a	Belief that vaccines are promoted by authorities and corporations to advance their financial interests	92	13
Doubting effectiveness ^a	Mistrust of vaccine benefit due to a perceived lack of safety, effectiveness, and/or protectiveness	87	12
Preference for natural immunity ^a	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

^aVAX scale vaccine attitude.

- Waning immunity
- Waning vaccine effectiveness
- Emergence of novel (more or less pathogenic) variants

COVID-19, coronavirus disease 2019.1.

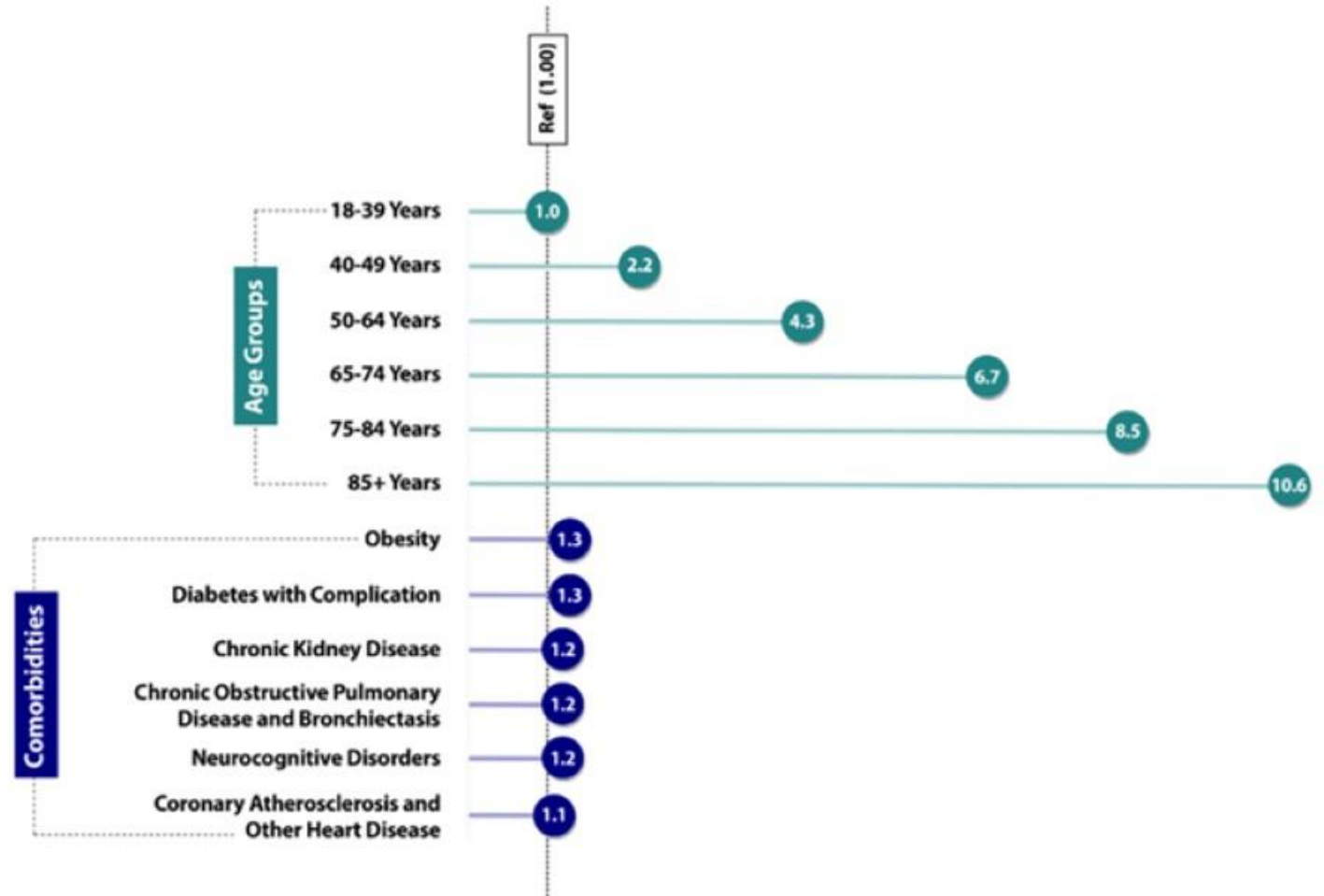
1. COVID-19 vaccine doses. Available at: <https://ourworldindata.org/covid-vaccinations> Accessed 24 February 2024. 2. Willingness to get vaccinated against COVID-19. Available at: <https://ourworldindata.org/grapher/covid-vaccine-willingness-and-people-vaccinated-by-month> Accessed 24 February 2024. 3. Zimmerman T, et al. *Vaccine*. 2023;41(1):136-144.

Risk Factors for Severe COVID-19

Age is the most important risk factor for severe COVID-19

Factors that put patients at risk for severe COVID-19:

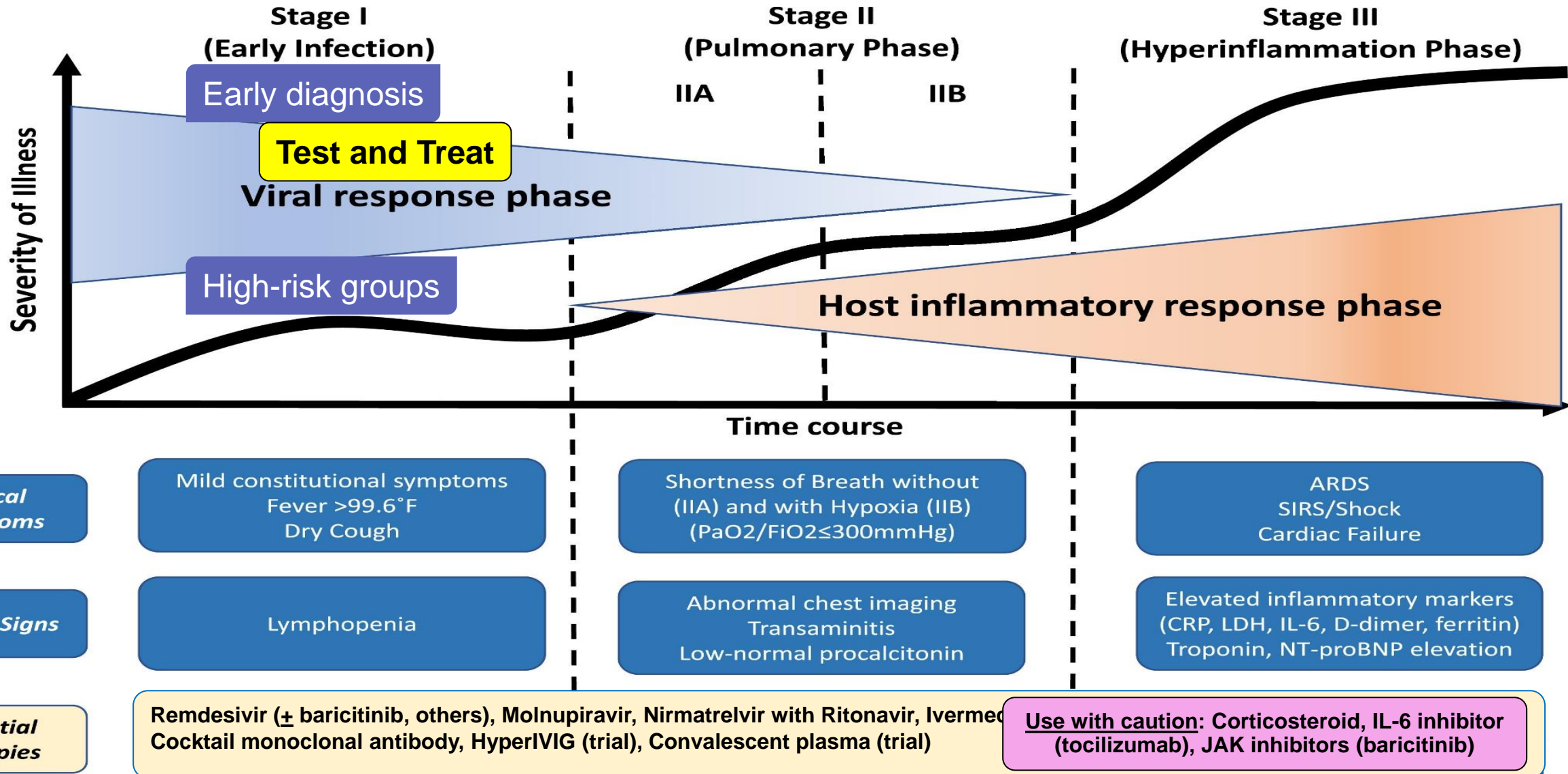
- Age
- Underlying medical conditions
- Being unvaccinated or not fully vaccinated
- Being immunocompromised



Ref, reference.

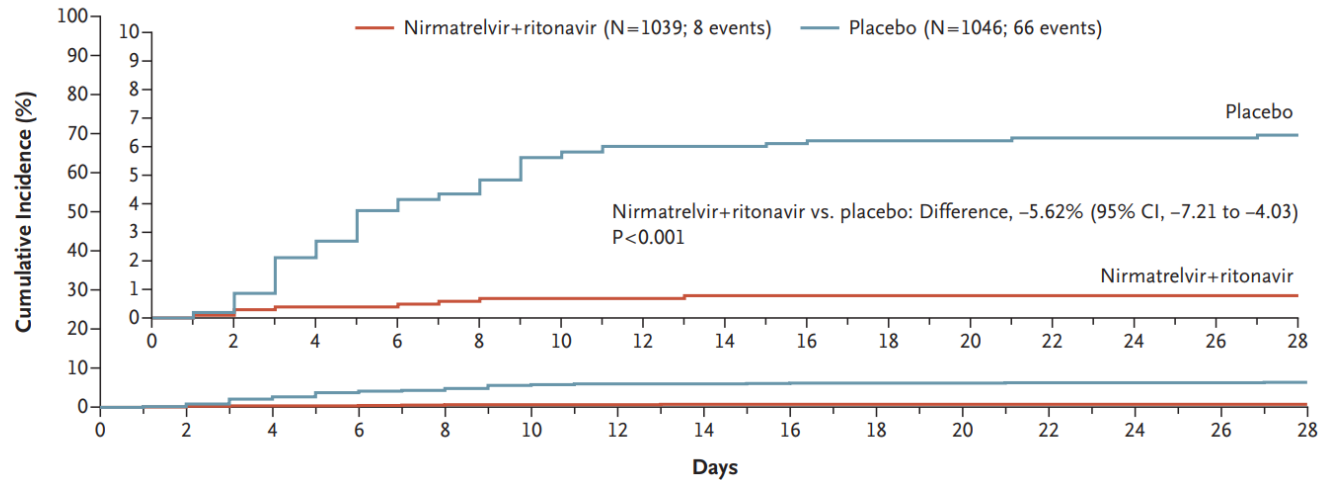
CDC. Updated February 9, 2023. Accessed November 15, 2023. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>

COVID-19 illness: A clinical–therapeutic staging proposal



Oral Nirmatrelvir for high-risk, nonhospitalized, unvaccinated adults with COVID-19: Phase 3 Randomized Trial¹

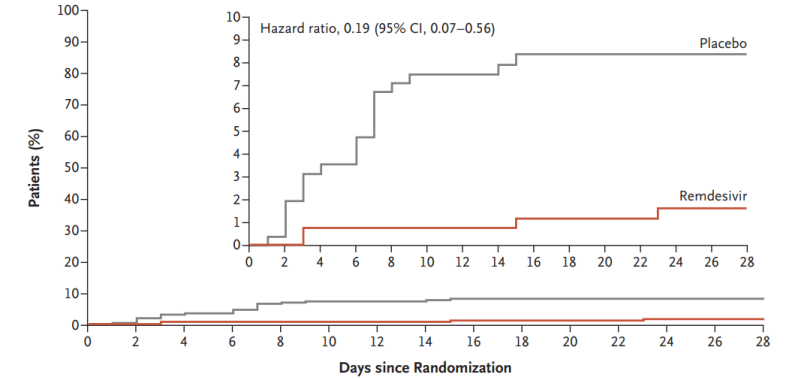
Covid-19–Related Hospitalization or Death from Any Cause through Day 28 among Patients Treated ≤5 Days after Symptom Onset



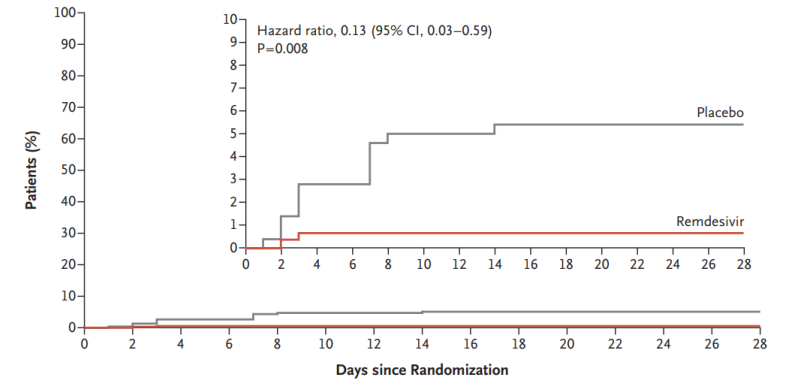
No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
NMV-r	1039	1034	1023	1013	1007	1004	1002	1000	997	995	993	993	993	993	992
Placebo	1046	1042	1015	990	977	963	959	959	955	953	951	948	948	948	945

IV Remdesivir in outpatients with mild to moderate COVID-19: PINETREE Randomized Study²

Covid-19–Related Medically Attended Visit or Death from Any Cause

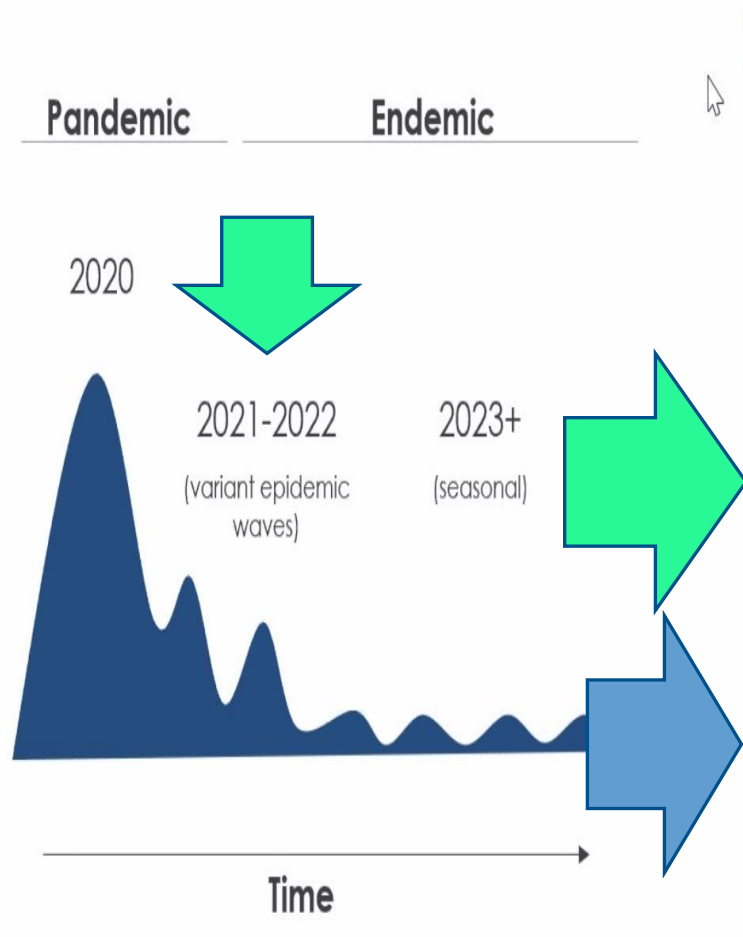


Covid-19–Related Hospitalization or Death from Any Cause



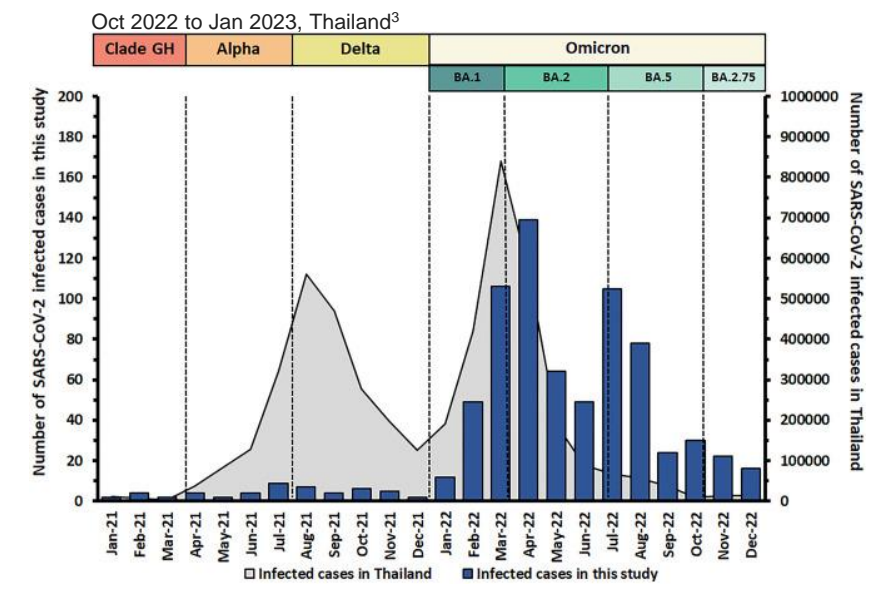
No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
Placebo	283	280	272	271	265	264	264	263	262	261	261	260	256	250	227
Remdesivir	279	276	272	272	271	268	268	268	264	264	264	264	260	252	226

Post-pandemic immunity after **immunization and natural infection** will maintain endemic **COVID-19** immunity to human coronaviruses (natural infection): < 1 year¹



Stage	Focus for vaccines
Pandemic Initial waves	<ul style="list-style-type: none"> Heavy focus on protecting high-risk populations Mostly ancestral virus vaccine
Variant epidemics Reinfection waves	<ul style="list-style-type: none"> Focus to suppressing transmission of variants Speed & adaptability are critical
Endemic Seasonal	<ul style="list-style-type: none"> <u>Multi-valent approaches with broadest immunity</u> <u>Focus on toddlers and seasonal protection against waning immunity in high-risk (e.g., 65+)</u>

COVID-19 vaccine will stop pandemic²



- Maintain immunity 80–90%
Natural booster or vaccination (booster-risk groups– duration ?)
- New variant of SARS-CoV2 VOC
(New vaccine for specific VOC ?)

Non-pharmacologic interventions: non-restriction?
Effective treatment: Remdesivir, Nirmatrelvir with Ritonavir, Molnuperavir
COVID-19 vaccination (many platforms)

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

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VOC, variants of concern.
 1. Milne G, et al. *Lancet Respir Med.* 2021;9(12):1450-1466. 2. Veldhoen M, Simas JP. *Nat Rev Immunol.* 2021;21(3):131-132. 3. Chansaenroj J, et al.. *Sci Rep.* 2023;13(1):15595.

Current COVID-19 (Omicron era)

- **Lower disease severity** compared to infection due to previous SARS-CoV-2 variants¹
- **High levels of population immunity** acquired through vaccination and/or natural infection¹

Once a high population immunity threshold (from infection or vaccination) is attained, the pandemic transitions to an endemic phase¹

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

Despite high vaccination and prior infection rates, immunity may be insufficient to protect from mild infection and transmission (even less so, when new variants emerge), but may still markedly decrease serious outcomes.¹

In May 2023, WHO declared the end to the COVID-19 global health emergency, but urged for continued preparedness

WHO has advised that it is now time to move toward the long-term management of SARS-CoV-2 as an ongoing health issue, notably due to the remaining uncertainties posed by the potential evolution of the virus.



WHO advises that all partners and States Parties dedicate sustained attention and resources to preparedness and resilience for emerging threats, including:

- Sustaining capacities and remaining prepared for **future events/outbreaks**
- Integrating COVID-19 vaccination into **life course vaccination programs**, as well as maintaining efforts to increase vaccine coverage for high-priority groups
- Strengthening regulatory authorities to support **long-term availability and supply** of vaccines, diagnostics, and therapeutics

The end of the COVID-19 pandemic¹

There are **no widely accepted, quantitative definitions** for the end of a pandemic such as COVID-19.

The end of the pandemic and the **transition to endemicity may be defined based on:**

High proportion (70% ?) of the global population having immunity by natural infection or vaccination (heterogeneity/new VOC).

Other considerations:

- Diminished death (normal death toll)
- Lower clinical burden (diminished pressure on health systems)
- Reduced actual and perceived personal risk
- Removal of restrictive measures
- Diminished public attention

Adjusting public health and social measures

WHO Interim guidance
Considerations COVID-19
public health measures
(30 March 2023)²

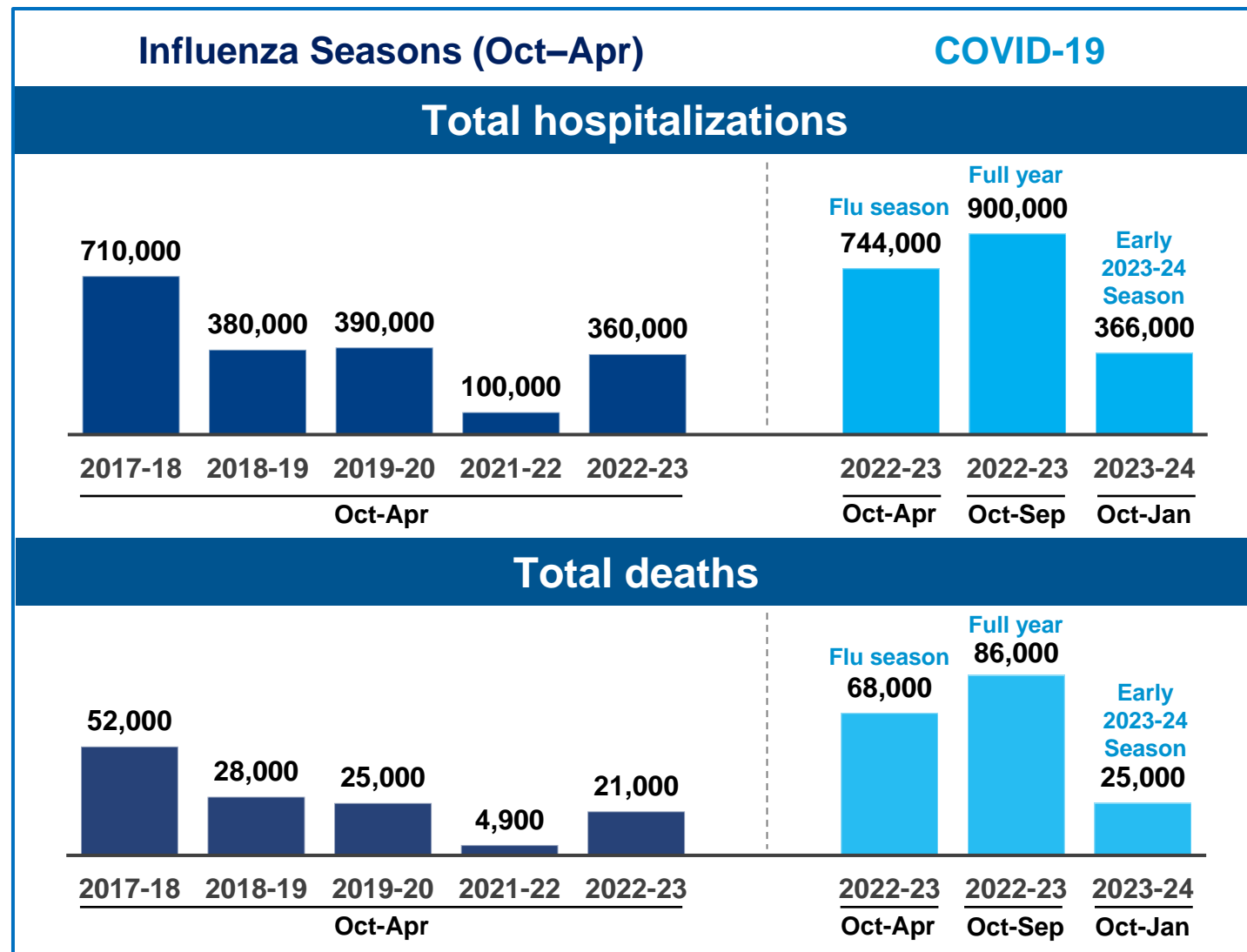
- Reduce transmission of SARS-CoV-2, cases of COVID-19 and post-COVID-19 condition and the risk of emergence of variants.
- Reduce morbidity and mortality due to COVID-19.
- Reduce impact on health systems.

Endemic or Seasonal: What 's mean?



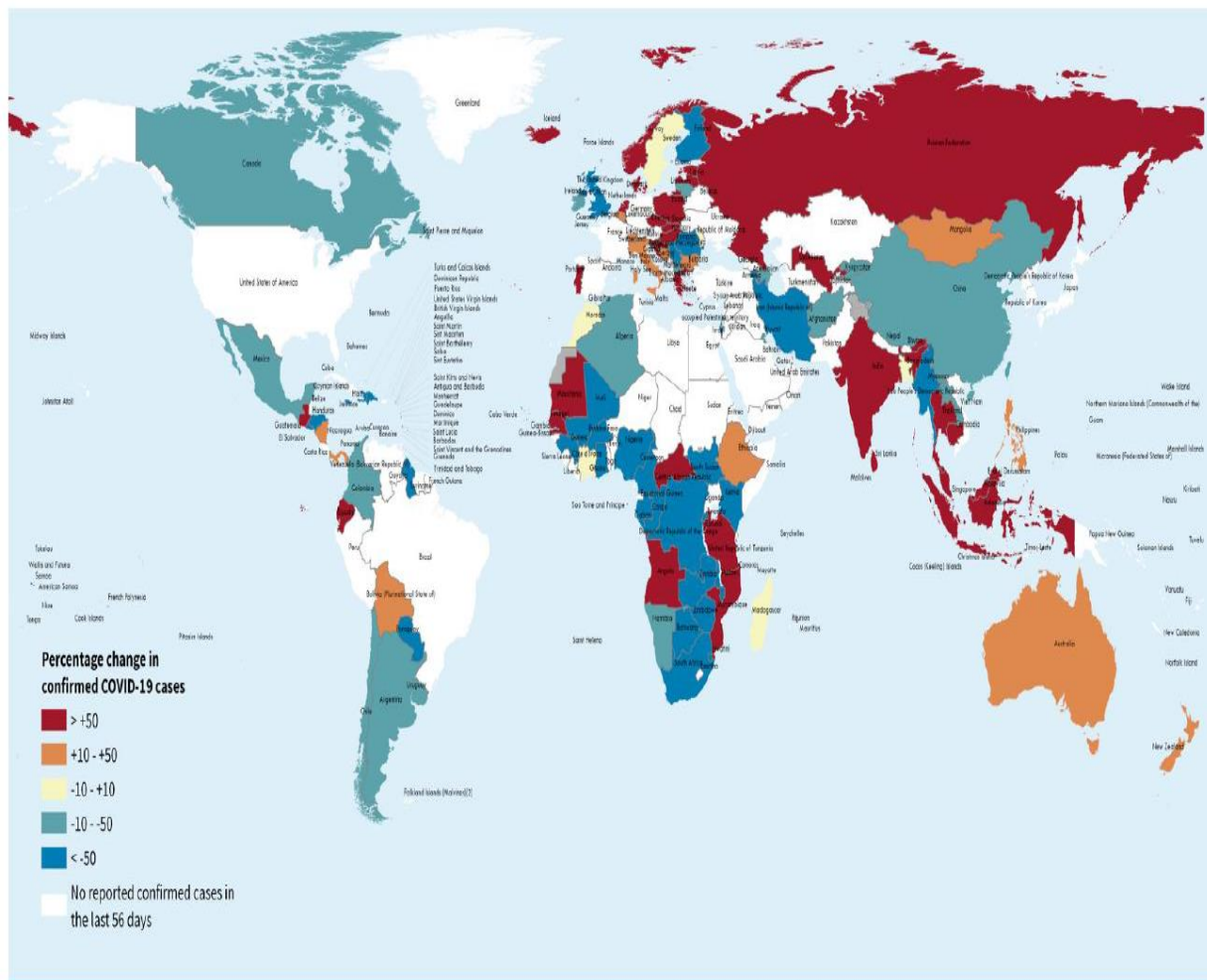
COVID-19 Still a Top Cause of Morbidity and Mortality

- COVID-19 10th leading cause of death in 2023¹
– 11th leading cause: flu & pneumonia
- Post-pandemic COVID-19 burden is comparable or higher than flu burden^{2,3}
- 2023–24 COVID-19 burden already higher than some prior flu seasons^{2,3}



COVID-19 epidemiological update – 22 December 2023

Figure 4. Percentage change in confirmed COVID-19 cases over the last 28 days relative to the previous 28 days, as of 17 December 2023**

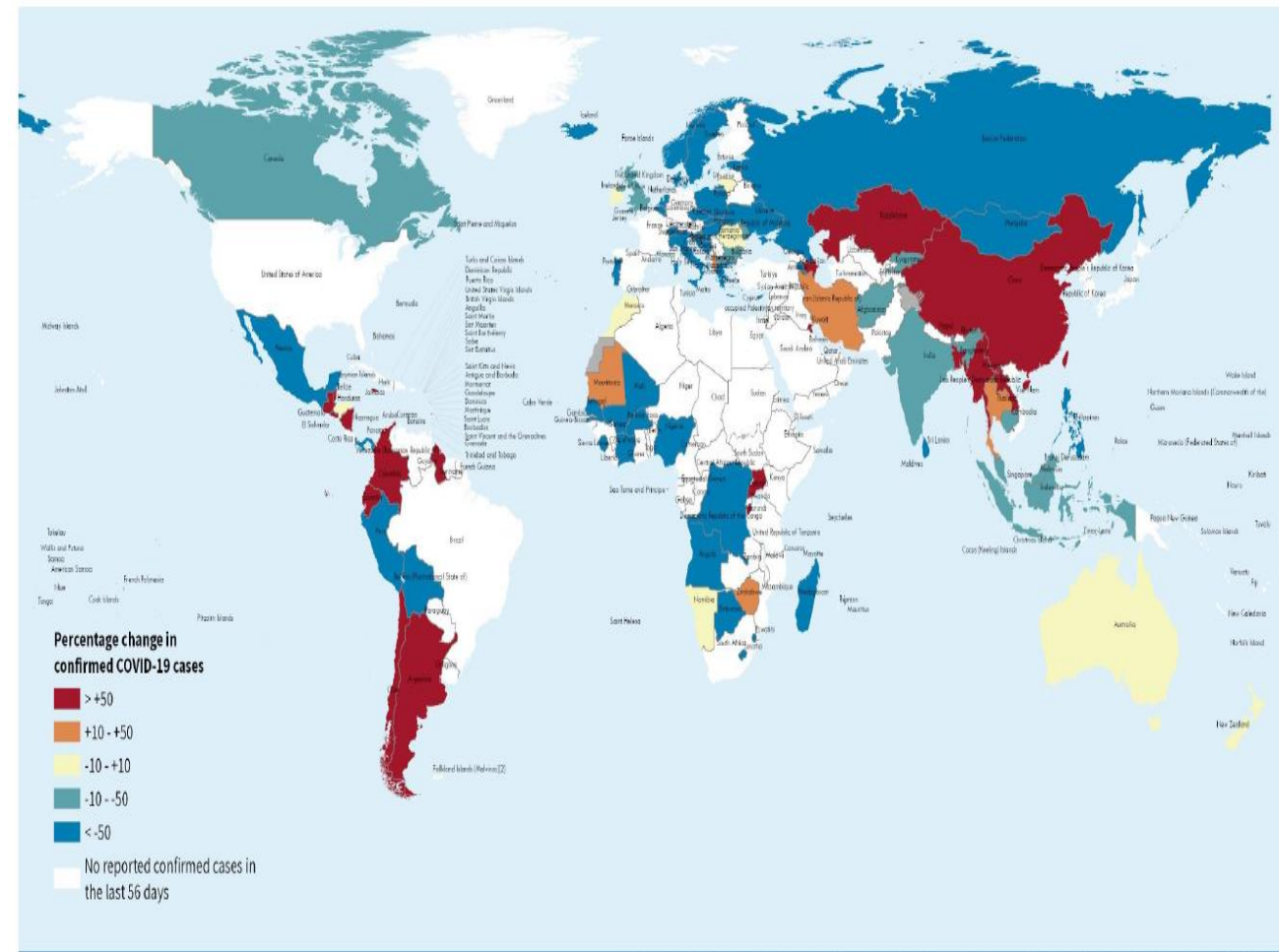


Data Source: World Health Organization
 Map Production: WHO Health Emergencies Programme
 Not applicable
 0 2,500 5,000 km
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COVID-19 epidemiological update – 16 February 2024

Figure 4. Percentage change in confirmed COVID-19 cases over the last 28 days relative to the previous 28 days, as of 4 February 2024**



Data Source: World Health Organization
 Map Production: WHO Health Emergencies Programme
 Not applicable
 0 2,500 5,000 km
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COVID-19 continues to pose health risks, including infections, hospitalizations, and death globally

WHO global overview: Events reported globally*



>17,930

new cases per day
(25 Sept–22 Oct 2023)



>3420

new hospitalizations per day
(18 Sept–15 Oct 2023)



>160

new deaths per day
(25 Sept–22 Oct 2023)



STRATEGIES FOROMICRON VARIANT / NEW VOC

- **Interruption of SARS-CoV-2 variant spread:** Maintaining present public health prevention measures, and early diagnosis (accuracy) and timely quarantine
- **Early diagnosis and Effective treatment (anti-COVID-19 agents/anti-inflammatory agents.....)**
- **COVID-19 vaccination**
 - **Improving COVID-19 vaccine coverage:** Primary COVID-19 vaccines and booster doses
- **Developing variant-specific vaccines:** (updated COVID-19 vaccine).....

*Globally, 93 countries reported COVID-19 cases, 38 reported deaths and 60 reported hospitalisations.

COVID-19, coronavirus disease 2019; WHO, World Health Organization.

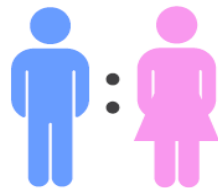
World Health Organization. Available at: <https://www.who.int/publications/m/item/COVID-19-epidemiological-update---27-october-2023> (accessed November 2023)..

ผู้เสียชีวิต จำนวน 8,950 ราย



อายุเฉลี่ย 71 ปี

- ต่ำสุด 1 เดือน
- สูงสุด 109 ปี



อัตราส่วน
เพศชายต่อเพศหญิง
เท่ากับ 1.2 : 1

ผู้ป่วยที่เคยติดเชื้อ **SAR-COV-2** มีความเสี่ยงที่จะ
มีผลกระทบทางสุขภาพภายหลังการป่วยจากโควิด-19

ประวัติการรับวัคซีน	ประวัติทางสุขภาพ
<ul style="list-style-type: none"> • ไม่ได้รับวัคซีน 4,568 ราย • รับวัคซีน 1 เข็ม 641 ราย • รับวัคซีน 2 เข็ม 2,706 ราย • รับวัคซีน 3 เข็มขึ้นไป 657 ราย • ไม่มีข้อมูล 378 ราย 	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>มีโรคประจำตัว 7,909 ราย</p> </div> <div style="text-align: center;"> <p>ปฏิเสธโรคประจำตัว 489 ราย</p> </div> <div style="text-align: center;"> <p>ไม่ระบุ 552 ราย</p> </div> </div>

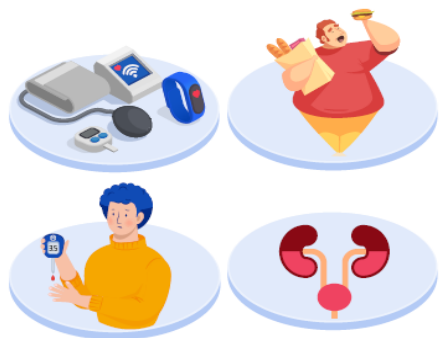
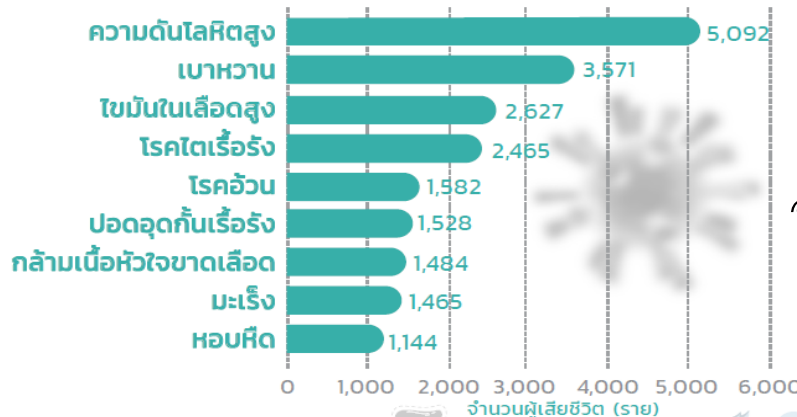
Long COVID*

ประมาณ

~24%

ของผู้ป่วยโควิด-19 มีภาวะ
Long COVID^{1-3†‡§}

มีโรคประจำตัว 7,909 ราย (ร้อยละ 88.37)



การป้องกัน

ประชาชนโดยเฉพาะ 7 กลุ่มเสี่ยง โดยเฉพาะกลุ่มเสี่ยงสูง ผู้สูงอายุ
ผู้มีโรคประจำตัว 7 กลุ่มโรค รวมถึงหญิงตั้งครรภ์ ยังจำเป็นต้องฉีดวัคซีน 2 เข็มแรก
หรือหากฉีดครบแล้วนาน 3-6 เดือน ควรได้รับเข็มกระตุ้น

ข้อมูลจาก : ทะเบียนผู้เสียชีวิต กรมควบคุมโรค

จัดทำ : 8 ก.ค. 2565

Global Burden of Disease Long COVID Collaborators^{1†}

จากการสำรวจและศึกษาการเกิดอาการ Long COVID หลังการ

เจ็บป่วยด้วยโรคโควิด-19 ทั่วโลก พบว่า....

~3 ใน 5 ราย พบความผิดปกติทางระบบหายใจ

~1 ใน 2 ราย พบปัญหาเกี่ยวกับการปวดตามร่างกาย/อารมณ์แปรปรวน

จากผลการศึกษาวิจัยต่างๆ พบว่าความเสี่ยงในการเกิด Long Covid สามารถลดลงได้จากการได้รับวัคซีนป้องกันโรคโควิด³⁻⁵

Covid-19: What's Next?

Overview:

- **End and Burden of Covid-19**
- **Strategies for Prevention and Control of Covid-19**

STRATEGIES FOROMICRON 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
- ***Early effective treatment (anticovid-19 agents/anti-inflammatory agents.....)***



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:

- Multivalent vaccine candidates

Why Is COVID-19 Testing Still Important?



Protecting those around the infected individual^[1]



Prevention of progression to severe disease in at-risk individuals^[1]



Distinguishing between different respiratory infections^[2]

Current Status of COVID-19 Testing

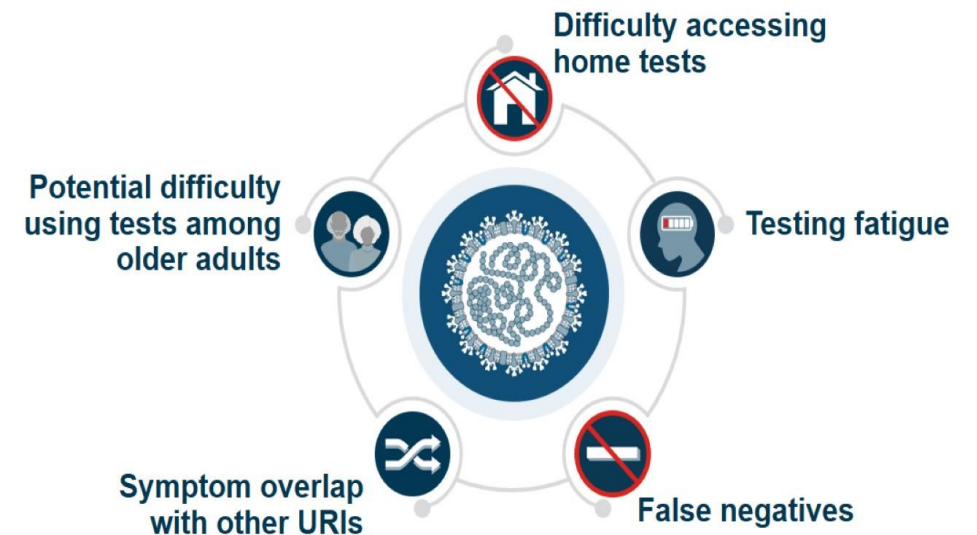
At height of pandemic

- PCR and antigen self testing were widely used
- Costs reimbursed in most countries
- Antigen testing required before travel
- PCR or antigen testing required for hospital admission

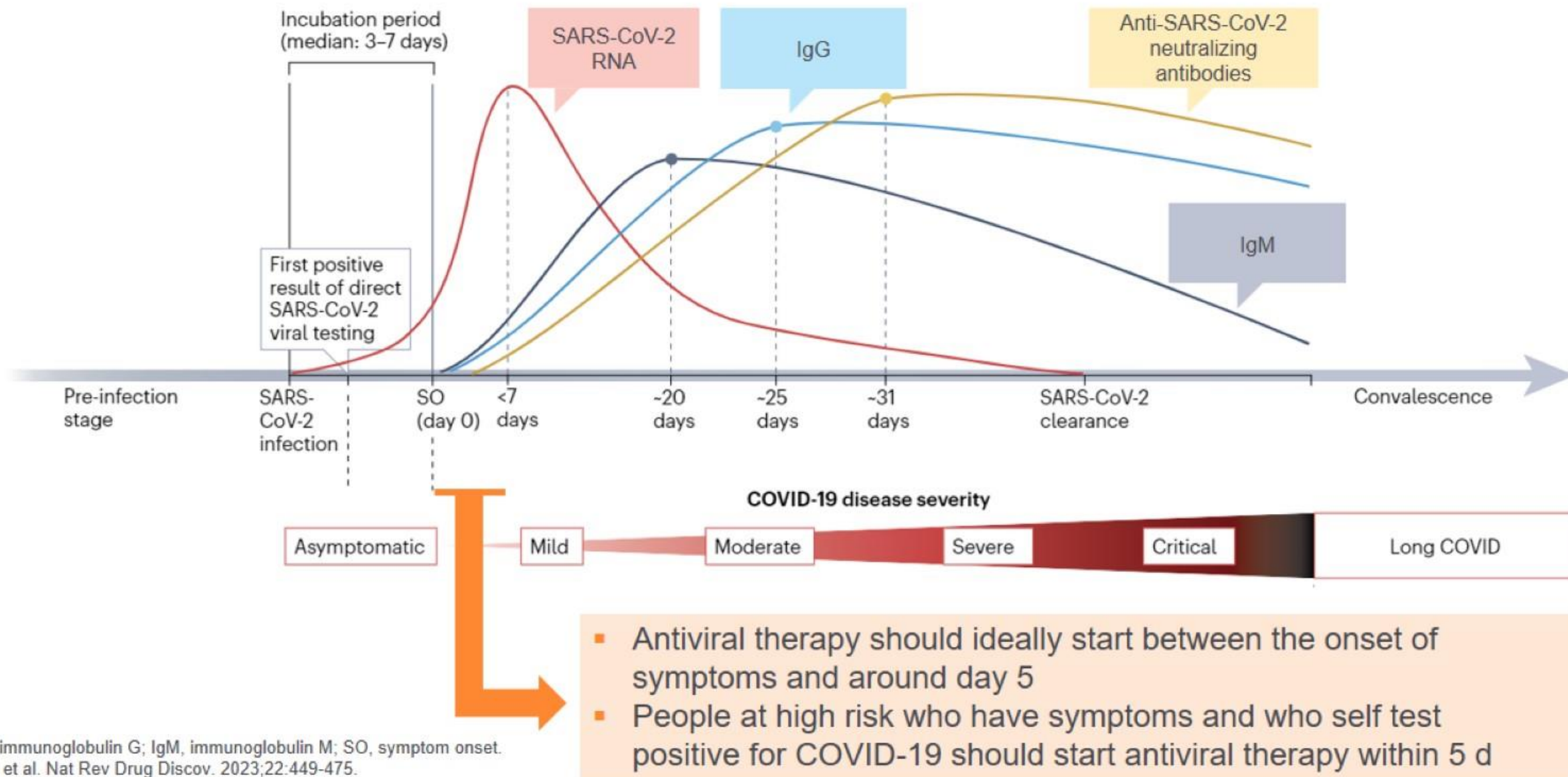
Now

- Widespread PCR testing no longer used
- PCR or antigen testing no longer required for hospital admission
- Costs not reimbursed
- Testing is underused

Challenges With COVID-19 Testing



When Can Antivirals Be Used to Treat COVID-19?



The Battle Against COVID-19

Where Do We Stand Now?



- We are approaching 4 y since the beginning of battle against SARS-CoV-2^[1]
- Unvaccinated individuals and those who have poor immune responses to vaccines are at a higher risk of mortality than are vaccinated ones^[2]
- Vaccine hesitancy remains a problem^[3]
- COVID-19 vaccine uptake is likely to depend on the severity of the new variants that will continue to evolve^[3]
- Few fully approved treatments for COVID-19 are currently available^[4]
- Resistance of variants has led to reversal of EUAs of all approved therapeutic mAbs^[5]
- Additional effective agents are needed
- Understanding how mAbs work and retain potency in the face of mutational change may help in the development of new therapeutic Abs and vaccines^[6]

Ab, antibody; EUA, Emergency Use Authorization; mAb, monoclonal antibody.

1. Negahdaripour M. Iran J Med Sci. 2020;45:81-82; 2. Ikeokwu AE, et al. Cureus. 2023;15:e43282; 3. Anderson R. Eur J Epidemiol. 2023. doi:10.1007/s10654-023-01066-5 [Epub ahead of print]; 4. NIH. Updated November 2, 2023. Accessed November 10, 2023. <https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf>; 5. McCreary EK, et al. JAMA Netw Open. 2023;6:e239702; 6. Zhou D, et al. Curr Opin Virol. 2023;61:101332.

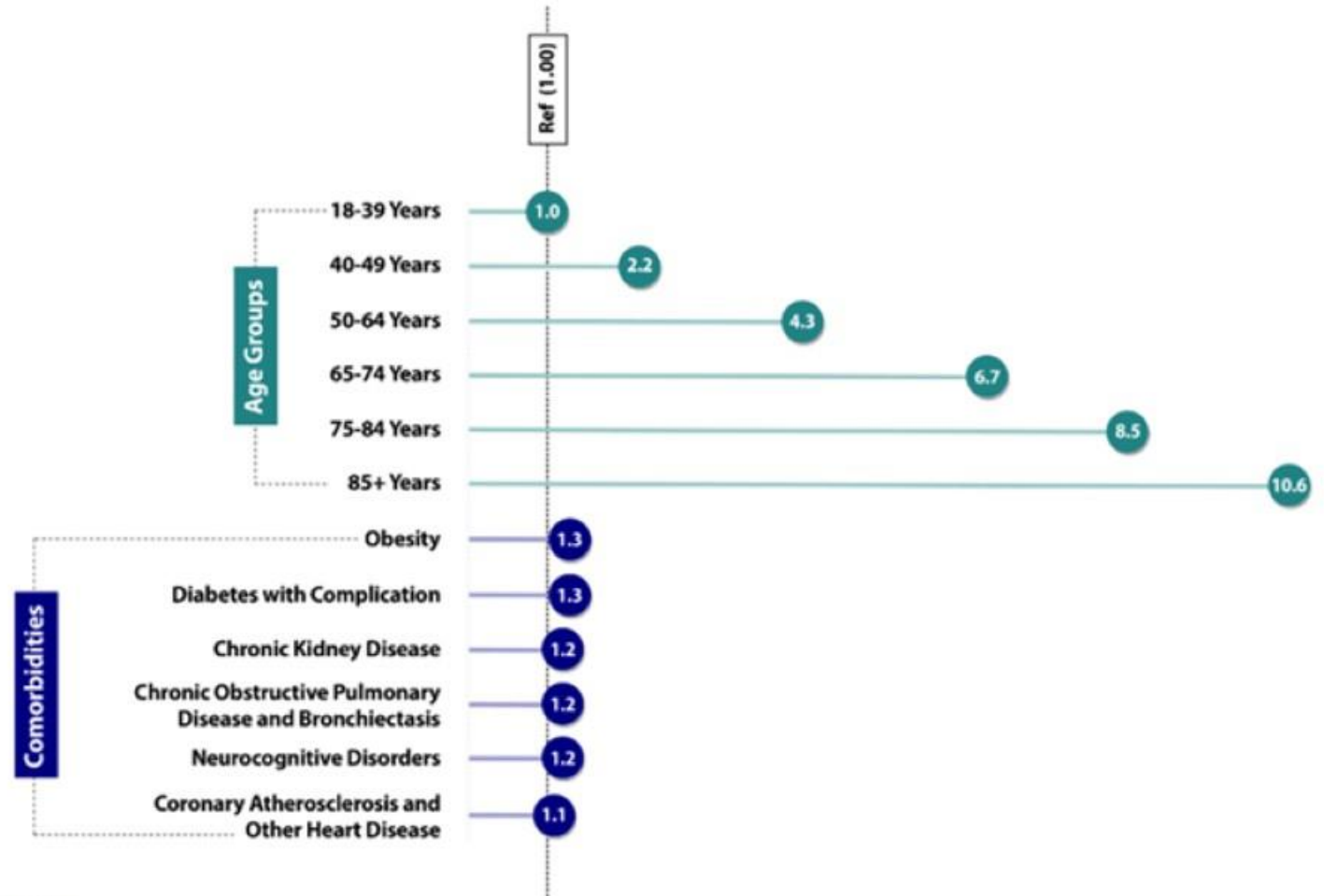
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Risk Factors for Severe COVID-19

Age is the most important risk factor for severe COVID-19

Factors that put patients at risk for severe COVID-19:

- Age
- Underlying medical conditions
- Being unvaccinated or not fully vaccinated
- Being immunocompromised



Ref, reference.

CDC. Updated February 9, 2023. Accessed November 15, 2023. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>

Antivirals Currently Approved for COVID-19

Drug Name	Type (Delivery Route)	Eligible Patients	Status	Adverse Events
RNA Polymerase Inhibitors				
Remdesivir ^[1,2]	Small molecule (IV)	Outpatients ^a ≤ 7 days after symptom onset, or inpatients	Approved by the FDA, EUA in many countries	Include difficulty swallowing, trouble breathing, headache, nausea, vomiting
Molnupiravir ^[1,3]	Small molecule (oral)	Outpatients ^a ≥ 18 y old and ≤ 5 days after symptom onset	Approved in the UK, EUA in many countries	Include diarrhea, nausea, vomiting, headache
Protease Inhibitors				
Nirmatrelvir-ritonavir ^[1,4]	Small molecule (oral)	Outpatients ^a ≤ 5 days after symptom onset	Approved in the UK and EU; EUA in many countries	Include blurred vision, dizziness, headache
Ensitrelvir ^[1,5]	Small molecule (oral)	Outpatients ^a ≤ 5 days after symptom onset	EUA in Japan; phase 3 trial ongoing	Include diarrhea and GI events

This activity includes discussion of off-license or unapproved therapies. Please consult your local SmPC, or its equivalent, for further information.

^aNonhospitalized patients with mild to moderate COVID-19 and at high risk for progression to severe COVID-19, including hospitalization or death (see drug labels).

EUA, emergency use authorization; EU, European Union; FDA, Food and Drug Administration; GI, gastrointestinal; SmPC, summary of product characteristics; UK, United Kingdom.

1. Li G, et al. *Nat Rev Drug Discov.* 2023;22:449-475; 2. Mayo Clinic. Remdesivir. Accessed November 17, 2023. www.mayoclinic.org/drugs-supplements/remdesivir-intravenous-route/side-effects/drg-20503608;

3. Mayo Clinic. Molnupiravir; Accessed November 17, 2023. www.mayoclinic.org/drugs-supplements/molnupiravir-oral-route/side-effects/drg-20524779; 4. Mayo Clinic. Nirmatrelvir And Ritonavir. Accessed

November 17, 2023. <https://www.mayoclinic.org/drugs-supplements/nirmatrelvir-and-ritonavir-oral-route/side-effects/drg-20528231?p=1>; 5. Shimizu R, et al. *Antimicrob Agent Chemo.* 2022;66:1-12.

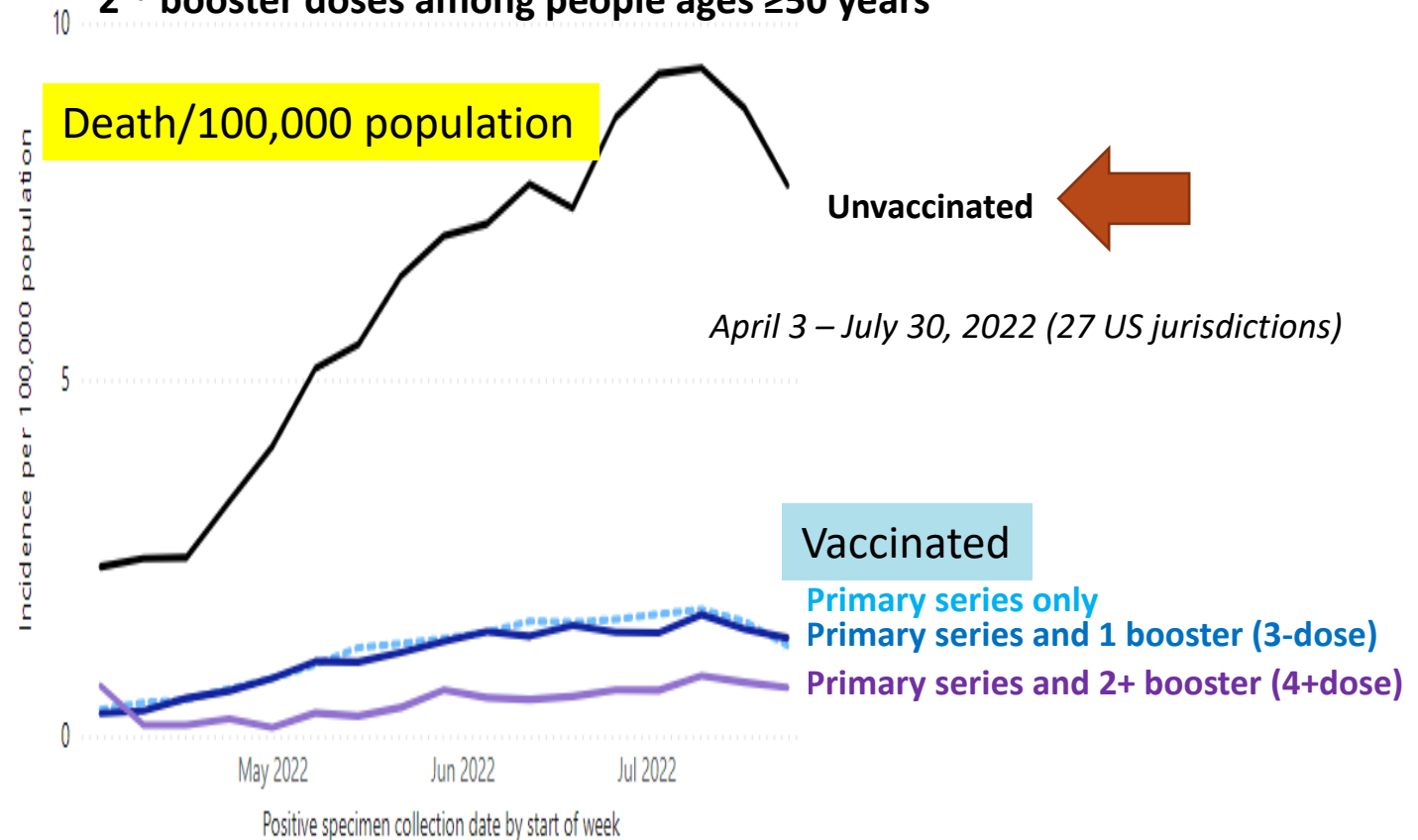


Seroprevalence by Vaccine and Infection History Among U.S. Adult Blood Donors by Age Group, January-June 2022

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

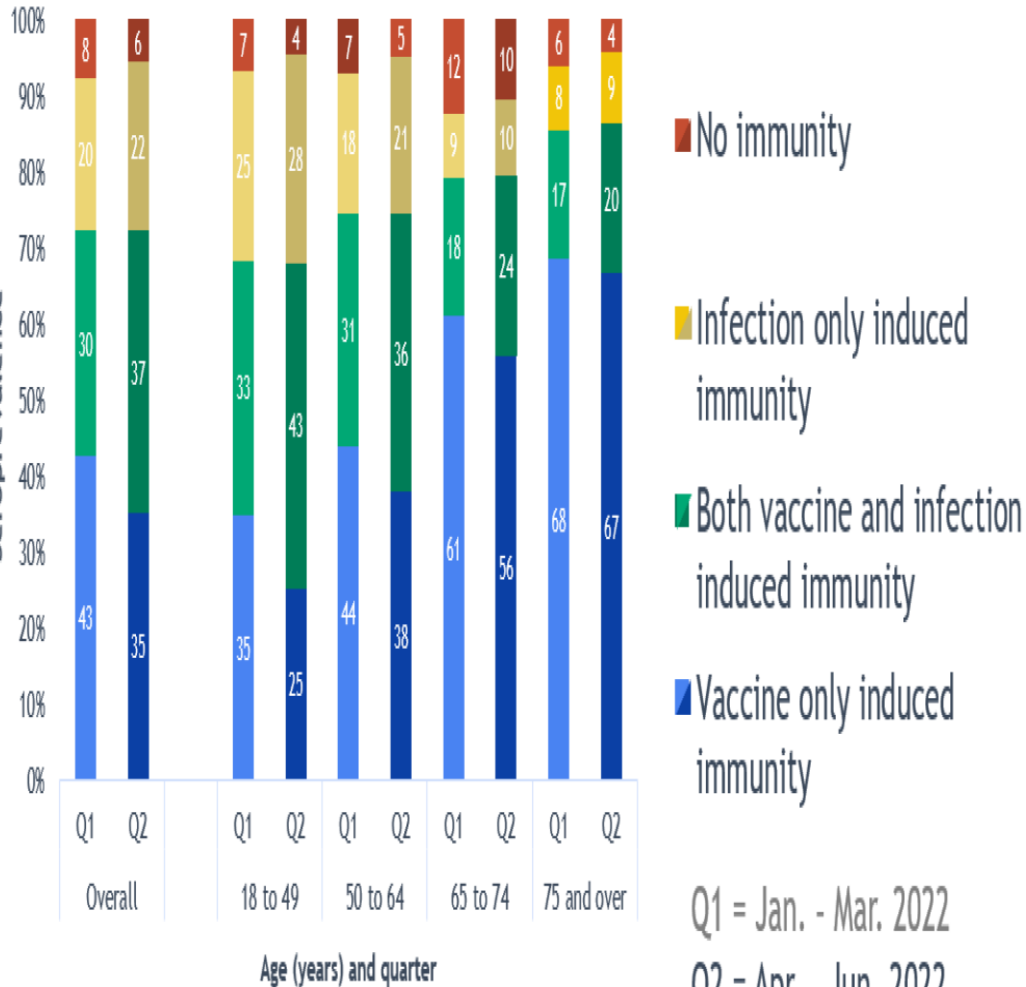
0 vs 2 vs 3 vs 4 dose

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



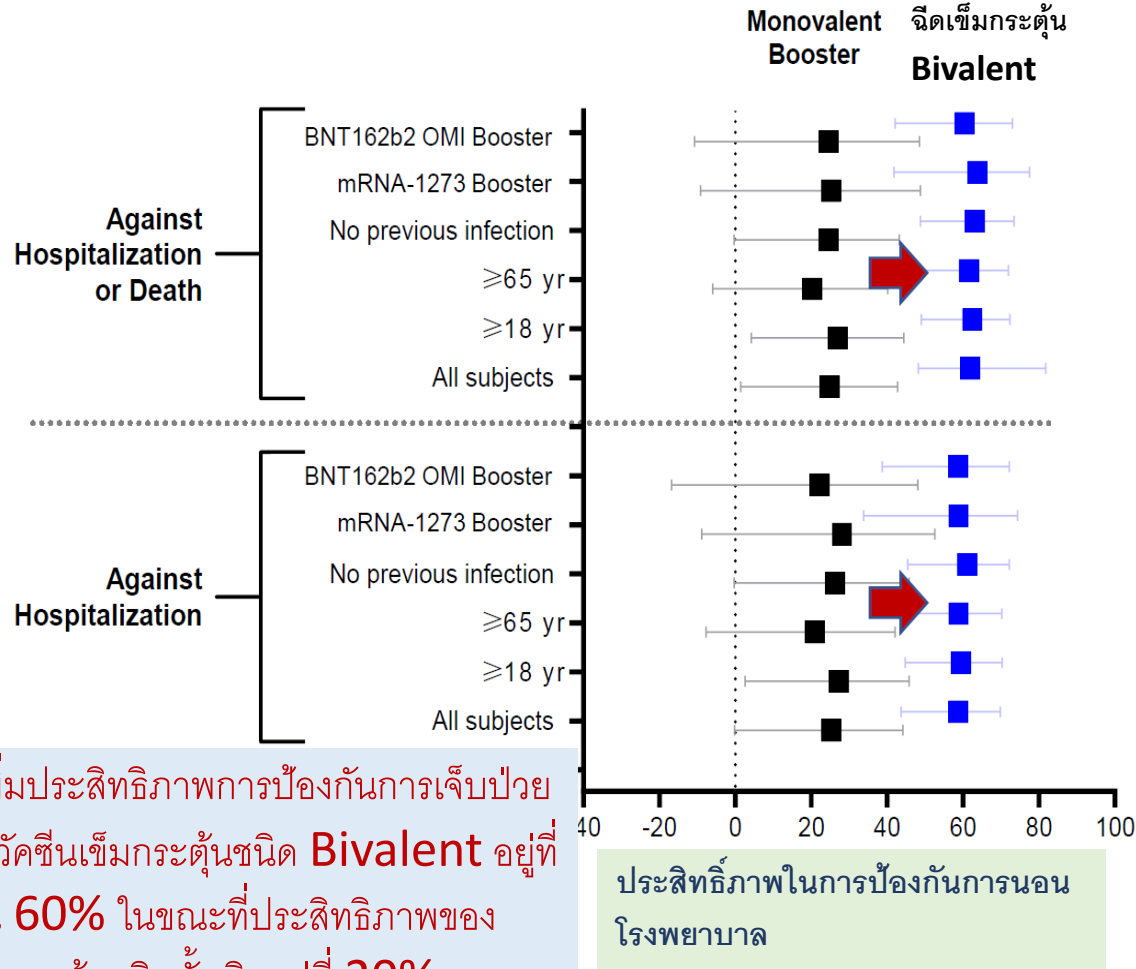
In July 2022, peoples ages ≥50 years with **≥ 2+ booster doses** had

- **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



ผลการเปรียบเทียบประสิทธิภาพของวัคซีนเข็มกระตุ้นชนิด 2 สายพันธุ์ (Bivalent) เทียบกับวัคซีนชนิดดั้งเดิมในการป้องกันการป่วยหนักจากสายพันธุ์โอมิครอน

อัตราการติดเชื้อโควิด19 รุนแรงต้องเข้านอนรักษาตัวในโรงพยาบาลในสหรัฐอเมริกาช่วงเดือนมกราคม 2021 ในกลุ่มที่ไม่ฉีดวัคซีน และฉีดเข็มกระตุ้น



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

ผลการเพิ่มประสิทธิภาพการป้องกันการเจ็บป่วยหนักของวัคซีนเข็มกระตุ้นชนิด **Bivalent** อยู่ที่ประมาณ **60%** ในขณะที่ประสิทธิภาพของวัคซีนเข็มกระตุ้นชนิดดั้งเดิมอยู่ที่ **20%**

ประสิทธิภาพในการป้องกันการนอนโรงพยาบาล

วัคซีนโควิดเข็มกระตุ้นชนิด Bivalent มีประสิทธิภาพการป้องกันการป่วยหนักได้ดีกว่าวัคซีนโควิดรุ่นเดิม

SARS-CoV-2 Hybrid Immunity: The Best of Both Worlds

Ninaad Lasrado¹ and Dan H. Barouch^{1,2}

¹Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; and ²Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard, Cambridge, Massachusetts, USA

The Journal of Infectious Diseases® 2023;228:1311–3

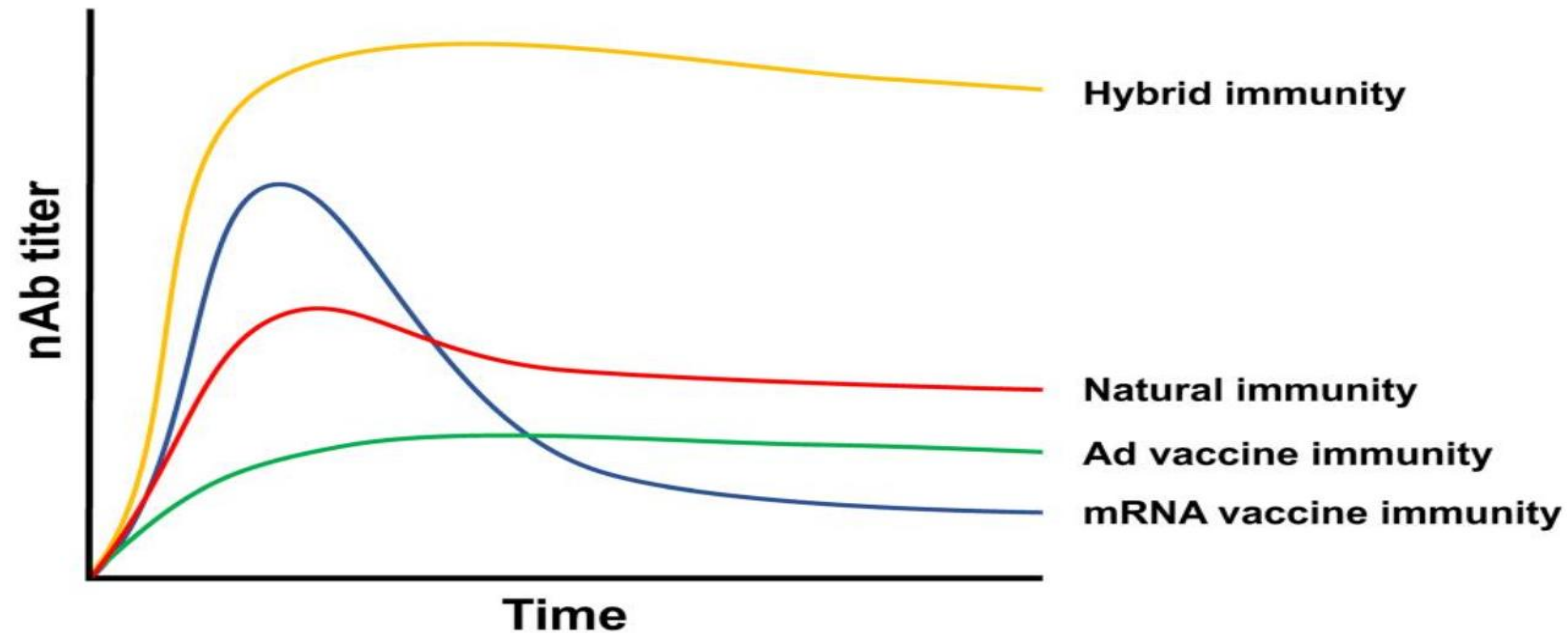


Figure 1. Magnitude and durability of nAb titers following SARS-CoV-2 infection, vaccination, and both. Schematic representation of nAb titers following natural infection (red line), adenovirus vector vaccination (green line), mRNA vaccination (blue line), and hybrid immunity (yellow line). mRNA vaccination results in robust nAb titers that wane rapidly, whereas adenovirus vector vaccination induce lower nAb titers that are more durable. Hybrid immunity results in higher magnitude and more durable nAb responses than that achieved with either vaccine immunity or natural immunity alone. Abbreviations: nAb, neutralizing antibody; Ad, adenovirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Who should get vaccinated and boosted? (WHO March 2023)

WHO's Strategic Advisory Group on Immunization (SAGE) updated the recommendations in the context of the circulating Omicron variant and high population immunity. outline three priority groups for COVID-19 vaccination.

High priority group:

- Older adults;
- Younger adults with significant comorbidities (e.g., diabetes and heart disease) or severe obesity;
- People, including children aged 6 months and older, with serious immunocompromising
- Pregnant persons;
- Frontline health workers.

For this group, WHO recommends receiving the primary series, first booster and additional booster doses 6 or 12 months after the last dose, depending on factors such as age and immunocompromising conditions.

Medium priority group:

- Healthy younger adults - adults without comorbidities under the age of 50 to 60 years
- Children/adolescents with severe obesity or comorbidities that put them at higher risk of severe COVID-19 infection.

For this group, WHO recommends the primary series and first booster dose.

Additional booster doses are not routinely recommended. However, health authorities may consider giving additional boosters doses when the benefits are warranted and there are no known safety issues.

Low priority group:

- Healthy children and adolescents ages 6 months to 17 years

Countries could consider vaccinating healthy children and adolescents with the primary series based on disease burden, cost-effectiveness and other health or program priorities and opportunity costs.

Short-term effectiveness of the XBB.1.5 updated COVID-19 vaccine against hospitalisation in Denmark: a national cohort study

Christian Holm Hansen; *Lancet Infect Dis* 2024 Published Online January 5, 2024

We conducted a cohort analysis using national electronic civil and health registry data to compare COVID-19 hospitalisation rates between **Oct 8 and Oct 26, 2023**, among people older than 65 years living in Denmark on Oct 1, 2023, who had received **the vaccine on or after Oct 1, 2023**, compared with those who had not.

	Population	Cumulative follow-up time, years	Average follow-up time, days	Events (rates per 100 person-years)	Adjusted hazard ratio (95% CI)
COVID-19 hospitalisation					
Vaccinated 7 or more days ago	442 247	12 019	9·9	21 (0·175)	0·239 (0·152–0·377)
Not yet vaccinated	867 645	35 023	14·7	243 (0·694)	ref
Negative control outcome: other hospitalisation					
Vaccinated 7 or more days ago*	441 754	11 996	9·9	899 (7·49)	0·848 (0·784–0·918)
Not yet vaccinated	867 645	34 950	14·7	2987 (8·55)	ref

Of those vaccinated, 90·4% (9·6%) received the vaccine by Pfizer-BioNTech (Moderna). *493 people were hospitalised during follow-up before vaccination and were therefore removed from the at-risk set.

Table: Event rates among people older than 65 years with and without the XBB.1.5 updated COVID-19 vaccine, from Oct 8 to Oct 26, 2023

Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalisation and admission to intensive care, the Netherlands, 9 October to 5 December 2 C Henri van Werkhoven; Euro Surveill. 2024;29(1):pii=2300703

Table COVID-19 hospitalisations and ICU admissions included in the analysis by seasonal vaccination status, and estimated vaccine effectiveness, the Netherlands, 9 October–5 December 2023 (n = 2,050)

Outcome	Age group (years)	Cases with 2023 seasonal vaccination	Cases without 2023 seasonal vaccination	VE (95% CI) COVID-19 hospitalisation
	≥ 60	295	1,755	70.7% (66.6–74.3)
	60–74	59	681	68.3% (58.3–75.9)
	75–84	150	756	73.9% (68.5–78.4)
	≥ 85	86	318	66.0% (56.4–73.5)
COVID-19 ICU admission	≥ 60	8	84	73.3% (42.2–87.6)

The Rates of Rare Adverse Events Caused by COVID-19 Vaccines

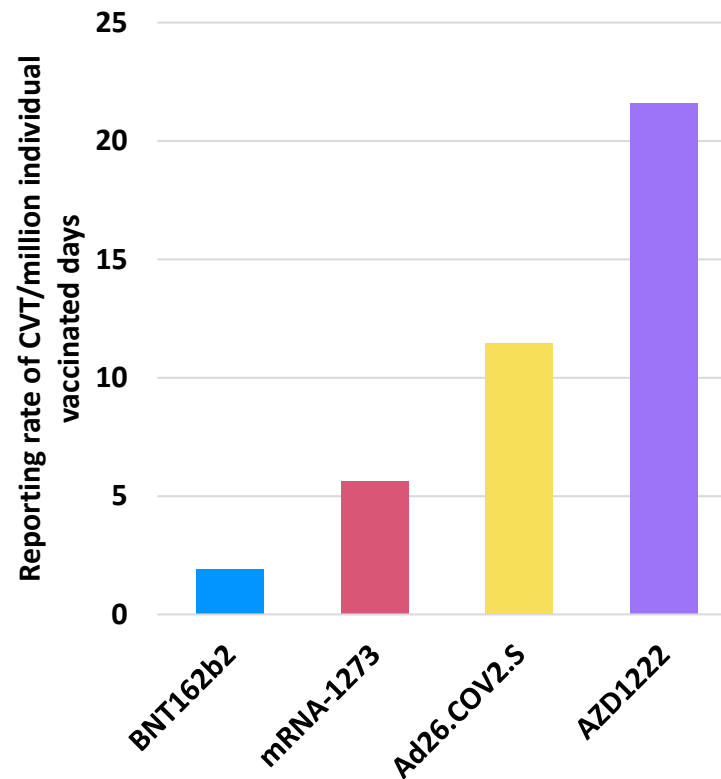
Cerebral venous thrombosis has a decreased reporting rate in BNT162b2 compared to **non-replicating viral vector vaccines** (AZD1222 and Ad26.COVS.2) per million individuals¹

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**²

Guillain-Barré Syndrome occurs at a higher rate after vaccination with **Ad26.COVS.2**, at **20.2 cases per million** doses administered, while there is **no increased risk** associated with **mRNA vaccines**²

The rates of anaphylaxis after BNT162b2 or mRNA-1273 vaccination currently present minimal concern due to a decrease in cases³

CVT was more prevalent in inactivated vaccines compared with mRNA vaccines¹



ANTI-VACCINE MOVEMENT MIGHT UNDERMINE PANDEMIC EFFORTS

Studies of social networks show that opposition to vaccines is small but far-reaching – and growing.

Nature | Vol 581 | 21 May 2020 |

Categories of anti-COVID-19 vaccine tweets and more representative tweets (most retweeted)*

Category	N (%)
Vaccine safety	
Adverse effects	250 (79.89)
New strain of SARS-CoV2	22 (7.03)
Vaccine efficacy	
COVID-19 vaccine is ineffective	24 (54.55)
COVID-19 vaccine could work or does not	16 (36.36)
Vaccine importance	
It is better to be COVID-19-positive and acquire natural immunity	19 (44.19)
Government and pharmaceutical industries are allies	24 (55.81)

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

Primary covid-19 vaccination:

Primary -1 dose of updated covid-19 vaccination for unvaccinated persons age **18 years and over with or without prior covid-19 infection**

Booster covid-19 vaccination:

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

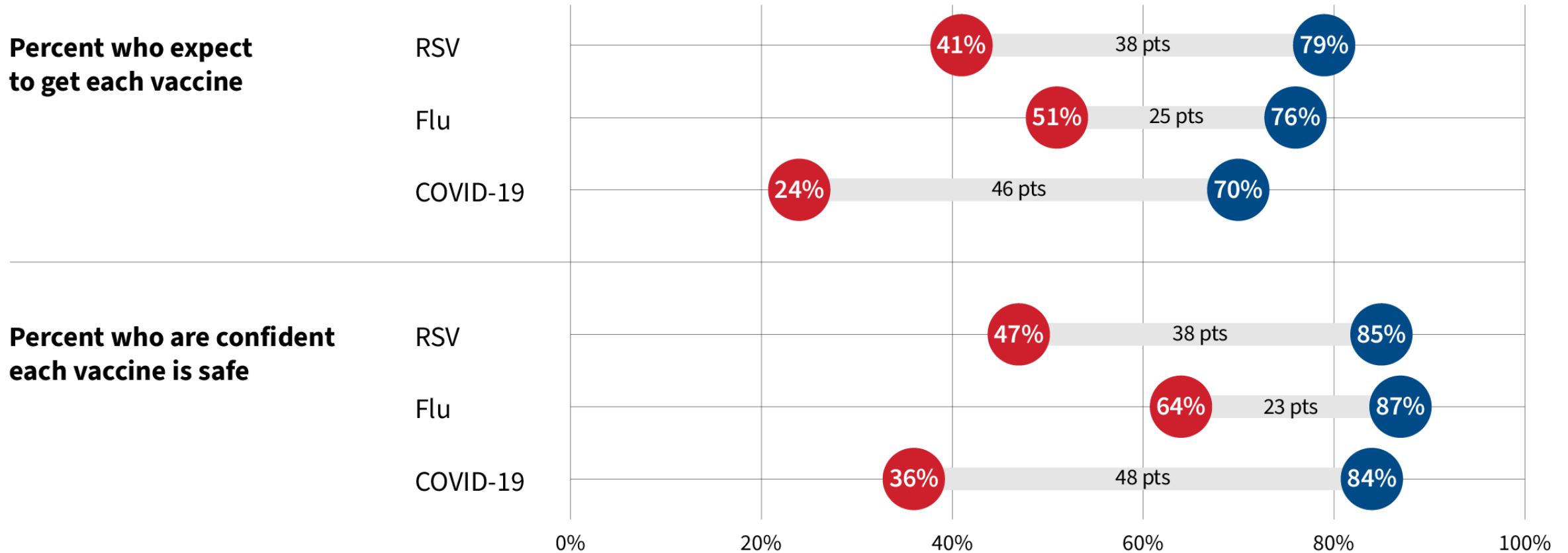
1. **Healthy persons age 65 years and over (or 50 years and over ?)**
2. **Persons age 18 years and over at higher risk of severe COVID-19**
3. More targeted offer to protect those persons at higher risk of severe COVID-19.
 - **Health-care workers and social care workers**
 - Residents in a care home 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 administered 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

Republicans Much Less Likely to View Vaccines as Safe, Intend to Get Them; Biggest Differences in Partisan Views of COVID-19 Vaccine

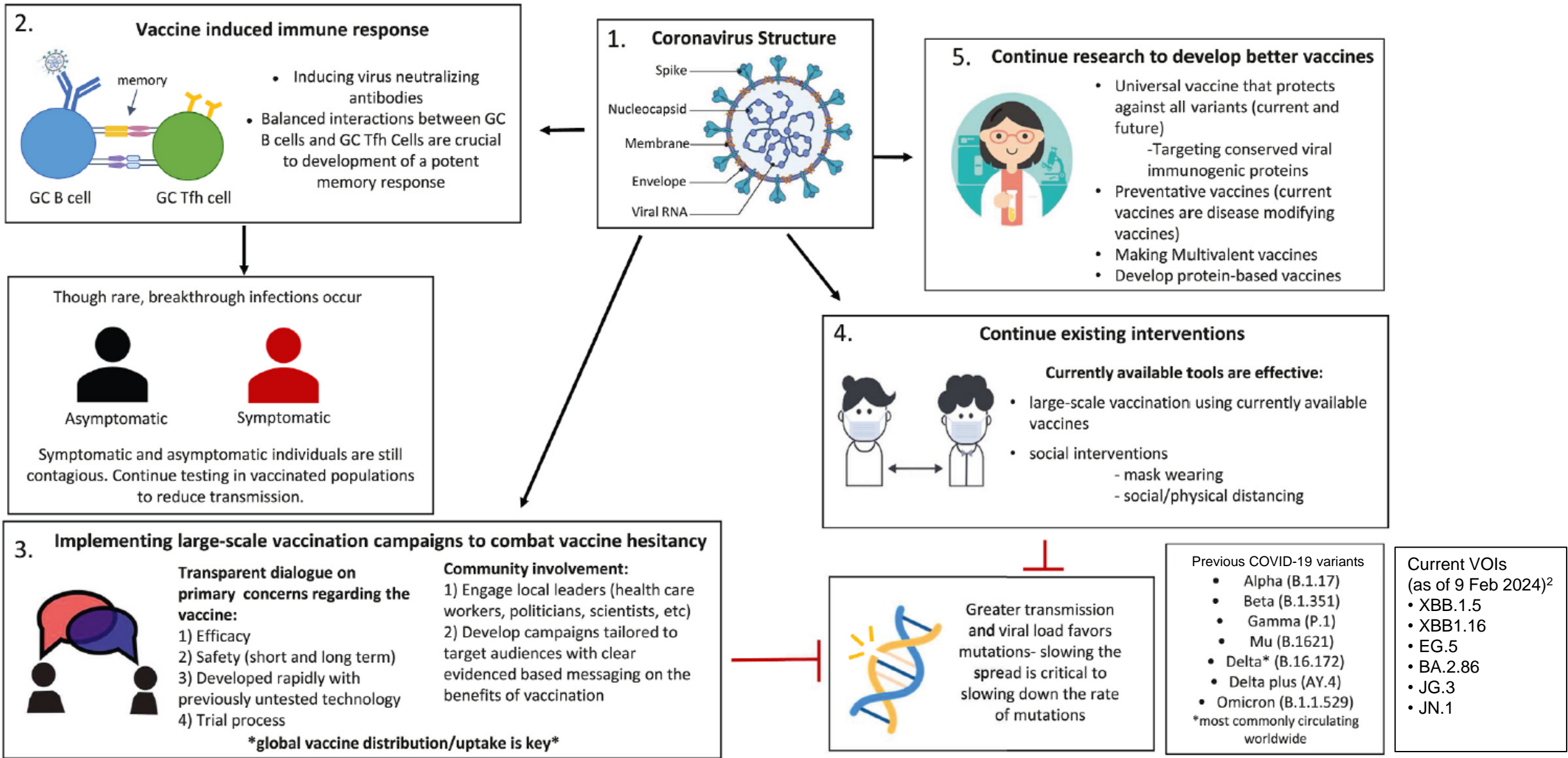
● Republicans ● Democrats ■ Percentage point gap



NOTE: RSV vaccine questions are only among adults ages 60 and older. See topline for full question wording

SOURCE: KFF COVID-19 Vaccine Monitor (Sept. 6-13, 2023)

Mitigating COVID-19 Now and Beyond



Current Challenges and Future Strategies

High morbidity and mortality, Effect on world economy

Duration of immunity with current vaccines

Emergence of variants

Enhanced transmissibility

Compromised immunity

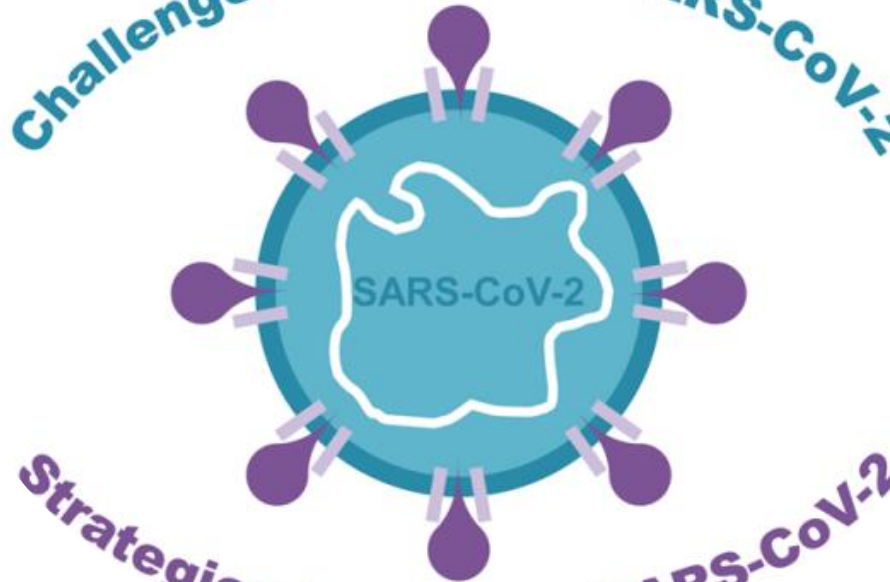
Incomplete detection of variants

Efficacy of vaccines in use

Unfair global vaccine distribution

Vaccine storage and transportation

Challenges in fighting SARS-CoV-2



Strategies to combat SARS-CoV-2

Antiviral therapies

Non-pharmaceutical interventions

Global genomic surveillance

Universal vaccination

Developing a test to detect all variants

Study impact of mutations on vaccines

Induction of trained immunity by BCG

Functional characterization of variants

Fair vaccine distribution

Reduce the risk of emergence of new variants

Multivalent vaccine effective against all the variants of SARS-CoV-2 or seasonal vaccination similar to the influenza vaccines?

Control the current pandemic and prevent future pandemics due to SARS-CoV-2

Reflecting on our collective pandemic response as a global community uncovers critical learnings to carry forward

Future Pandemics In Our Lifetime Are Likely

Increased surveillance of pathogens with pandemic potential could trigger preparations earlier, enabling a quicker response

Improved coordination among governments, industry, NGOs is needed to more effectively address the needs of the global community

Diversify response across preparedness tactics, manufacturers, and product technologies to help mitigate single-source risks

Establish proactive funding mechanisms to ensure equitable access to critical products during a crisis

Harmonize global regulatory pathways through standardization of requirements to enable accelerated time to market for products

Better understand behaviors leading to vaccine hesitancy and leverage insights to develop strategies aimed at increasing uptake

Bolster health systems' ability to address public health emergencies through access to critical products (e.g., PPE, essential medicines) and training

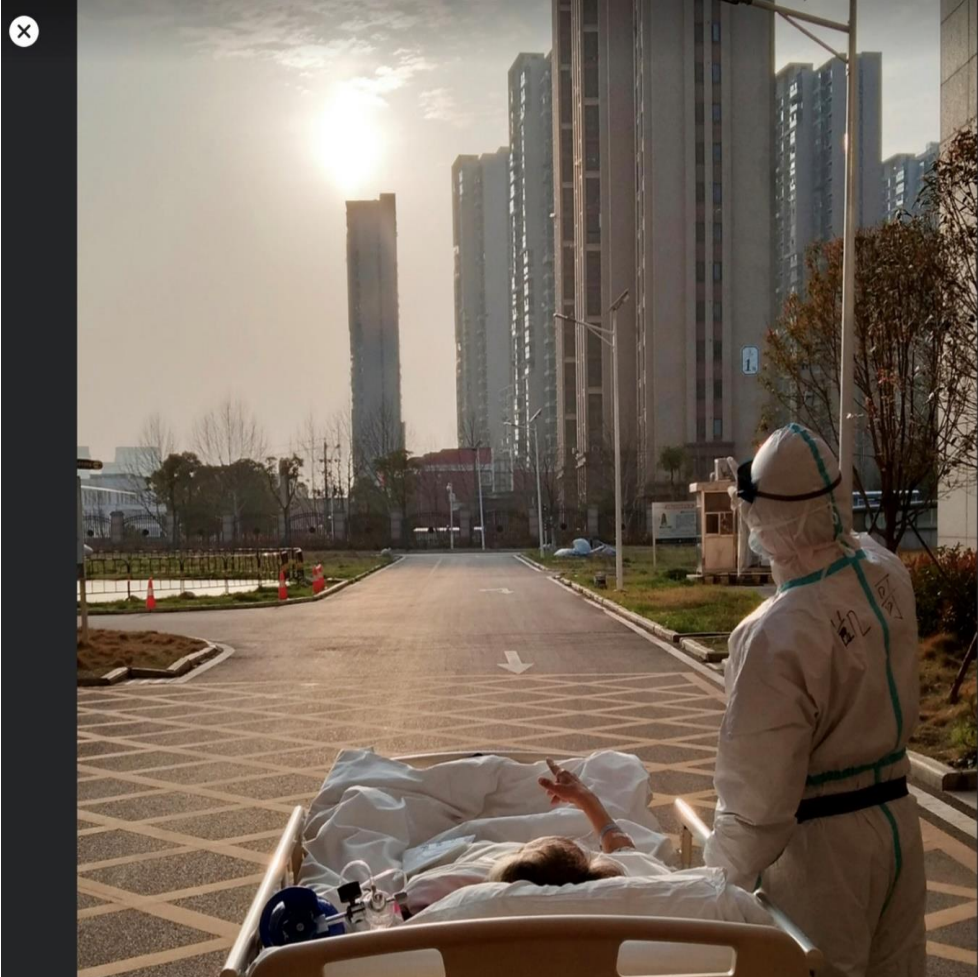
Utilize vast amounts of existing data to inform decision making on pandemic policy and response

What do we need to do better moving forward?

A modern disease: The virulence and global spread is in many respects a *function of modern times*. *Urbanization, mass migration, global transport and trade, and overcrowding accelerate the spread of pandemics*, which ignore national borders, social class, economic status, and even age.

PPE, personal protective equipment; NGO, non-governmental organization.

1. Williams BA, et al. *NPJ Vaccines*. 2023;8(1):178. 2. Gong W, et al. *Int Rev Immunol*. 2023;42(6):393-414. 3. World Health Organization Interim Report May 2023. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2023.1 (accessed February 2024).



**“You don’t
make the
timeline.
The virus
makes the
timeline.”**

Dr. Anthony Fauci

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Thank you

