COVID-19 Update

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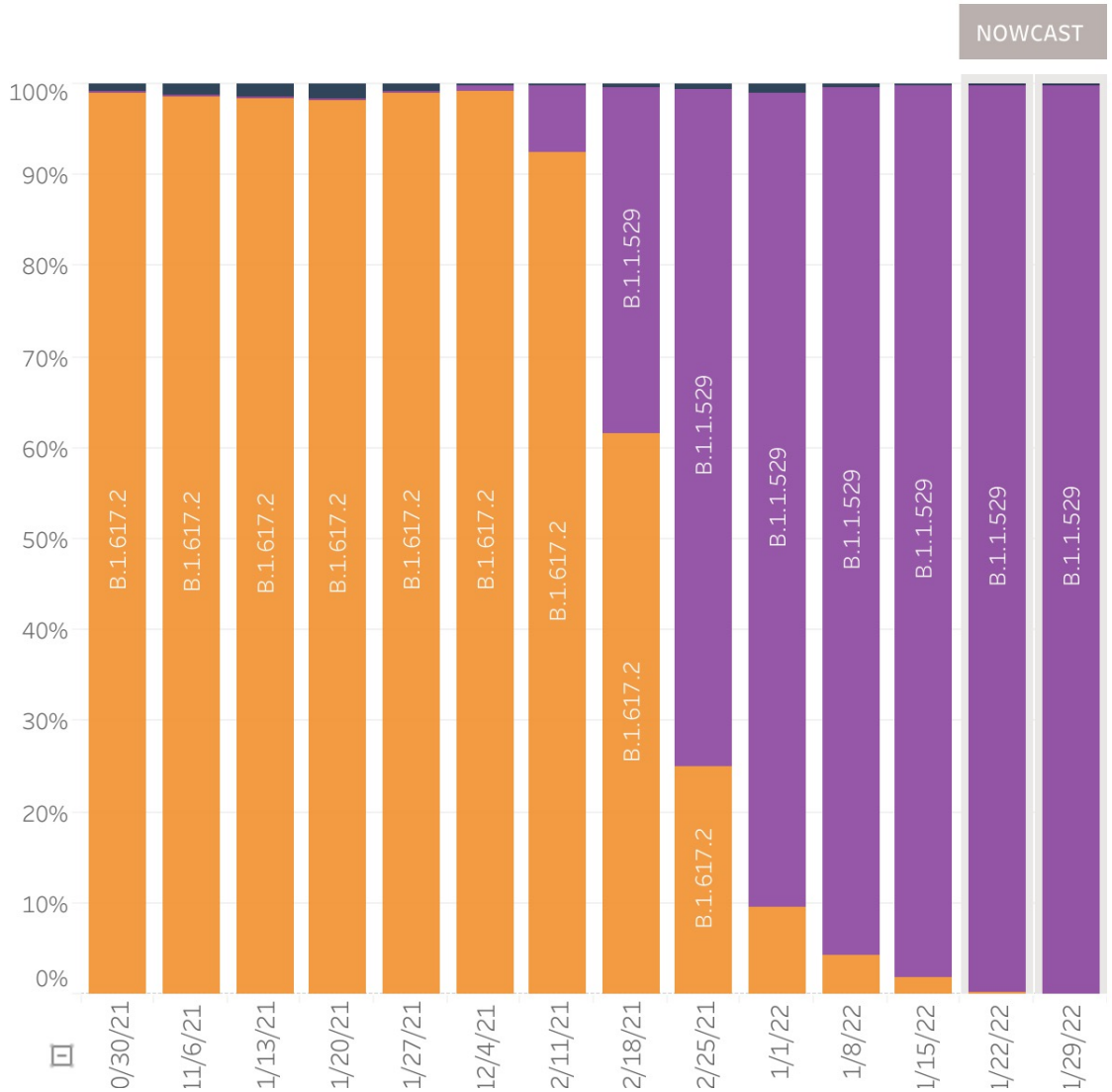
Outline

- Epidemiology
- Vaccine/Immunology
- Treatment

United States: 10/24/2021 – 1/29/2022



United States: 1/23/2022 – 1/29/2022 NOWCAST

USA

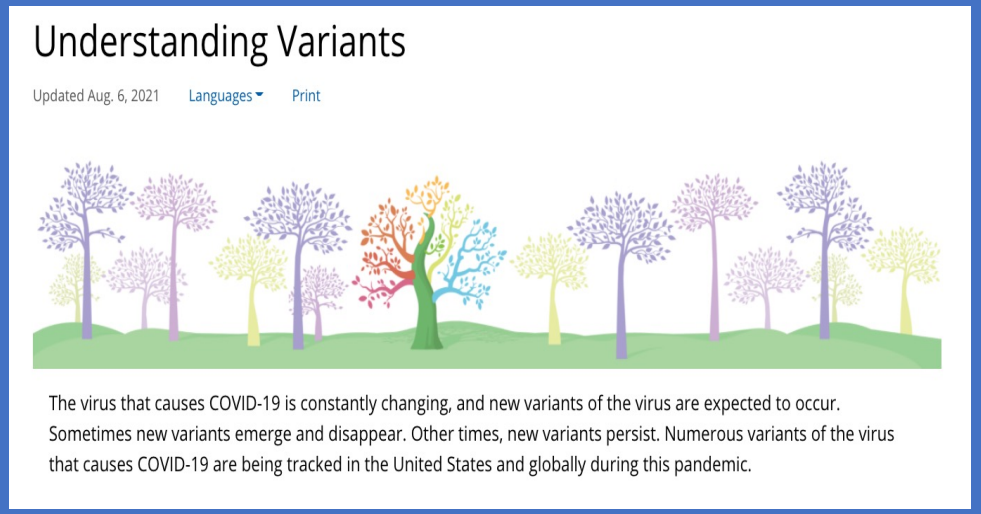
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	99.9%	99.9-100.0%
Delta	B.1.617.2	VOC	0.1%	0.0-0.1%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

Variants of concern (VOC): WHO Working Definition

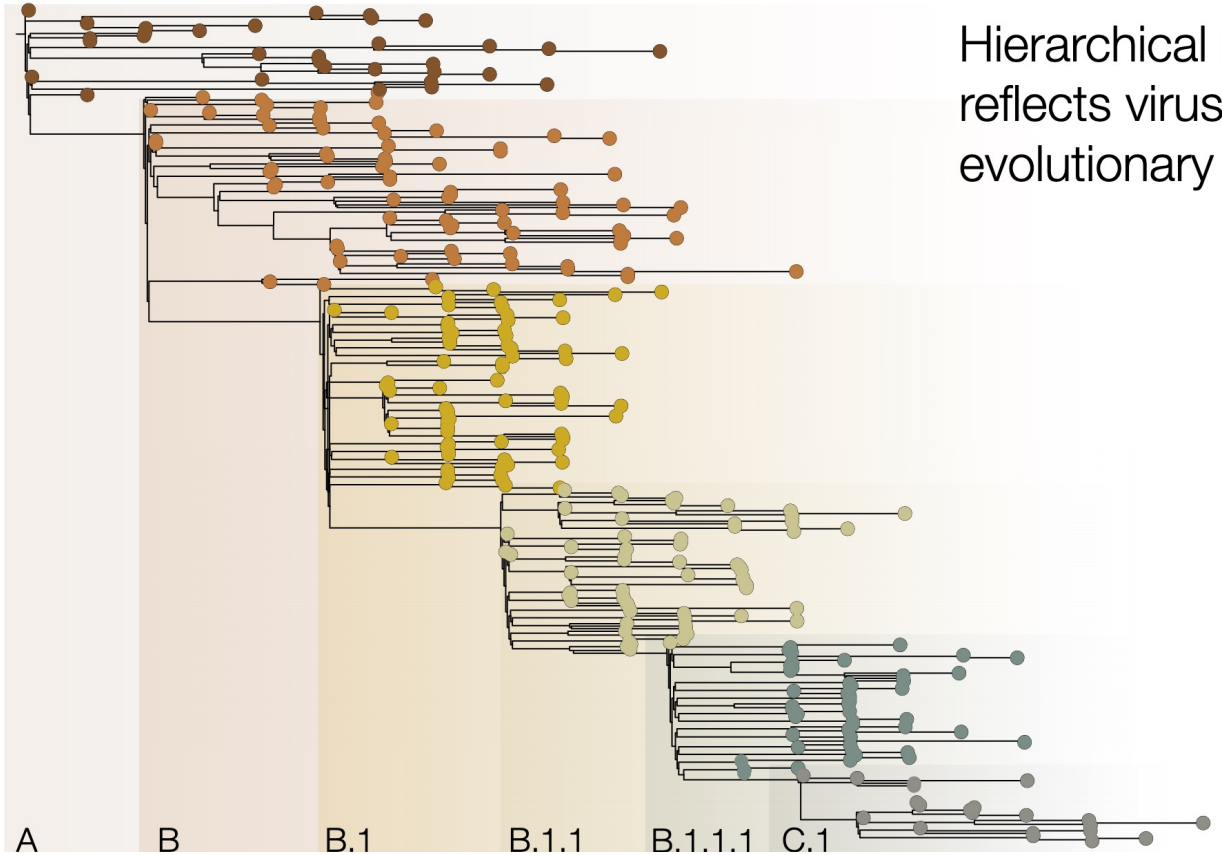


A SARS-CoV-2 VOC has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

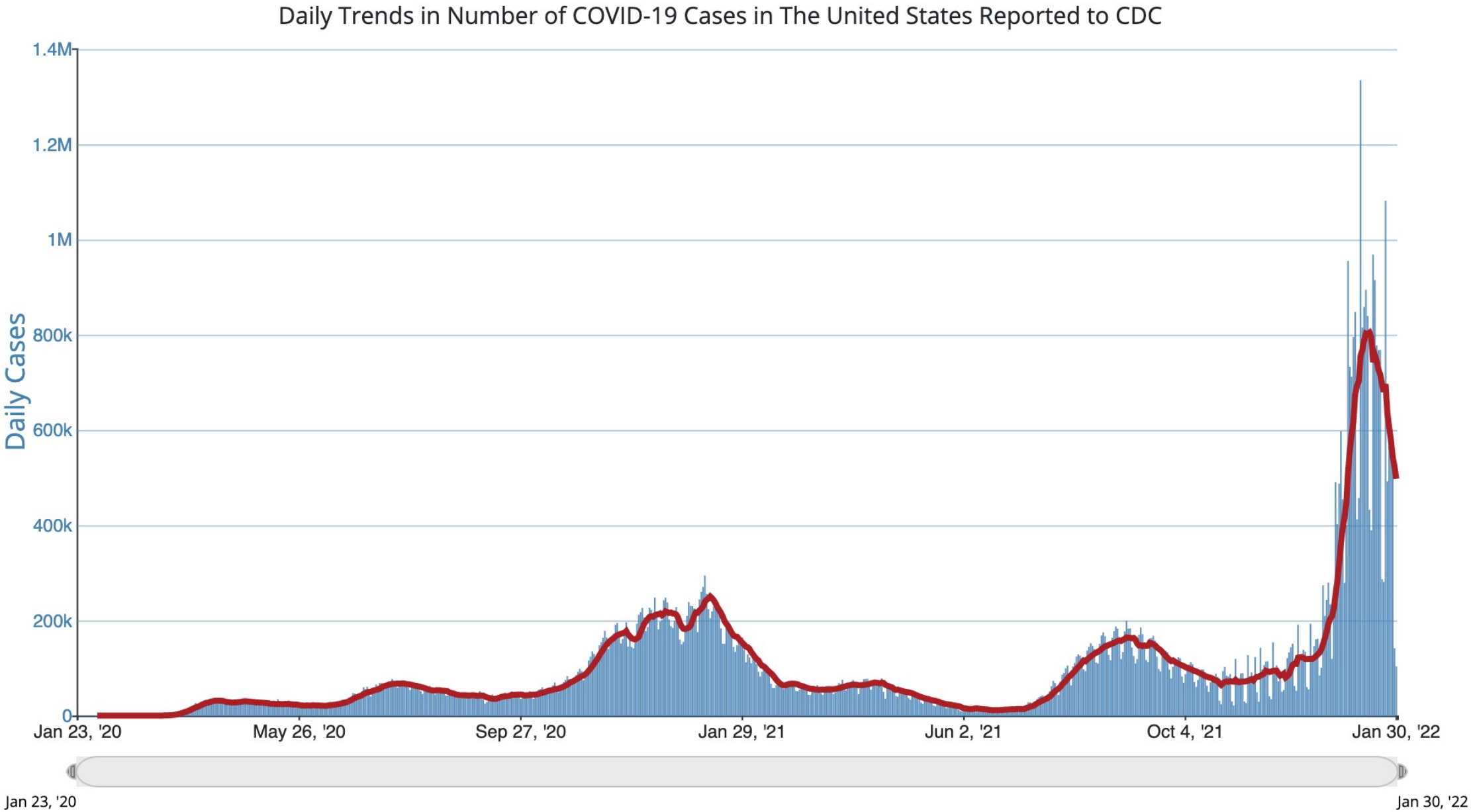
- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in clinical disease presentation; OR
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

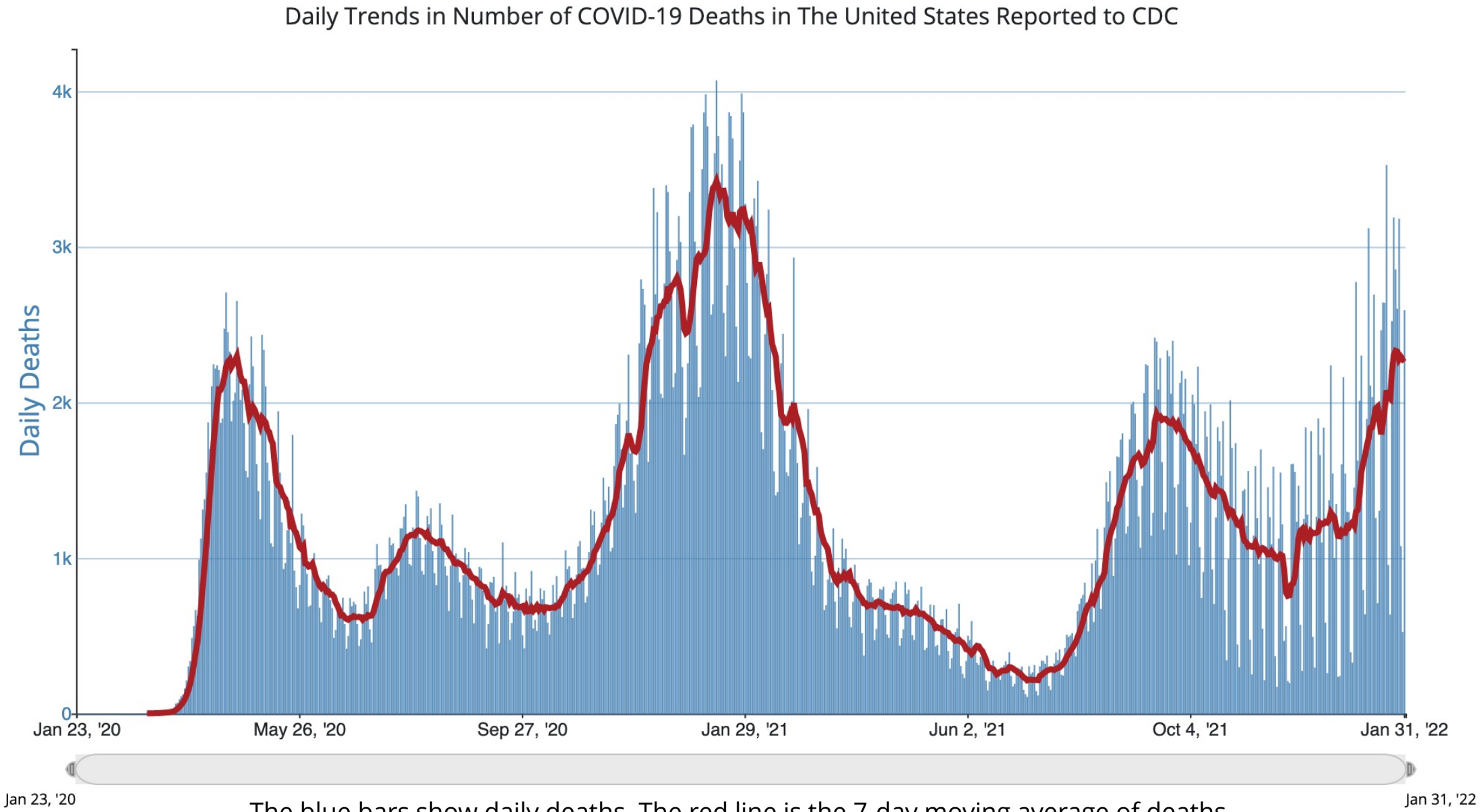
BA.2 Variant “The Son of Omicron”



- BA.2 has been detected in 49 countries and 17 states in the U.S., With over 10,800 cases reported
- **No evidence yet of**
  - Increase in transmissibility, virulence OR
  - Clinical disease presentation OR
  - Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.
- Information is obtained from global COVID variant tracker supported by the CDC and NIH



The blue bars show daily cases. The red line is the 7-day moving average of cases.



The blue bars show daily deaths. The red line is the 7-day moving average of deaths.

COVID-19 Weekly Deaths per 100,000 Population by Race/Ethnicity, United States

March 01, 2020 - February 05, 2022*

Jurisdiction

US

3/7/2020 2/5/2022

Cases

Sex

Age - All Groups

Pediatric Case Proportions

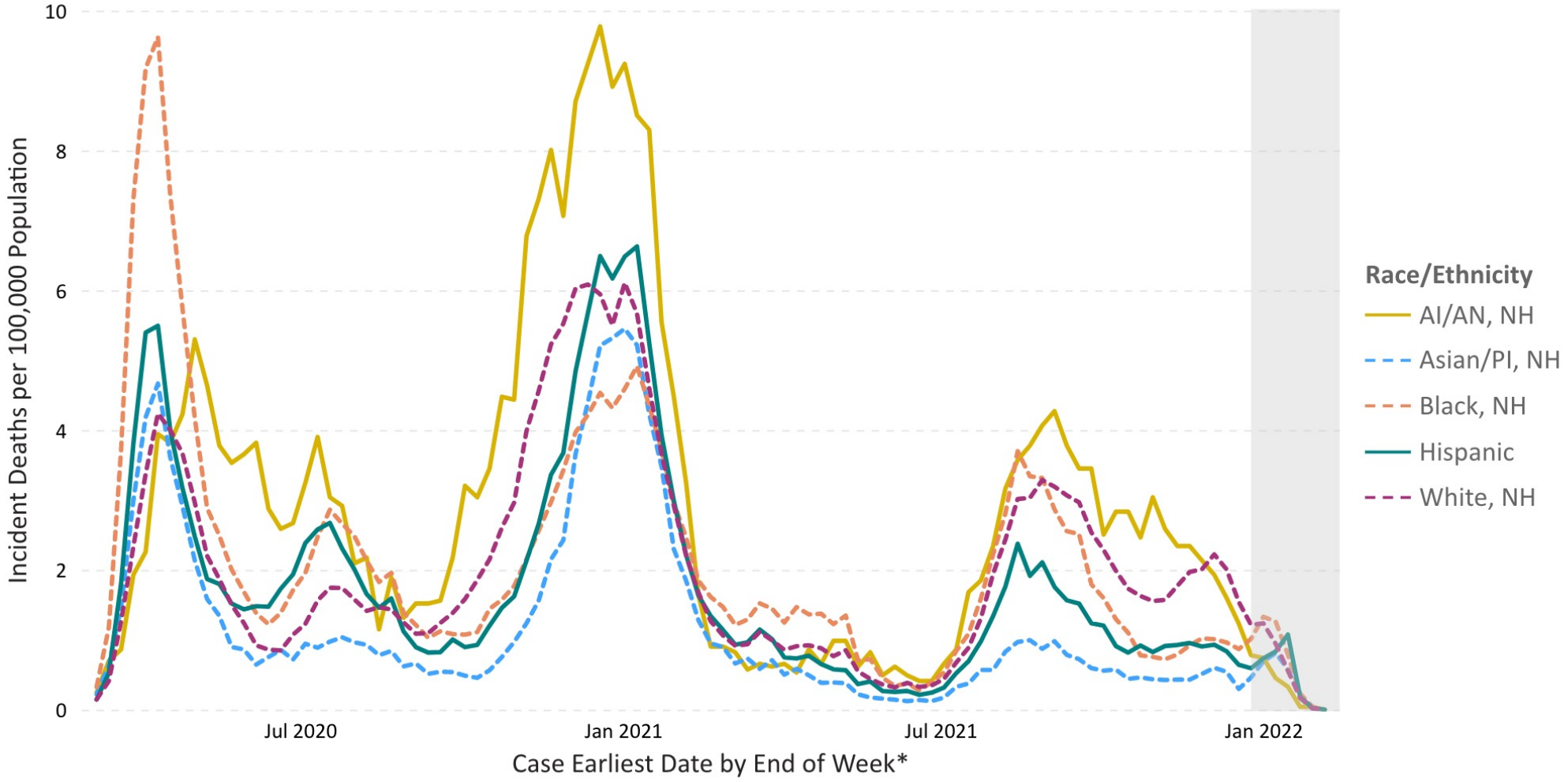
Race/Ethnicity

Deaths

Sex

Age - All Groups

Race/Ethnicity



US: The most recent line level case record was reported during the week ending on Feb 05, 2022. Percentage of deaths among reported cases - 1.33%. Percentage of deaths reporting race by date - 83.26%.

US territories are included in case and death counts but not in population counts. Potential six-week delay in case reporting to CDC denoted by gray bars. AI = American Indian, AN = Alaska Native, NH = Non-Hispanic, PI = Pacific Islander. Excludes cases with unknown or multiple races.

*Case Earliest Date is the earliest of the clinical date (related to illness or specimen collection and chosen by a defined hierarchy) and the Date Received by CDC. The date for the current week extends through Saturday.

Last Updated: Feb 01, 2022

Source: CDC COVID-19 Case Line-Level Data, 2019 US Census, HHS Protect; Visualization: Data, Analytics & Visualization Task Force and CDC CPR DEO Situational Awareness Public Health Science Team

COVID-19 Weekly Deaths per 100,000 Population by Age Group, United States

March 01, 2020 - February 05, 2022*

Jurisdiction

US

3/7/2020 2/5/2022

Cases

Sex

Age - All Groups

Pediatric Case Proportions

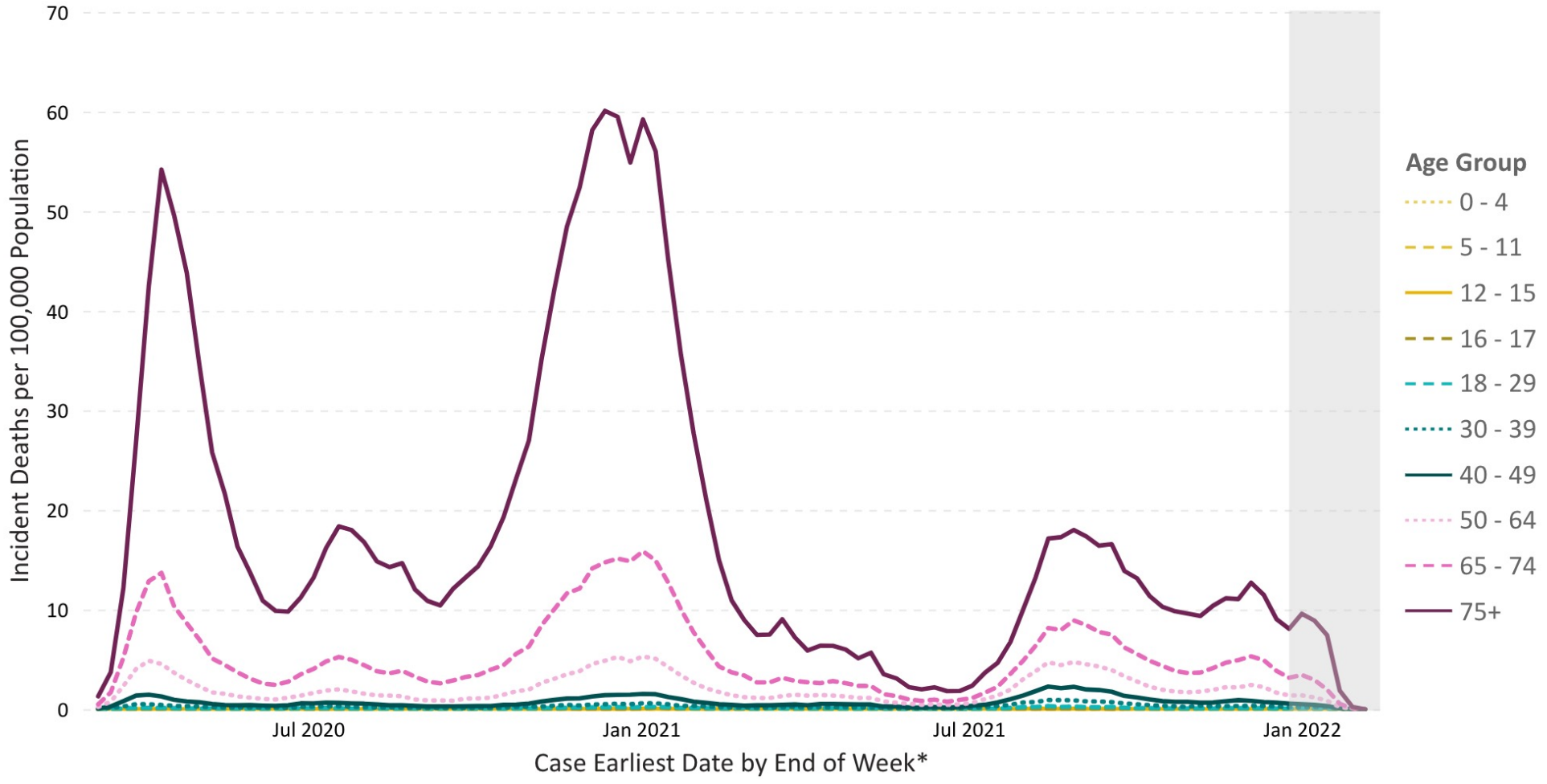
Race/Ethnicity

Deaths

Sex

Age - All Groups

Race/Ethnicity



US: The most recent line level case record was reported during the week ending on Feb 05, 2022. Percentage of deaths among reported cases - 1.33%. Percentage of deaths reporting age by date - 99.96%.

US territories are included in case and death counts but not in population counts. Potential six-week delay in case reporting to CDC denoted by gray bars.

*Case Earliest Date is the earliest of the clinical date (related to illness or specimen collection and chosen by a defined hierarchy) and the Date Received by CDC. The date for the current week extends through Saturday.

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Underlying Medical Conditions and Severe Illness Among 540,667 Adults Hospitalized With COVID-19, March 2020–March 2021

What is already known about this topic?

- Severe COVID-19 illness in adults has been linked to age and underlying medical conditions.

What is added by this cross-sectional study of 540,667 adults hospitalized with COVID-19?

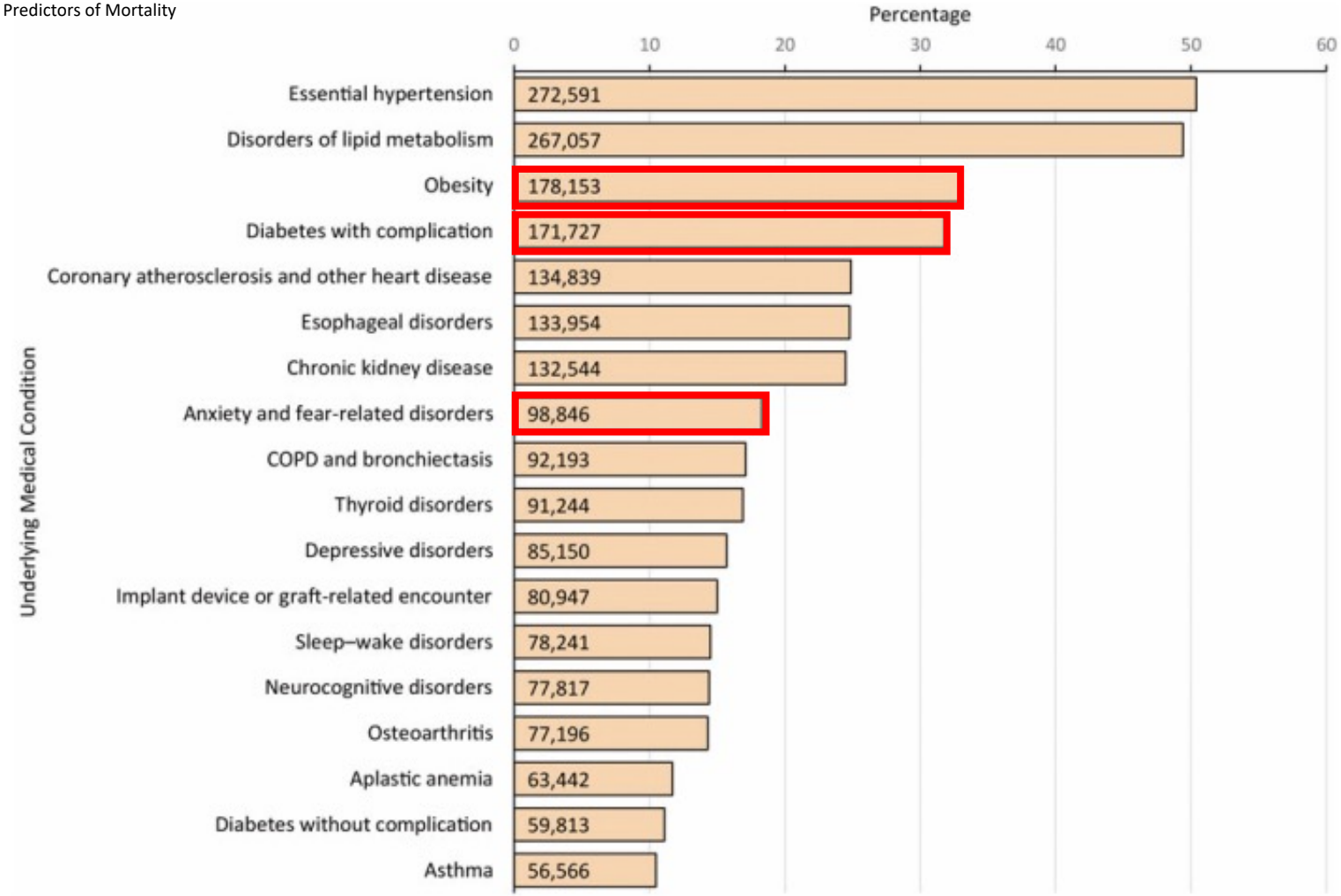
- 94.9% had at least 1 underlying medical condition.
- Hypertension and disorders of lipid metabolism were the most frequent
- Obesity, diabetes with complication, anxiety disorders, and the total number of conditions were the strongest risk factors for severe COVID-19 illness.

What are the implications for public health practice?

- Preventing COVID-19 in populations with these underlying conditions and multiple conditions should remain a public health priority, with targeted mitigation efforts and ensuring high uptake of vaccine, when available, in these individuals and their close contacts

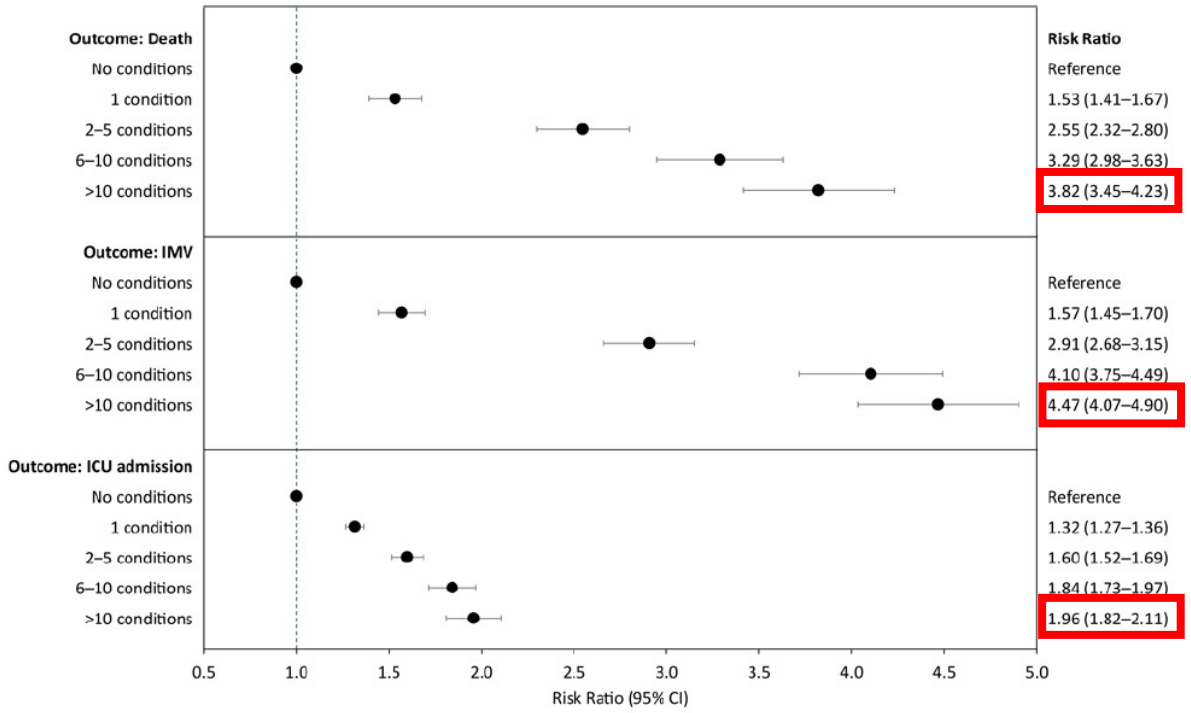
Lyudmyla K eta al.; Preventing Chronic Disease, Public Health Research, Practice and PolicyVolume 18 — July 1, 2021

Associated with the Highest Predictors of Mortality



Prevalence of the most frequent underlying medical conditions in a sample of adults hospitalized with COVID-19 in Premier Healthcare Database Special COVID-19 Release. Underlying medical conditions were defined by using Chronic Condition Indicator to identify chronic International Classification of Diseases, Tenth Revision, Clinical Modification codes; 2) aggregating the codes into a smaller number of categories by using the Clinical Classifications Software Refined (CCSR); 3) a clinical review of CCSR categories that classified CCSR codes as "likely underlying," "indeterminate," or "likely acute"; and 4) including only "likely underlying" CCSR categories and excluding "indeterminate" and "likely acute" CCSR categories. Patients coded with both CCSR categories of "diabetes with complication" and "diabetes without complication" (n = 55,141) were classified as having diabetes with complication. The following frequent (present in ≥10.0% of patients) "indeterminate" CCSR categories were excluded: cardiac dysrhythmias (n = 124,367 [23.0%]), heart failure (n = 104,858 [19.4%]), other specified nervous system disorders (n = 89,929 [16.6%]), other specified and unspecified nutritional and metabolic disorders (n = 89,337 [16.5%]), coagulation and hemorrhagic disorders (n = 75,766 [14.0%]), and diseases of white blood cells (n = 57,765 [10.7%]). Abbreviation: COPD, chronic obstructive pulmonary disease.
Relative risk of death in the full model was 3

- **Underlying Medical Conditions and Severe Illness Among 540,667 Adults Hospitalized With COVID-19, March 2020–March 2021**



Risk ratio (95% CI) of death, invasive mechanical ventilation (IMV), and admission to intensive care unit (ICU), by the number of underlying medical conditions among adults hospitalized with COVID-19 in the Premier Healthcare Database Special COVID-19 Release. Each panel contains the results of a single generalized linear model with Poisson distribution and log link function, adjusted for age group, sex, race/ethnicity, payer type, hospital urbanicity, US Census region of hospital, admission month, and admission month squared as controls. Patients who died without ICU care or IMV wereexcluded from the sample when estimating the model with the outcome of ICUcare or IMV, respectively.

Lyudmyla K et al; Preventing Chronic Disease, Public Health Research, Practice and PolicyVolume 18 — July 1, 2021

Vaccines

- Moderna COVID-19 Vaccine FDA approved
- Pfizer applying for FDA approval for COVID-19 vaccine for children 6 months – 5 years of age

Does the world need an Omicron vaccine? What researchers say

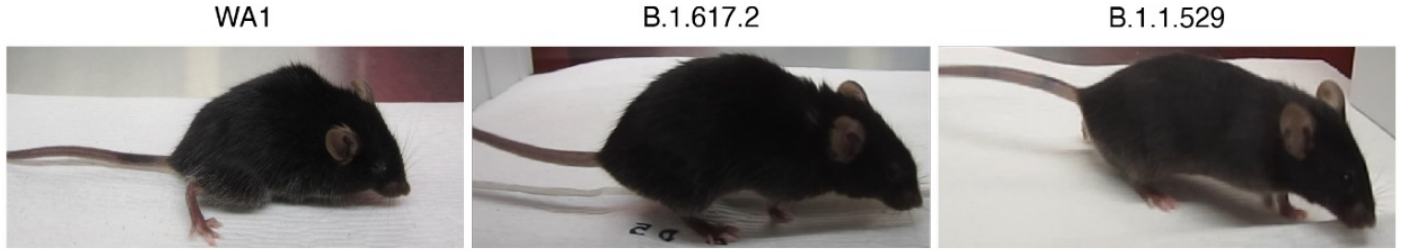
Public-health specialists are debating the need for a shot targeting the variant, now causing a record-breaking surge in COVID-19 cases.

- It might not be worthwhile because Omicron cases could plummet before manufacturers can finalize the vaccines.
- How useful the shot might be against future variants.
- Real-world data suggest that a third dose of a messenger-RNA-based vaccine, such as those made by Pfizer and Moderna, protects most people infected with Omicron against severe illness, at least in the short term.

Nature News: 28 January 2022

Limited cross-variant immunity after infection with the SARS-CoV-2 Omicron variant without vaccination

Question	Animal Study: Inoculated mice with different SARS-CO-2 Variants and measured	Human Study
• Will rampant spread of Omicron lead to mass immunization, accelerating the end of the pandemic.	• Viral replication • Cytokine response • Variant specific neutralizing antibodies.	• Tested human sera for neutralizing antibodies in vaccinated and unvaccinated individuals with delta infections



100 % 7-day Mortality

60 % 7-day Mortality

0 % 7-day Mortality

Suryawansh RK et al. medRxiv preprint https://doi.org/10.1101/2022.01.13.22269243 ; this version posted January 17, 2022.

Limited cross-variant immunity after infection with the SARS-CoV-2 Omicron variant without vaccination: RESULTS

Mice Neutralizing Immune response

- Infection with Delta, but not Omicron, induces broad immunity in mice.
- **Sera from Omicron-infected mice only neutralize Omicron**
- Sera from Delta-infected mice are broadly effective against Delta and other VOCs, including Omicron.

Mice Pro-inflammatory cytokine response

- Both WA1 and Delta elicited a highly pro-inflammatory cytokine response
- **Omicron elicited a milder proinflammatory cytokine response**

Mice Viral replication

- Both Wa1 and Delta replicated to similar titers in the respiratory tracts and lungs of infected mice as well as in human airway organoids.
- **Pulmonary viral replication, disease progression were markedly reduced with Omicron infection.**

medRxiv preprint https://doi.org/10.1101/2022.01.13.22269243 ; this version posted January 17, 2022.

Limited cross-variant immunity after infection with the SARS-CoV-2 Omicron variant without vaccination: RESULTS

Analysis of human sera: Non vaccinated individuals infected with Delta

- These sera effectively neutralized WA1 and Delta (>50%), Omicron strains (<50%).

Analysis of human Sera: Vaccinated individuals with breakthrough infections.

- Delta breakthrough infections: Neutralization was observed for all strains tested (less intense with Omicron)
- Omicron breakthrough infections: showed the highest level of protection (>80%) against all strains, including Omicron

Conclusions

- Omicron infection enhances preexisting immunity elicited by vaccines (HUMAN DATA),
- Omicron infection on its own may not induce broad, cross-neutralizing humoral immunity in unvaccinated individuals (ANIMAL DATA).
- These findings suggest that Omicron infection can effectively boost existing immunity conferred by the vaccination against other variants, eliciting “hybrid immunity” that is effective against not only itself but also other variants.

medRxiv preprint https://doi.org/10.1101/2022.01.13.22269243 ; this version posted January 17, 2022.

Homologous and Heterologous Covid-19 Booster Vaccinations: Methods

Phase 1–2, open-label clinical trial conducted at 10 sites in the United States

- Adults who had completed a Covid-19 vaccine regimen at least 12 weeks earlier and had no reported history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection received a booster injection with one of three vaccines:
  - mRNA-1273 (Moderna) at a dose of 100 µg
  - Ad26.COV2.S (Johnson & JohnsonJanssen) at a dose of 5×1010 virus particles
  - BNT162b2 (Pfizer–BioNTech) at a dose of 30 µg.

The primary end points on trial days 15 and 29 were:

- Safety
- Reactogenicity
- Humoral immunogenicity

NEJM, January 26, 2022. DOI: 10.1056/NEJMoa2116414

Homologous and Heterologous Covid-19 Booster Vaccinations: Results

Of the 458 participants who were enrolled in the trial

- 154 received mRNA-1273, 150 received Ad26.COV2., 153 received BNT162b2 as booster vaccines

Reactogenicity was similar to that reported for the primary series.

- More than half the recipients reported having injection-site pain, malaise, headache, or myalgia.

For all combinations:

- Antibody neutralizing titers against a SARS-CoV-2 D614G pseudovirus: Increased by a factor of 4 to 73

Heterologous boosters increased titers by a factor of 6 to 73

- Homologous boosters increased neutralizing antibody titers by a factor of 4 to 20

Spike-specific T-cell responses increased in all except for:

- The homologous Ad26.COV2.S-boosted subgroup.

Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults who had completed a primary Covid-19 vaccine regimen at least 12 weeks earlier.

NEJM, January 26, 2022. DOI: 10.1056/NEJMoa2116414

Different Scenarios to Enhance Your Immune Response to COVID-19

Vaccinated and Boosted + Omicron Infection

- Best immunogenic option unless you die in the process

Vaccinated and Boosted and not infected with Omicron

- Best Safest Option, you don’t have to die

Not Boosted

- Flip of a coin

Not vaccinated

- Start Praying

Remdesivir Receives EUA for Patients < 12 years old or Pediatric Patients Weighing 3.5-40 Kg

- Remdesivir peds

This EUA is for the use of VEKLURY to treat COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg *or* pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing who are:

Hospitalized, *or*

Not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

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[1] https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.

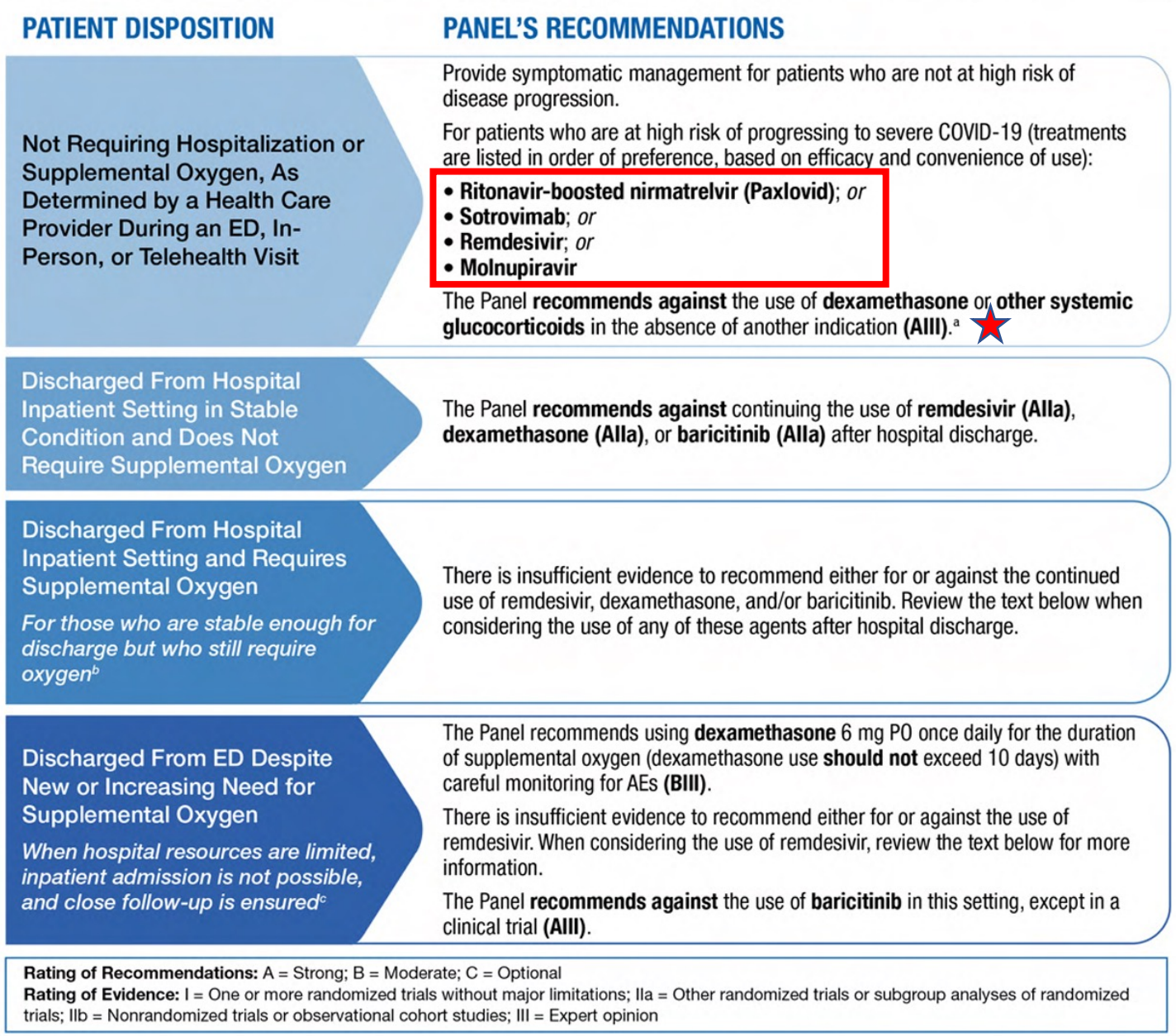
Management of Nonhospitalized Patients with COVID-19

Summary Recommendations
• Management of nonhospitalized patients with acute COVID-19 should include providing supportive care, considering the use of COVID-19-specific therapy for patients who have a high risk for disease progression, taking steps to reduce the risk of SARS-CoV-2 transmission (including isolating the patient), and advising patients on when to contact a health care provider and seek an in-person evaluation **(AIII)**.
• When possible, patients with symptoms of COVID-19 should be triaged via telehealth visits to determine whether they require COVID-19-specific therapy and in-person care **(AIII)**.
• Patients with dyspnea should be referred for an in-person evaluation by a health care provider and should be followed closely during the initial days after the onset of dyspnea to assess for worsening respiratory status **(AIII)**.
• Management plans should be based on a patient's vital signs, physical exam findings, risk factors for progression to severe illness, and the availability of health care resources **(AIII)**.
• See Therapeutic Management of Nonhospitalized Adults With COVID-19 for specific recommendations on using pharmacologic therapy in nonhospitalized patients.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

https://www.covid19treatmentguidelines.nih.gov/

NIH Treatment Guidelines

For Patients that Do Not Require Hospitalization



PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider During an ED, In-Person, or Telehealth Visit	Provide symptomatic management for patients who are not at high risk of disease progression. For patients who are at high risk of progressing to severe COVID-19 (treatments are listed in order of preference, based on efficacy and convenience of use): • **Ritonavir-boosted nirmatrelvir (Paxlovid)**; *or* • **Sotrovimab**; *or* • **Remdesivir**; *or* • **Molnupiravir** The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[a]
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[b]	There is insufficient evidence to recommend either for or against the continued use of remdesivir, dexamethasone, and/or baricitinib. Review the text below when considering the use of any of these agents after hospital discharge.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[c]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not** exceed 10 days) with careful monitoring for AEs **(BIII)**. There is insufficient evidence to recommend either for or against the use of remdesivir. When considering the use of remdesivir, review the text below for more information. The Panel **recommends against** the use of **baricitinib** in this setting, except in a clinical trial **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

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