Indian Country Infectious Disease ECHO COVID-19 Update

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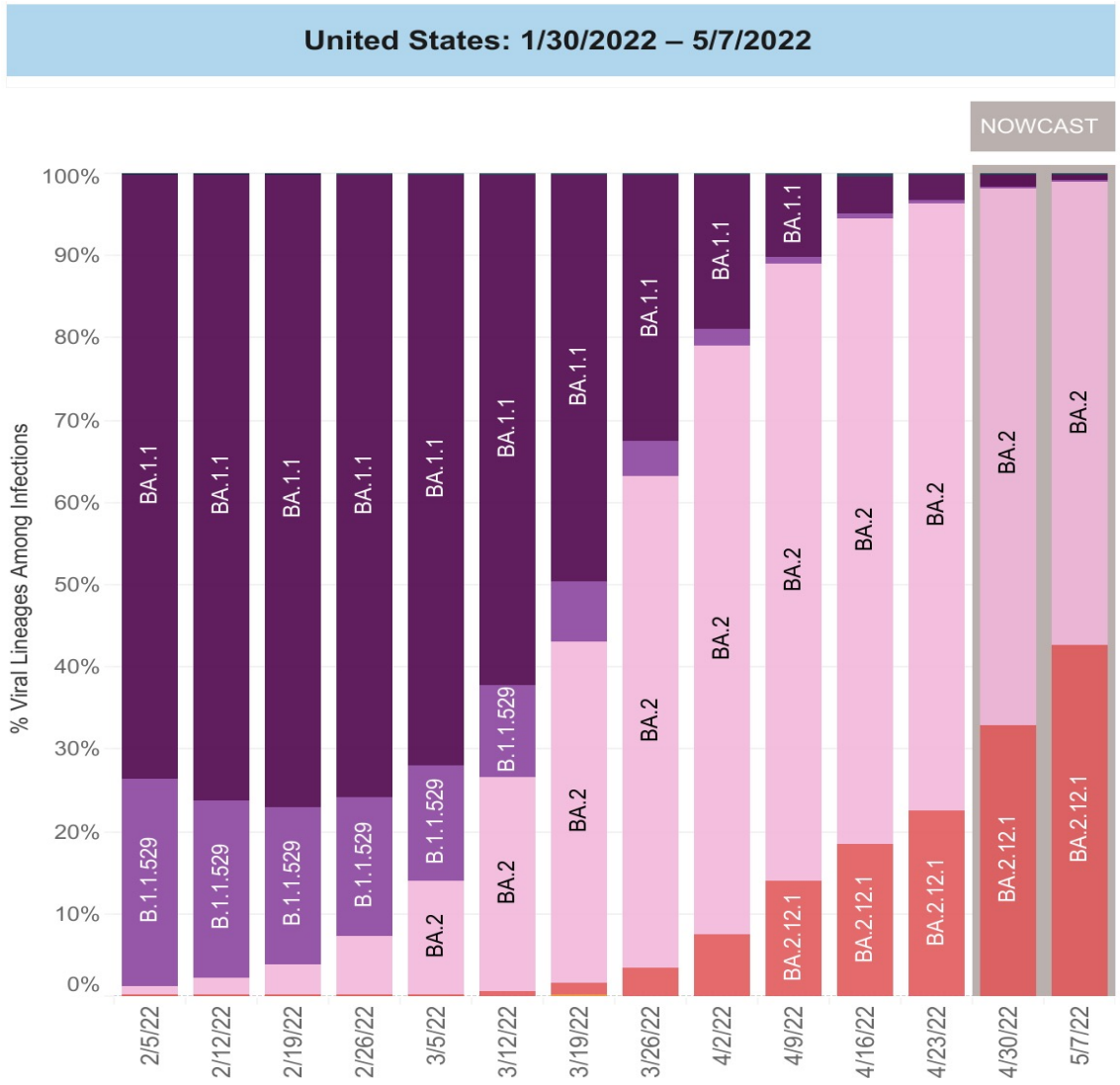


United States: 5/1/2022 – 5/7/2022 NOWCAST

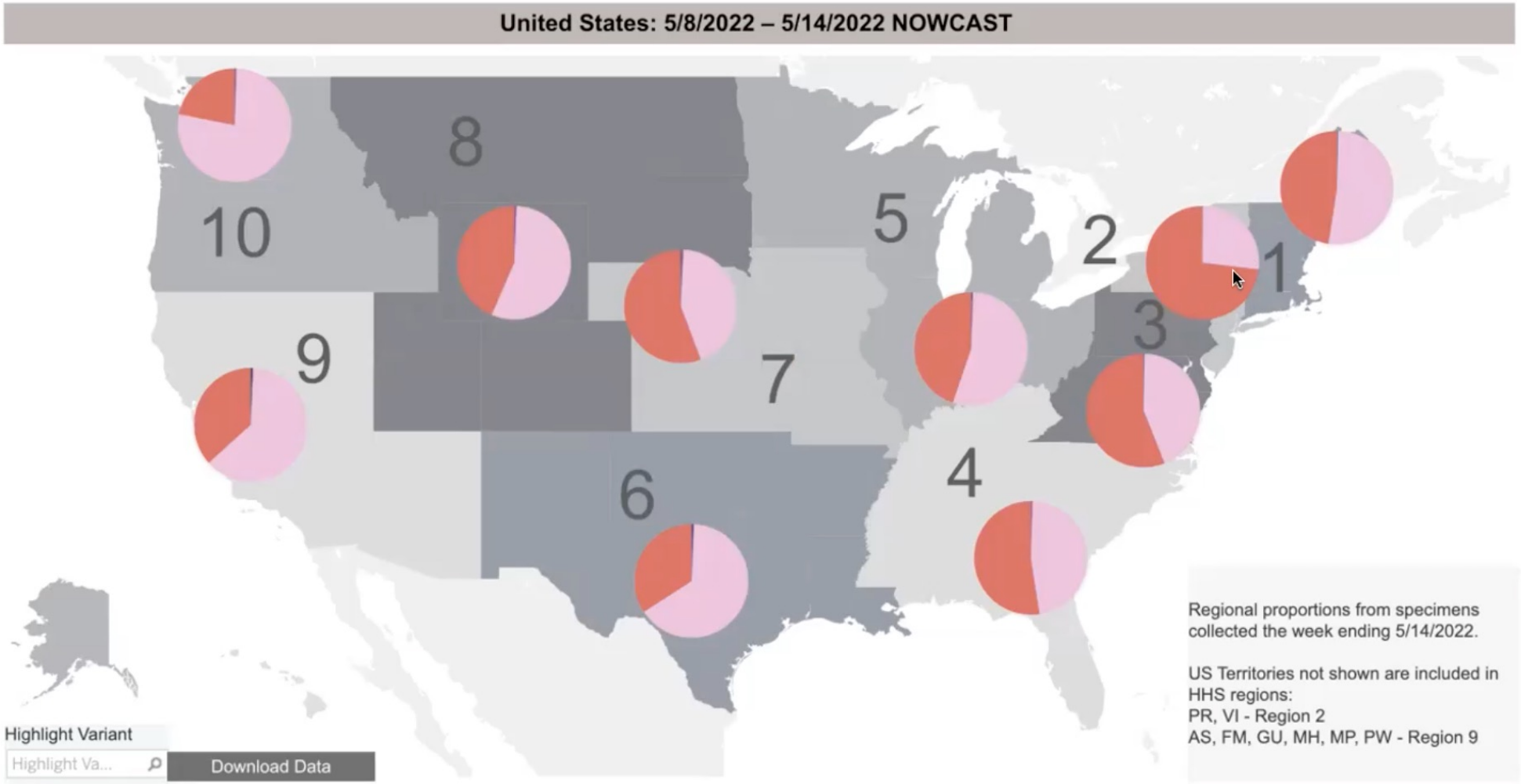
USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2	VOC	56.4%	49.3-63.3%
	BA.2.12.1	VOC	42.6%	35.6-49.9%
	BA.1.1	VOC	0.6%	0.5-0.8%
	B.1.1.529	VOC	0.2%	0.1-0.4%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.2%	0.1-0.3%

* 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.3, BA.4, BA.5 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggreagated with BA.2.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

COVID-19 Variants in the USA



Lineages called using pangolin v4.0.6 and pangolin-data v1.8.
Lineage BA.1.1 and its sublineages are aggregated with B.1.1.529 at the regional level as they currently cannot be reliably called in each region.

Updated May 17, 2022

Omicron

Increased transmissibility

- Secondary attack rate in households with **omicron** vs **delta**: **31%** vs **21%**

Unvaccinated individuals

- Have higher transmissibility compared with full vaccinated individuals

Among vaccinated people It is 2.7-3.7 times more transmissible than delta

WHO Label: Omicron

Pango Lineage: B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5 lineages (Pango lineage)[a]

Spike Protein Substitutions: A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

Nextstrain clade (Nextstrain)[b]: 21K

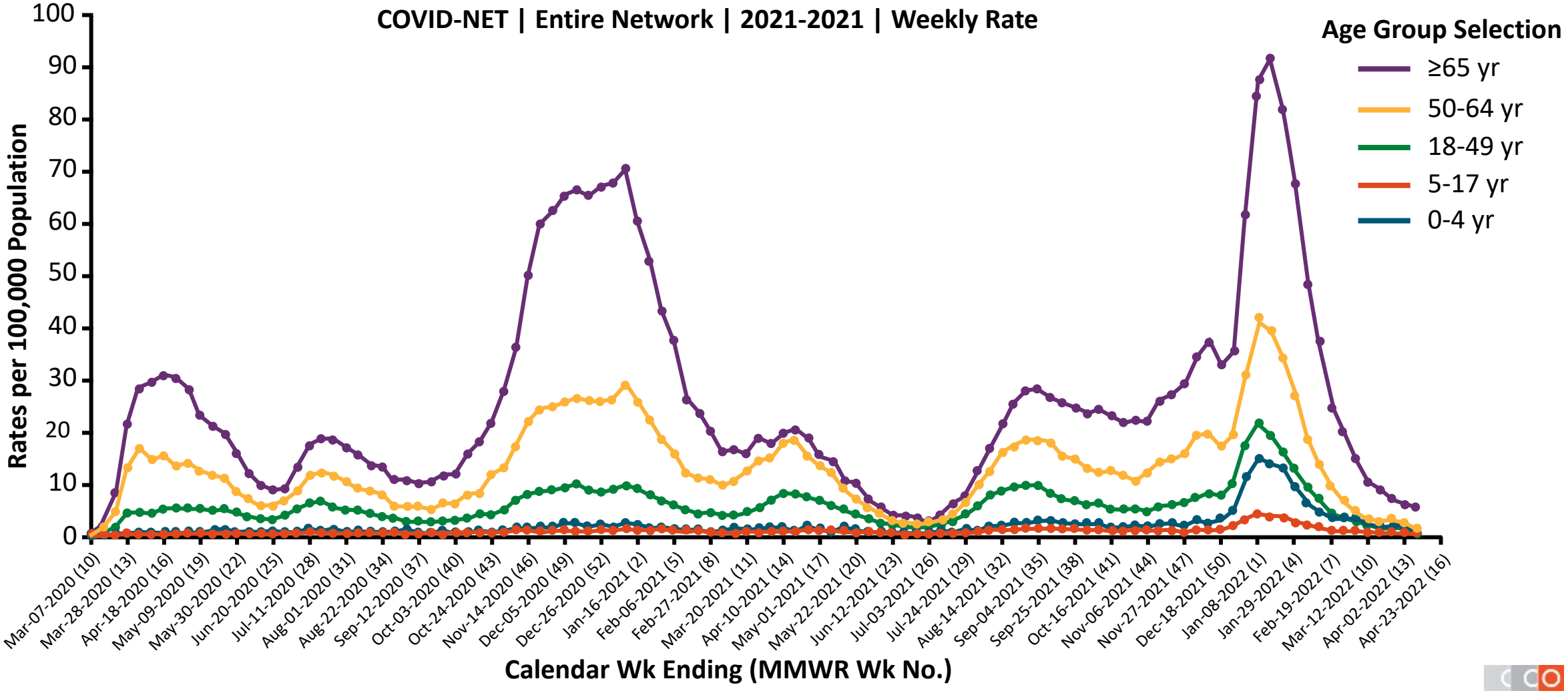
First Identified: South Africa

Attributes:

- Potential increased transmissibility
- Potential reduction in neutralization by some EUA monoclonal antibody treatments
- Potential reduction in neutralization by post-vaccination sera

Lyngse. medRxiv. 2021;[Preprint], covid.cdc.gov/covid-data-tracker/#variant-proportions.

COVID-NET: Lab-Confirmed COVID-19–Associated Hospitalization Rates Stratified by Age

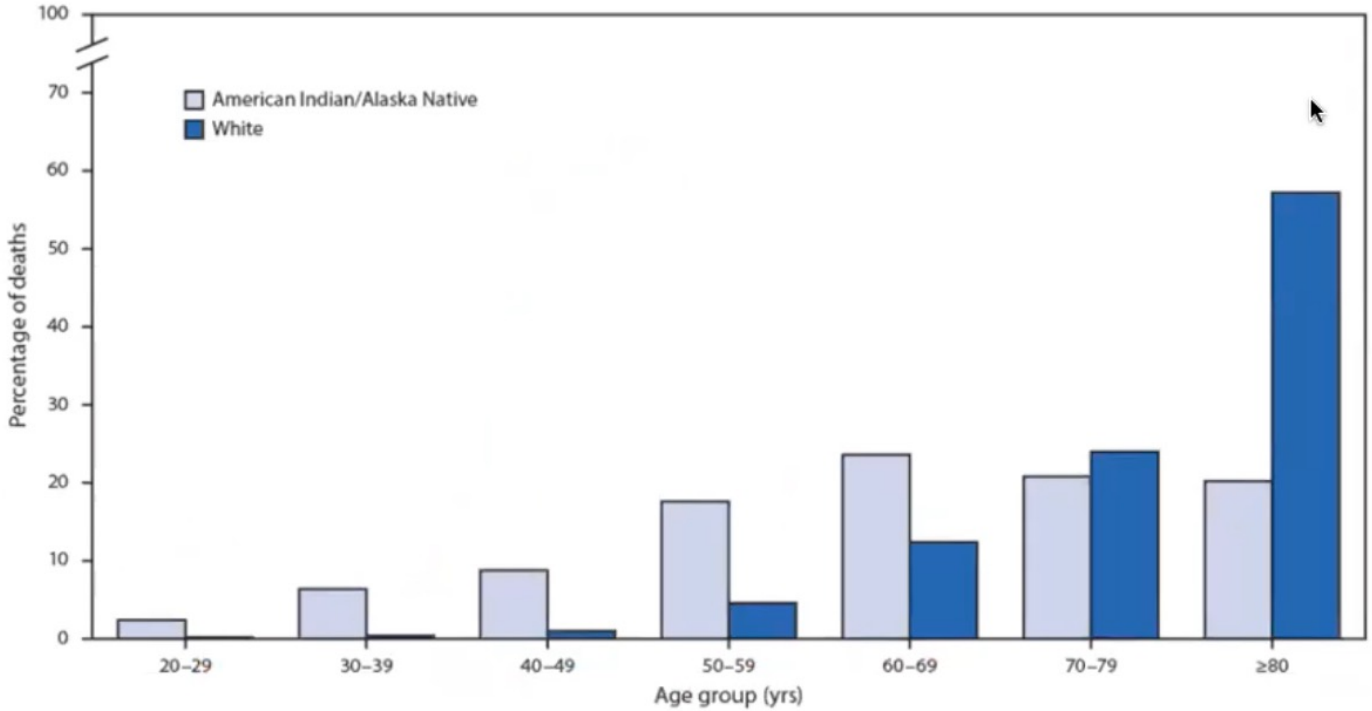


gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

Slide credit: clinicaloptions.com

Arrazola J, Masiello MM, Joshi S, et al. COVID-19 Mortality Among American Indian and Alaska Native Persons — 14 States, January–June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1853–1856.

FIGURE. Percentage distribution of COVID-19–associated deaths among American Indian/Alaska Native* and non-Hispanic White persons aged ≥20 years, by age group† — 14 states,§ January 1–June 30, 2020



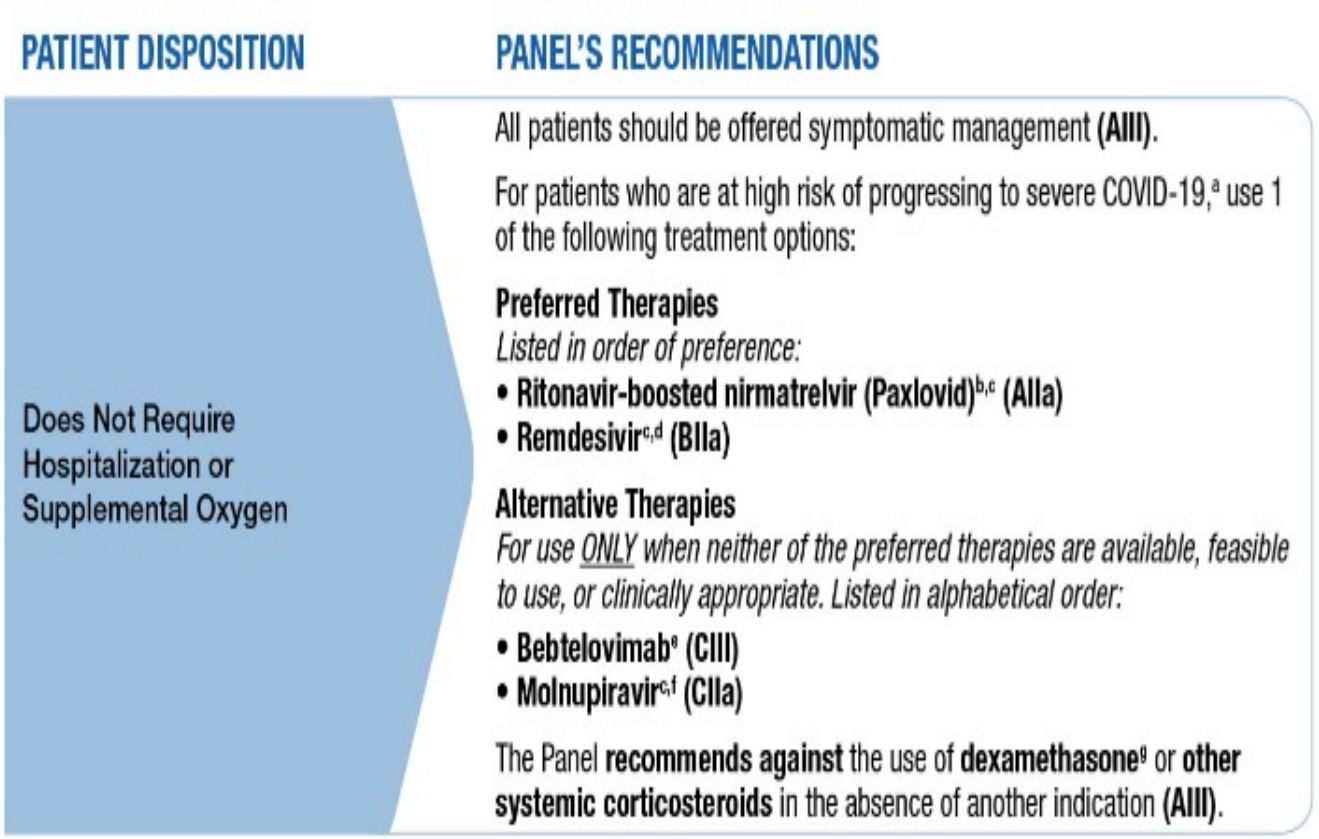
Abbreviation: COVID-19 = coronavirus disease 2019.

* Includes Hispanic and non-Hispanic ethnicities.

† Percentages by age group are not age-adjusted.

§ Alaska, Arizona, Louisiana, Minnesota, Mississippi, Nebraska, New Mexico, New York, North Dakota, Oklahoma, Oregon, South Dakota, Utah, and Washington.

COVID-19 Treatment Recommendations for Symptomatic Outpatients Patients



PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Does Not Require Hospitalization or Supplemental Oxygen	All patients should be offered symptomatic management **(AIII)**. For patients who are at high risk of progressing to severe COVID-19,[a] use 1 of the following treatment options: **Preferred Therapies** *Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)[b,c] (AIIa)** • **Remdesivir[c,d] (BIIa)** **Alternative Therapies** *For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:* • **Bebtelovimab[e] (CIII)** • **Molnupiravir[c,f] (CIIa)** The Panel **recommends against** the use of **dexamethasone[g]** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

- **Criteria for treatment**
  - Confirmed diagnosis
  - Mild to moderate symptoms
  - At least 1 risk factor for progression

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/clinical-management-summary/

Memorandum Explaining Basis for Declining Request for Emergency Use Authorization of Fluvoxamine Maleate Updates

On December 21, 2021, the FDA received a submission requesting (EUA) of fluvoxamine maleate for the "outpatient treatment of adults 24 years and older to prevent progression to severe COVID19 and/or hospitalization".

- The request is primarily based on results from the TOGETHER trial, a randomized, double-blind, placebo-controlled platform trial in high-risk, symptomatic adult outpatients in Brazil.

The primary endpoint was a composite of

- Emergency room visits due to the clinical worsening of COVID-19 (defined as remaining under observation for greater than 6 hours) and
- Hospitalization due to progression of COVID-19 (defined as worsening of viral pneumonia and/or complications), up to 28 days after randomization.

While the study met its primary endpoint, the results were primarily driven by a reduction in the emergency department visits lasting greater than 6 hours

- The treatment benefit of fluvoxamine was not persuasive when focusing on clinically meaningful outcomes such as proportion of patients experiencing hospitalizations or hospitalizations and deaths.
- FDA has determined that the data are insufficient to conclude that fluvoxamine may be effective in the treatment of nonhospitalized patients with COVID-19 to prevent progression to severe disease and/or hospitalization.
- The FDA has determined that the criteria for issuance of an EUA are not met and is declining to issue an EUA covering fluvoxamine for the treatment of COVID-19 at this time.

Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. WHO Solidarity Trial Consortium: METHODS

Solidarity enrolled consenting adults (aged ≥18 years) recently hospitalized with, definite COVID-19 and no contraindication to any of the study drugs, regardless of any other patient characteristics.

Participants were randomly allocated, in equal proportions between the locally available options, to receive whichever of the four study drugs

- lopinavir, hydroxychloroquine, IFN-β1a, or remdesivir were locally available at that time or no study drug (controls).
- All patients also received the local standard of care. No placebos were given.

The protocol-specified primary endpoint was:

- In-hospital mortality, subdivided by disease severity.

Secondary endpoints were:

- Progression to ventilation if not already ventilated, and time-to-discharge from hospital.

The Lancet: Published:May 02, 2022DOI:https://doi.org/10.1016/S0140-6736(22)00519-0

Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. WHO Solidarity Trial Consortium: METHODS

Findings

- Between March 22, 2020, and Jan 29, 2021, 14, 304 potentially eligible patients were recruited from 454 hospitals in 35 countries in all six WHO regions. Of which 14 221 patients were enrolled, including 8275 randomly allocated (1:1) either to remdesivir (ten daily infusions, unless discharged earlier) or to its control (allocated no study drug although remdesivir was locally available).
- Overall, 602 (14·5%) of 4146 patients assigned to remdesivir died versus 643 (15·6%) of 4129 assigned to control (mortality rate ratio [RR] 0·91 [95% CI 0·82–1·02], p=0·12).
- Of those already ventilated, 151 (42·1%) of 359 assigned to remdesivir died versus 134 (38·6%) of 347 assigned to control (RR 1·13 [0·89–1·42], p=0·32).
- Of those not ventilated but on oxygen, 14·6% assigned to remdesivir died versus 16·3% assigned to control (RR 0·87 [0·76–0·99], p=0·03).
- Of 1730 not on oxygen initially, 2·9% assigned to remdesivir died versus 3·8% assigned to control (RR 0·76 [0·46–1·28], p=0·30).
- Combining all those not ventilated initially, 11·9% assigned to remdesivir died versus 13·5% assigned to control (RR 0·86 [0·76–0·98], p=0·02) and 14·1% versus 15·7% progressed to ventilation (RR 0·88 [0·77–1·00], p=0·04).
- The non-prespecified composite outcome of death or progression to ventilation occurred in 19·6% assigned to remdesivir versus 22·5% assigned to control (RR 0·84 [0·75–0·93], p=0·001).
- A meta-analysis of mortality in all randomised trials of remdesivir versus no remdesivir yielded similar findings.

Interpretation

- Remdesivir has no significant effect on patients with COVID-19 who are already being ventilated. Among other hospitalised patients, it has a small effect against death or progression to ventilation (or both).

The Lancet: Published:May 02, 2022DOI:https://doi.org/10.1016/S0140-6736(22)00519-0

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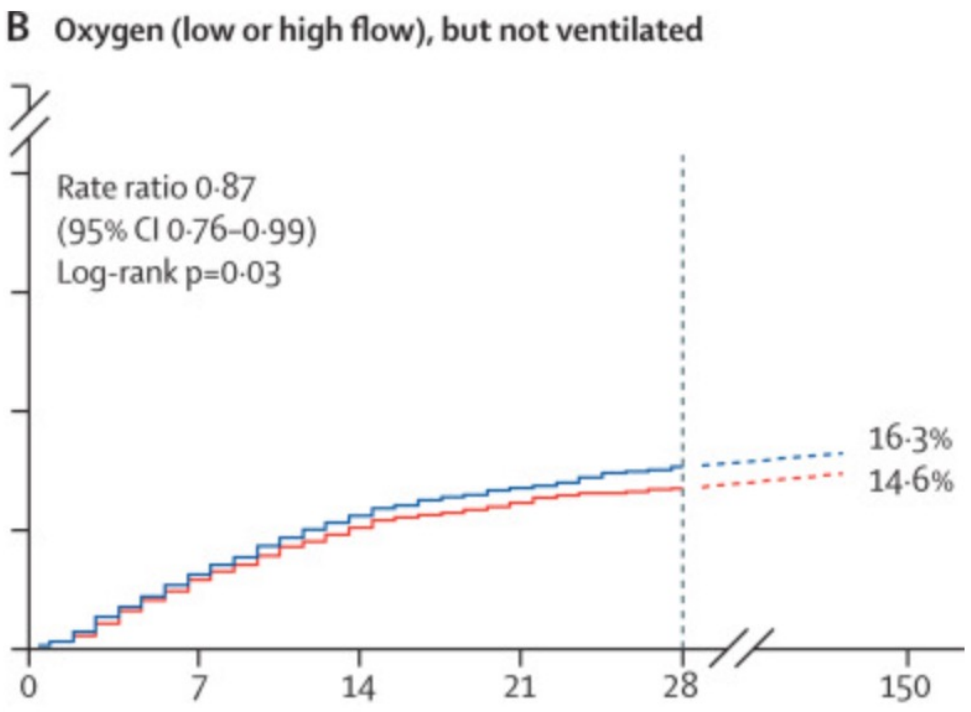

Death Outcome

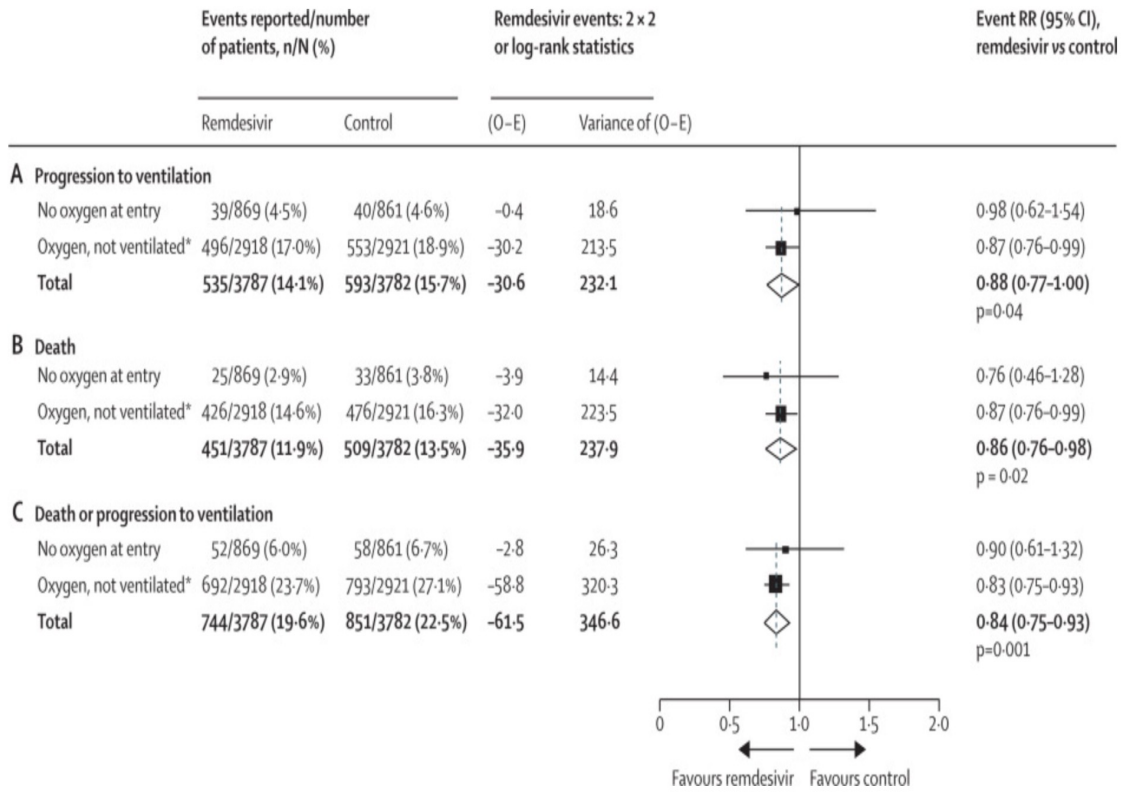

Figure 3 Secondary outcome of ventilation initiation for remdesivir *vs* its control in patients not already ventilated at study entry

Baricitinib Receives FDA Approval for the Treatment of Hospitalized Patients With COVID-19

The FDA previously granted emergency use authorization (EUA) to baricitinib for use in combination with remdesivir as a treatment for adults and pediatric patients hospitalized with COVID-19.

- The EUA was later updated to authorize the use of baricitinib as a standalone treatment.
- Baricitinib remains under EUA status for hospitalized patients aged 2 to 17 years who require supplemental oxygen, mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

The new indication of baricitinib is supported by two randomized, double-blind, placebo-controlled phase 3 studies that demonstrated mortality benefits

- ACTT-2
- COV-Barrier

Vaccine Update
Update March 29, 2022

- Second mRNA booster allowed for persons over age 50 or who are immunocompromised at least 4 months since the initial booster
  - Persons who received J and J vaccine and a booster dose at least 4 months ago may receive a second booster with an mRNA vaccine

- Pfizer-BioNTech COVID-19 Vaccine Booster Dose FDA approved for Children 5-11 years

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Expands Eligibility for Pfizer-BioNTech COVID-19 Vaccine Booster Dose to Children 5 through 11 Years

The FDA has determined that the known and potential benefits of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine for children 5 through 11 years of age at least five months after completing a primary series outweigh its known and potential risks

- **A booster dose can help provide continued protection against COVID-19 in this and older age groups.**

Data Supporting Effectiveness

- The EUA for a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine for children 5 through 11 years of age is based on FDA's analysis of immune response data in a subset of children from the ongoing randomized placebo-controlled trial that supported the October 2021 authorization of the Pfizer-BioNTech COVID-19 Vaccine primary series in this age group.
- Antibody responses were evaluated in 67 study participants who received a booster dose 7 to 9 months after completing a two-dose primary series of the Pfizer-BioNTech COVID-19 Vaccine. The antibody level against the SARS-CoV-2 virus one month after the booster dose was increased compared to before the booster dose.

FDA Evaluation of Safety

- The safety of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine in this age group was assessed in approximately 400 children who received a booster dose at least five months (range 5 to 9 months) after completing a two-dose primary series. The most commonly reported side effects were pain, redness and swelling at the injection site, as well as fatigue, headache, muscle or joint pain and chills and fever.