COVID-19 ECHO Update

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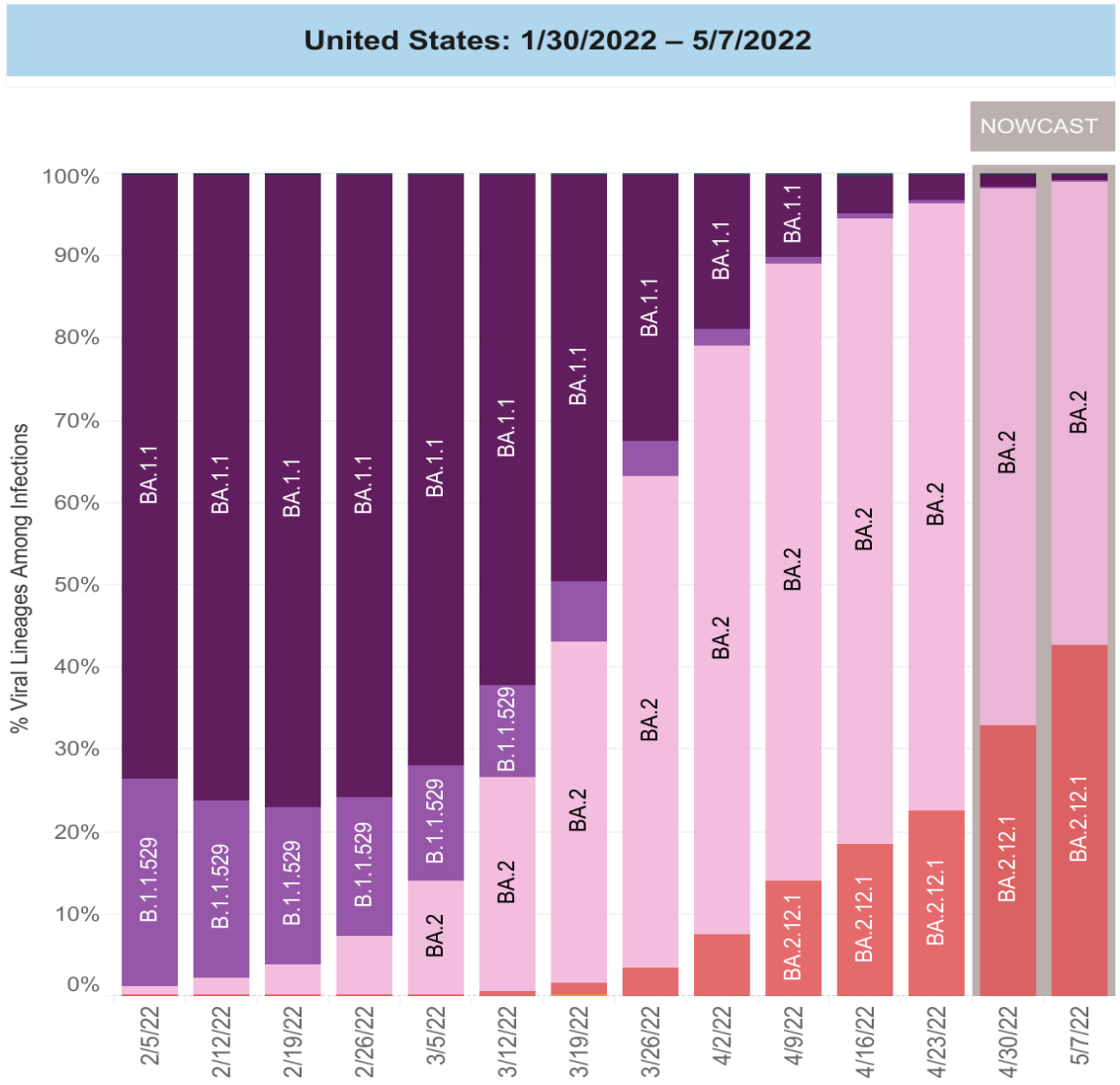


United States: 5/1/2022 – 5/7/2022 NOWCAST

USA

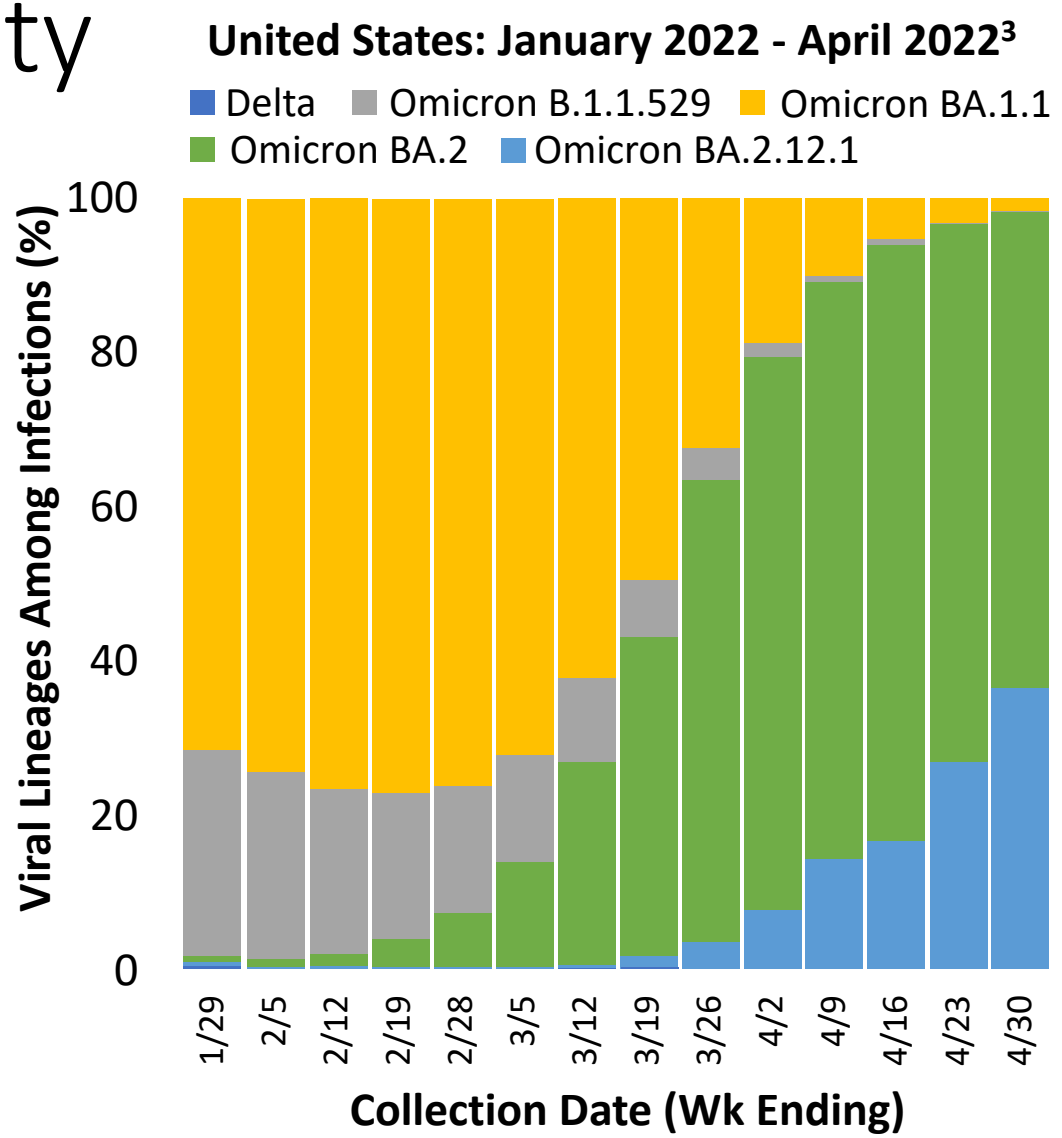
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2	VOC	56.4%	49.3-63.3%
	BA.2.12.1	VOC	42.6%	35.6-49.9%
	BA.1.1	VOC	0.6%	0.5-0.8%
	B.1.1.529	VOC	0.2%	0.1-0.4%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.2%	0.1-0.3%

* 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

Omicron: Transmissibility

- Omicron spreads rapidly[1,2]
  - Increased transmissibility[1]
    - Secondary attack rate in households with **omicron** vs **delta**: **31%** vs **21%**
    - Unvaccinated individuals have higher transmissibility compared with fully vaccinated individuals
    - **Omicron** is 2.7-3.7 times more transmissible than delta among vaccinated individuals[1]
  - **Immune evasion**



1. Lyngse. medRxiv. 2021;[Preprint]. Note: This study has not been peer reviewed.
2. cdc.gov/coronavirus/2019- ncov/variants/omicron-variant.html.
3. covid.cdc.gov/covid-data-tracker/#variant-proportions.

Slide credit: clinicaloptions.com

Cases Total 82,522,948

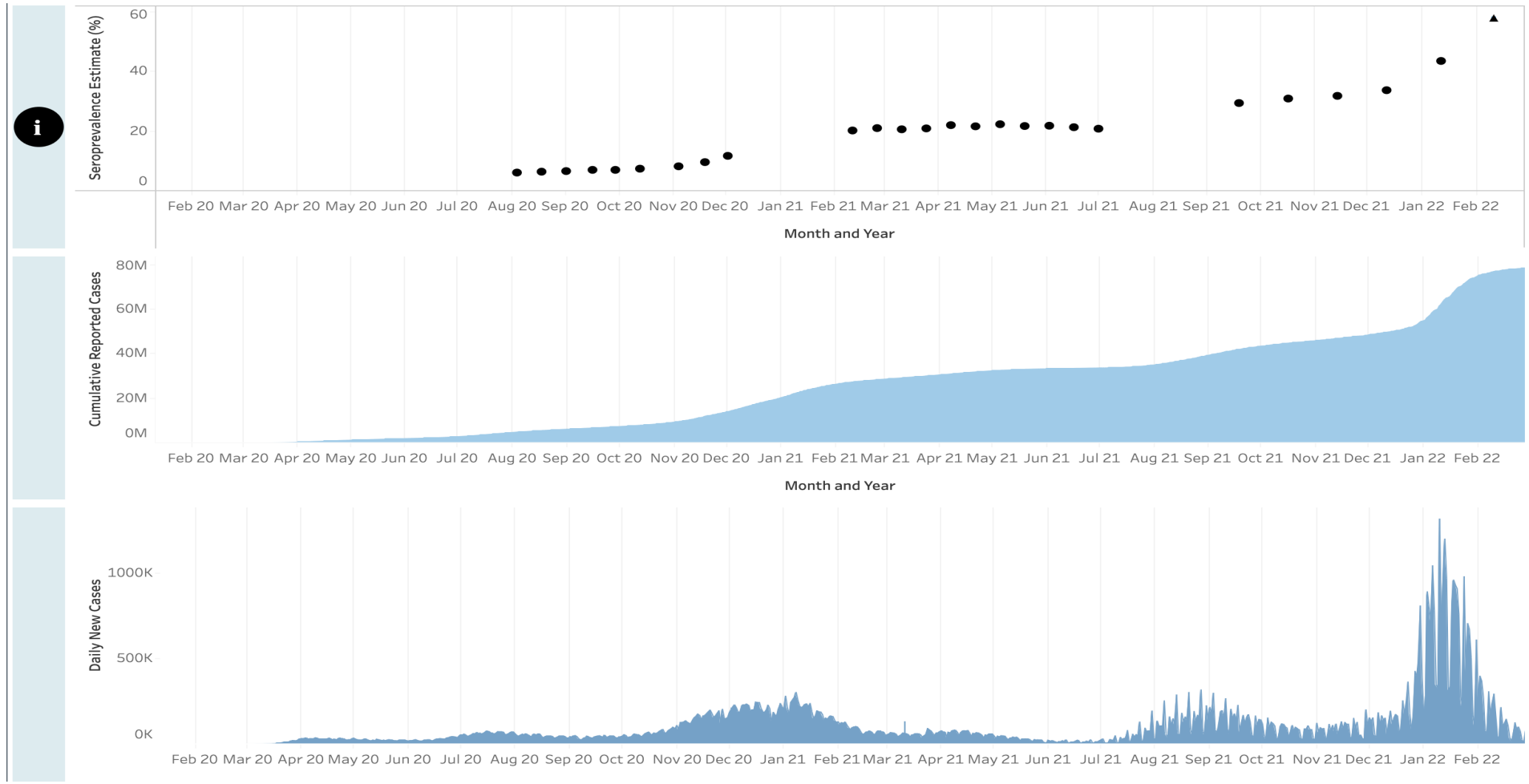
Case Trends

Deaths Total 997,468

Death Trends

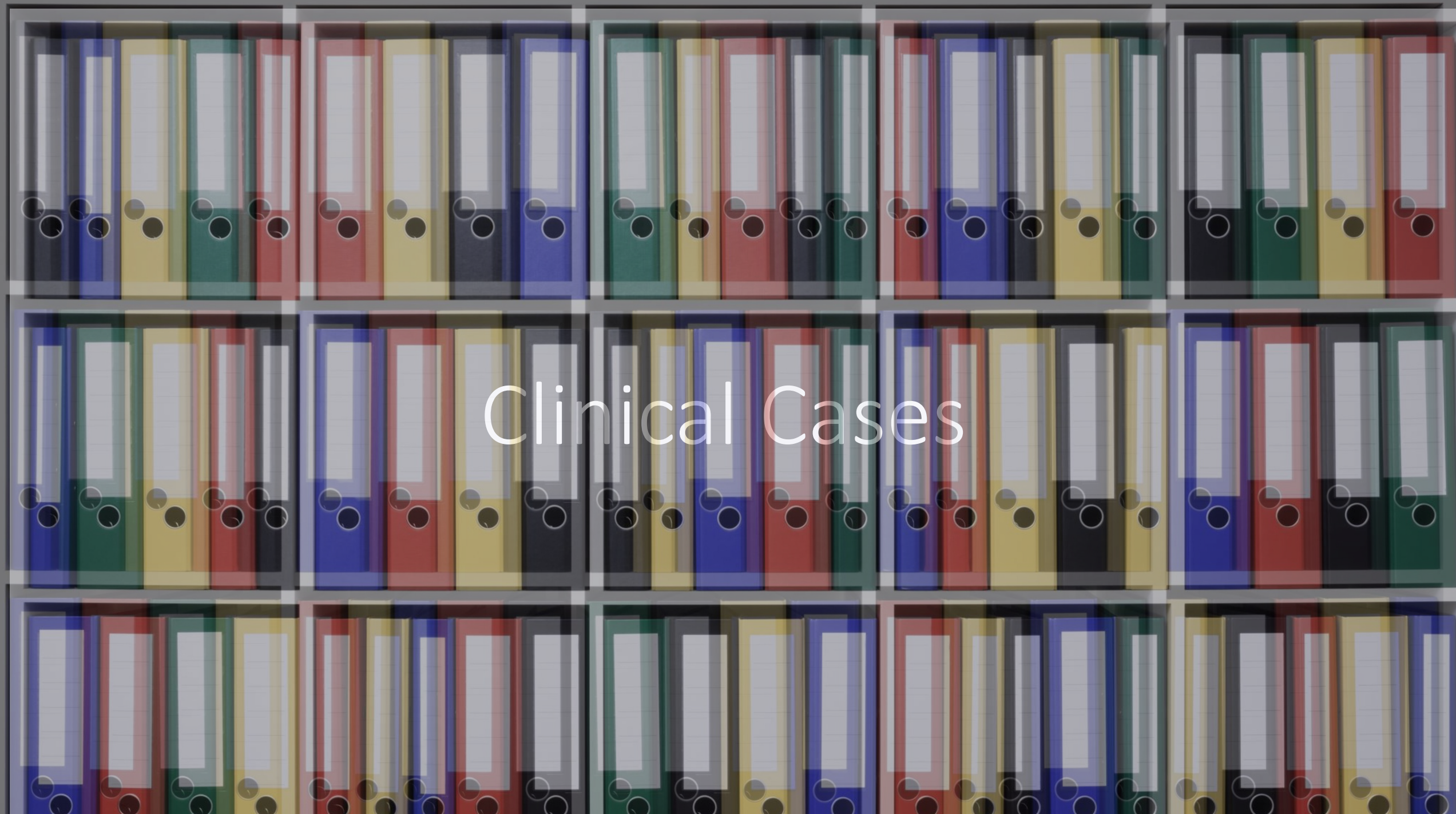
Current **Hosp.** 16,571

Admission Trends



CDC COVID Data Tracker: Trends in Cases and Deaths

Accessed May 18,2022, CDC.gov



Clinical Cases

Clinical Case # 1- September 2021

Mrs X is a 32-year-old female AI/AN patient without prior medical history that comes in for consultation

- She tested positive for SARS-CoV-2 (antigen home test).
- She is asymptomatic, was in a birthday party 5 days ago without wearing a mask.

Social History

- Works in a retail store, does not smoke nor drink alcohol
- Lives with her husband and does not have any children

Medical History:

- IUD
- Vaccinated x 2 with Moderna in April and May of 2021
- Does not take any medications

Physical exam

- Vitals: 37.5, 72, 122/84, 18, SaO2 98%, BMI24.5
- Alert and oriented
- Heart: RRR, No murmurs
- Lungs: Clear to auscultation

Clinical Case # 1- September 2021

How would you classify her disease severity?

- Asymptomatic or pre-symptomatic infection
- Mild illness
- Moderate illness
- Severe illness
- Critical illness

¿What risk factors does she have for disease progression?

What pharmacological treatment do you recommend?

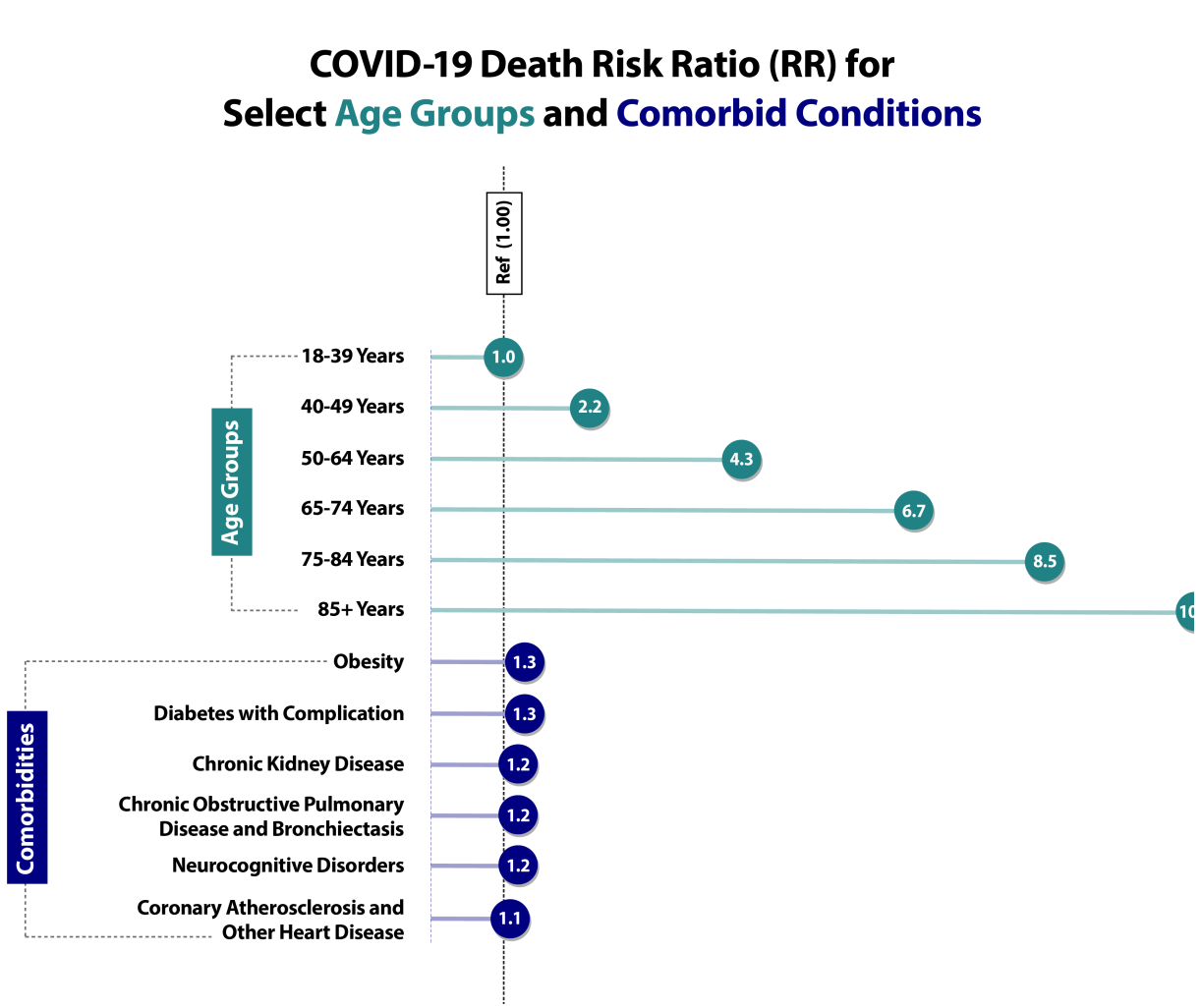
NIH Guidelines: Defining a COVID-19 Severity Spectrum

Stage	Characteristics
Asymptomatic or presymptomatic infection	▪ Positive virologic test for SARS-CoV-2 (ie, NAAT or antigen test) but no symptoms consistent with COVID-19
Mild illness	▪ Varied symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste or smell) but no shortness of breath, dyspnea, or abnormal chest imaging
Moderate illness	▪ SpO_2 ≥94% and lower respiratory disease evidenced by clinical assessment or imaging
Severe illness	▪ SpO_2 <94%, PaO_2/FiO_2 <300 mm Hg, respiratory rate >30 breaths/min, or lung infiltrates >50%
Critical illness	▪ Respiratory failure, septic shock, and/or multiorgan dysfunction

NIH COVID-19 Treatment Guidelines. Clinical spectrum of SARS-CoV-2 infection. Last updated October 19, 2021.

Slide credit: clinicaloptions.com

Risk Factors for Severe COVID-19 Outcomes



CDC.gov

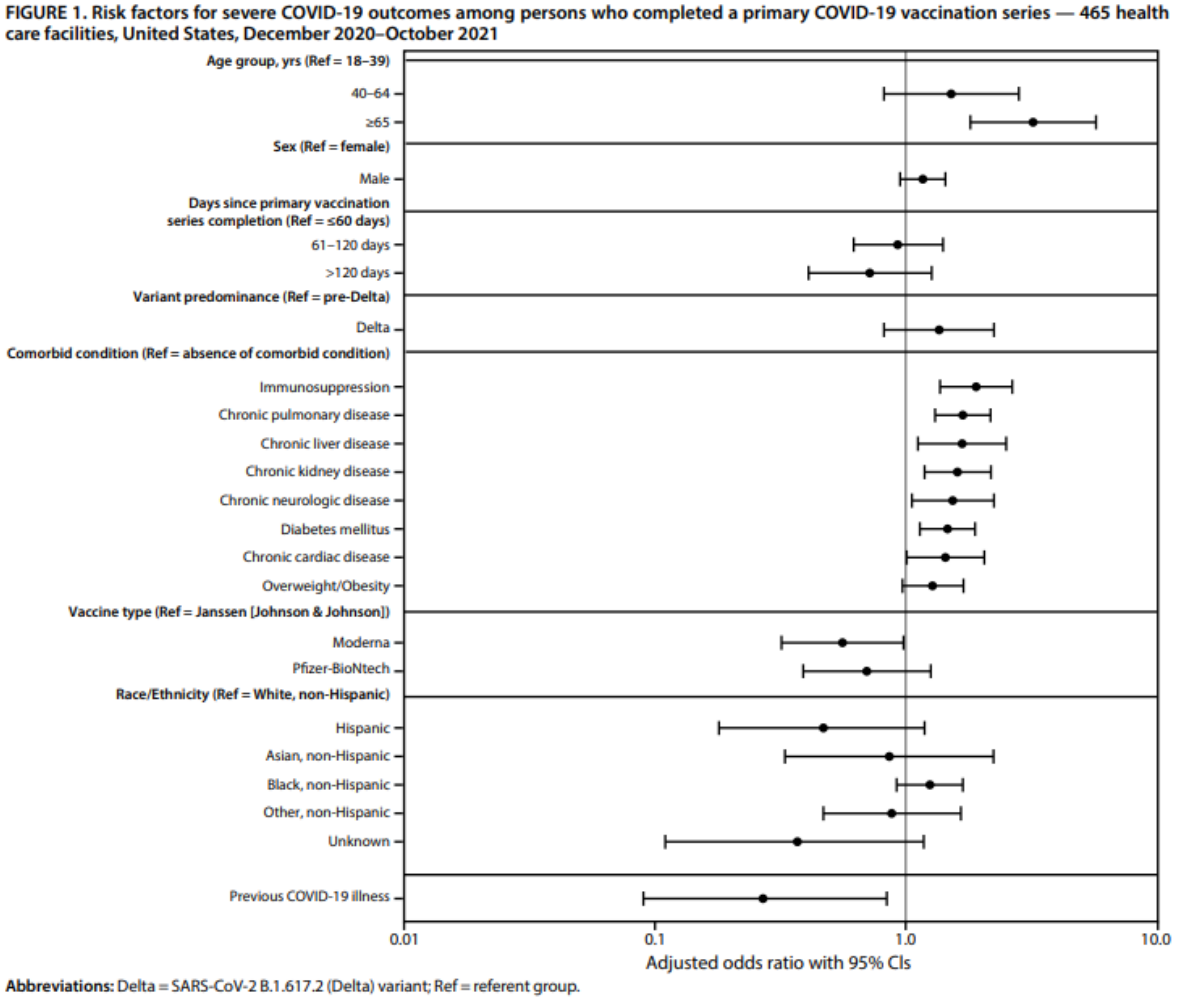


FIGURE 1. Risk factors for severe COVID-19 outcomes among persons who completed a primary COVID-19 vaccination series — 465 health care facilities, United States, December 2020–October 2021

Abbreviations: Delta = SARS-CoV-2 B.1.617.2 (Delta) variant; Ref = referent group.

Among 1,228,664 persons who completed primary vaccination during December 2020–October 2021, severe COVID-19–associated outcomes (0.015%) or death (0.0033%) were rare. Risk factors for severe outcomes included age ≥65 years, immunosuppressed, and six other underlying conditions. All persons with severe outcomes had at least one risk factor; 78% of persons who died had at least four. MMWR Morb Mortal Wkly Rep 2022;71:19–25 (

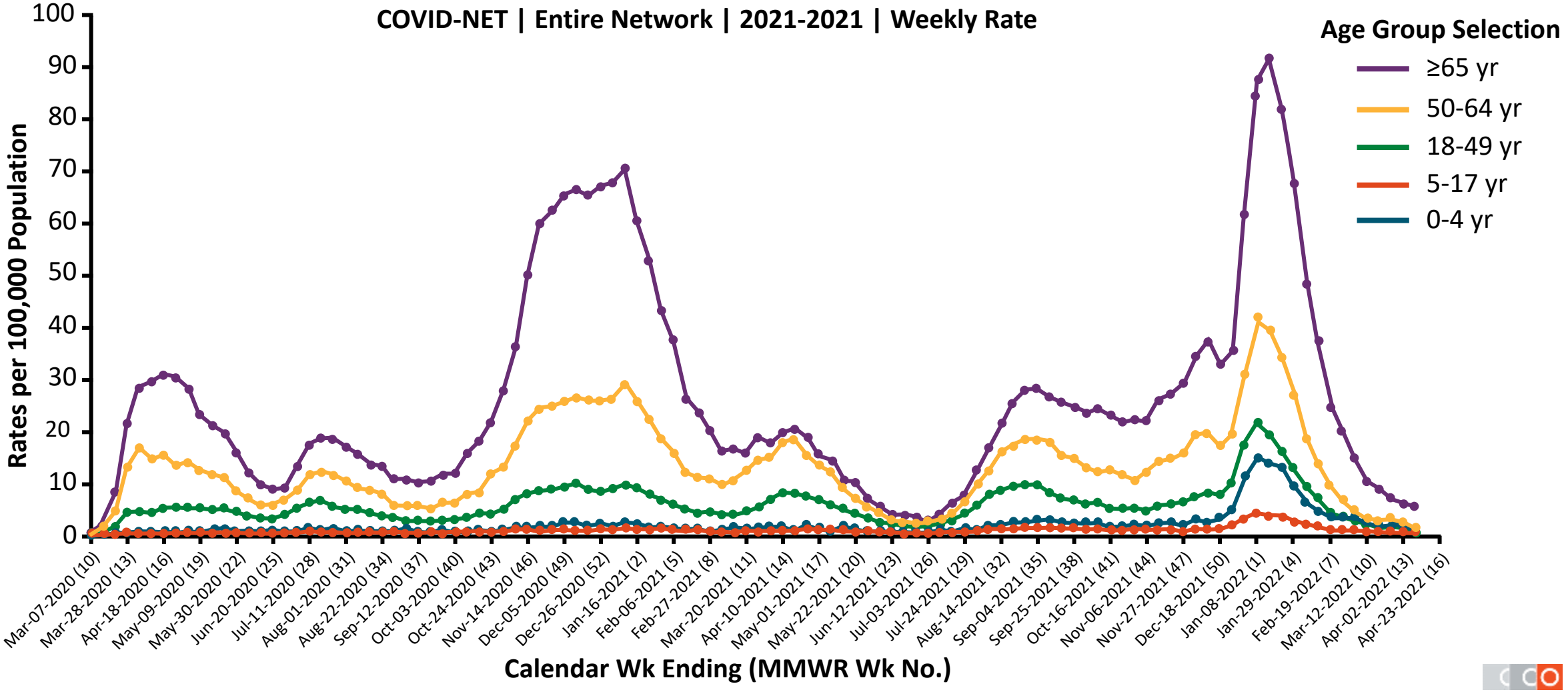
Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity

Updated Apr. 29, 2022 Print

Rate ratios compared to White, Non-Hispanic persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
Cases[1]	1.6x	0.7x	1.1x	1.5x
Hospitalization[2]	3.1x	0.8x	2.4x	2.3x
Death[3]	2.1x	0.8x	1.7x	1.8x

CDC.gov

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



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

Slide credit: clinicaloptions.com

Management of Asymptomatic Patients

- Reassurance
- Confirmation of antigen test
  - Not needed in the correct clinical scenario
- Isolation
  - 5, 7, 10 days?
- Retesting?
- No pharmacologic treatment needed
- Post exposure prophylaxis for contacts?

Clinical Case # 1- September 2021
2 Days Later

Patient returns with

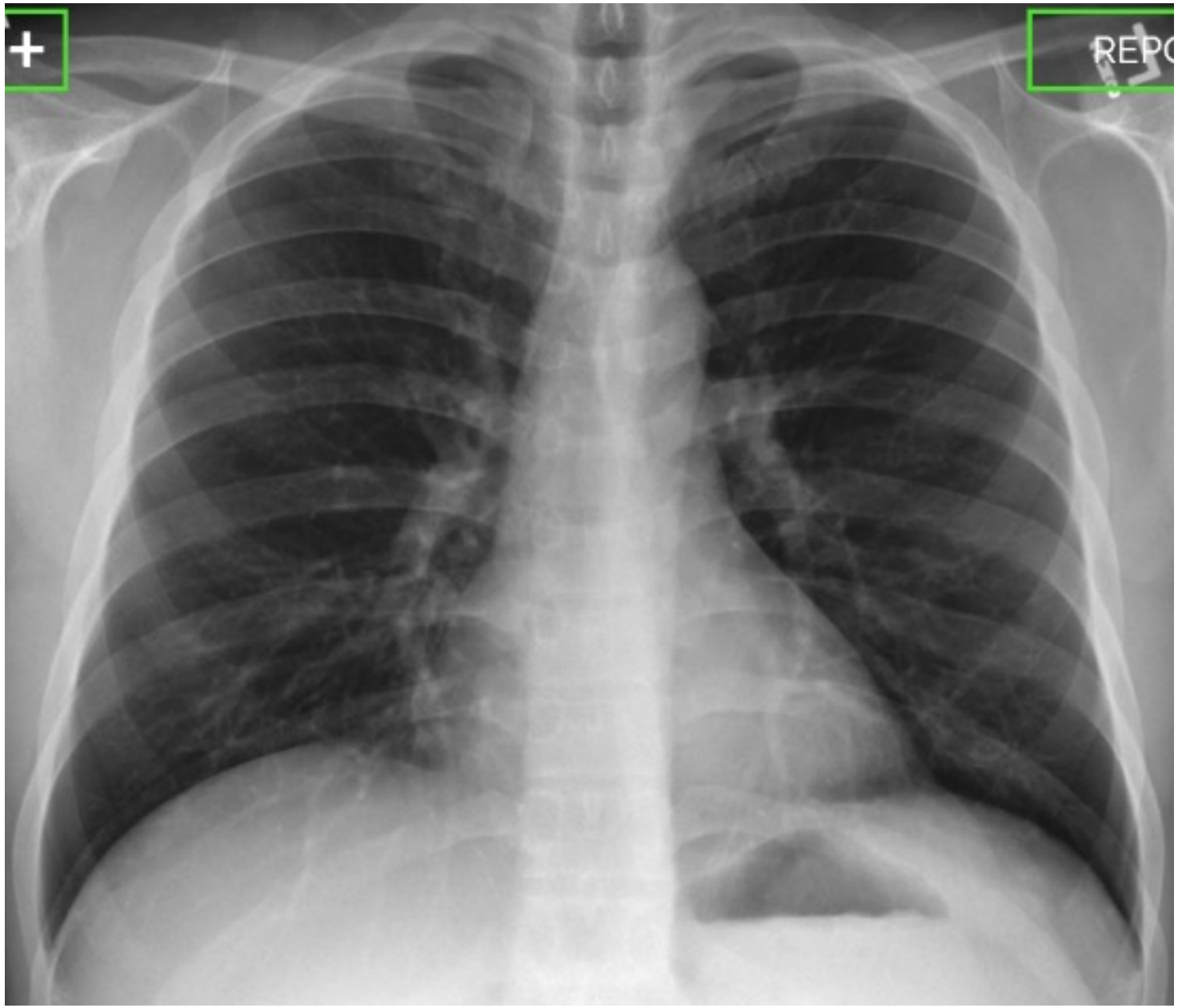
- Cough
- Nasal congestion
- Body aches
- Chills

Physical Exam

- T 38.8, HR 92, BP 122/84, RR 20, SaO2 96%, BMI 24.5

Lung exam

- Normal

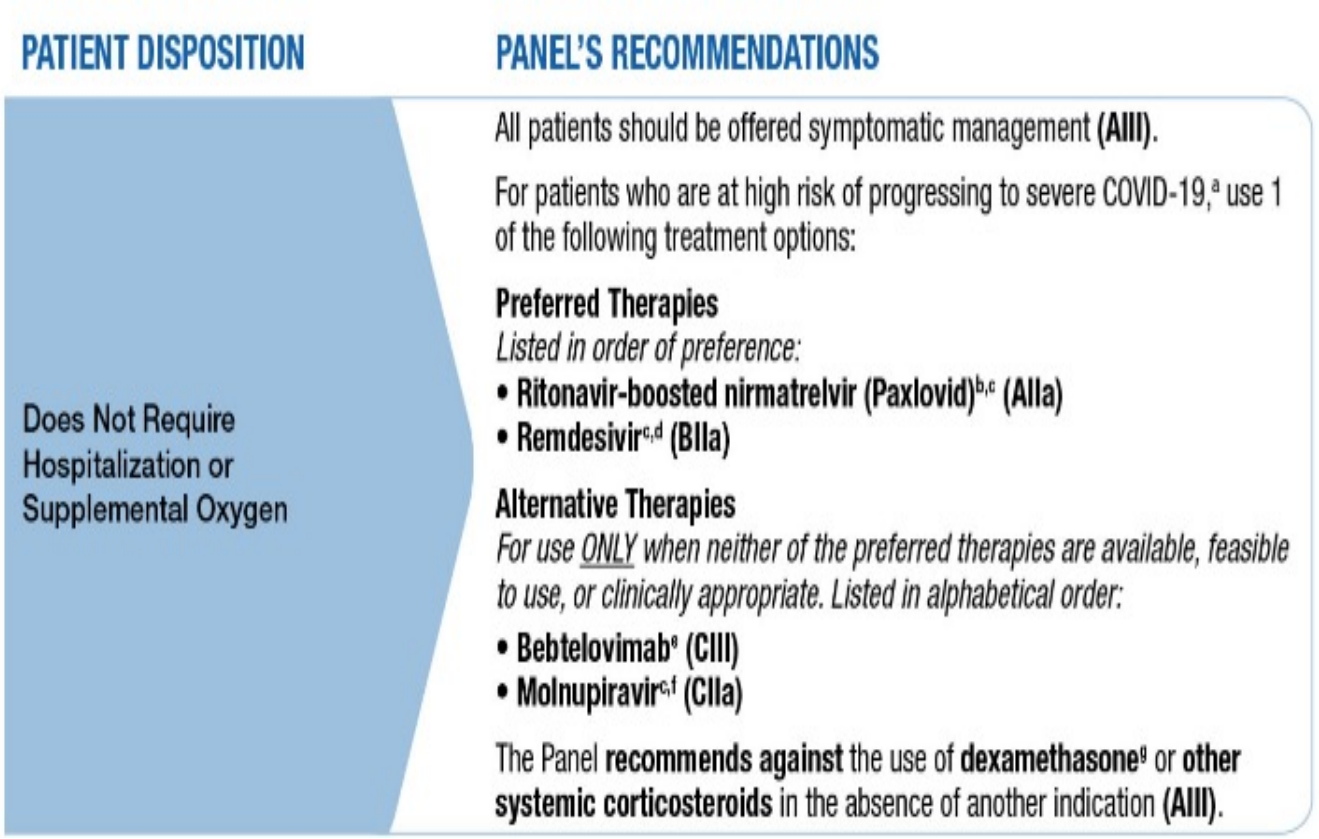


Clinical Case # 1- September 2021
2 Days Later

What is the first line of treatment for this patient

¿What is the most likely SARS-CoV-2 variant this patient has and does it matter?

COVID-19 Treatment Recommendations for Symptomatic Outpatients Patients

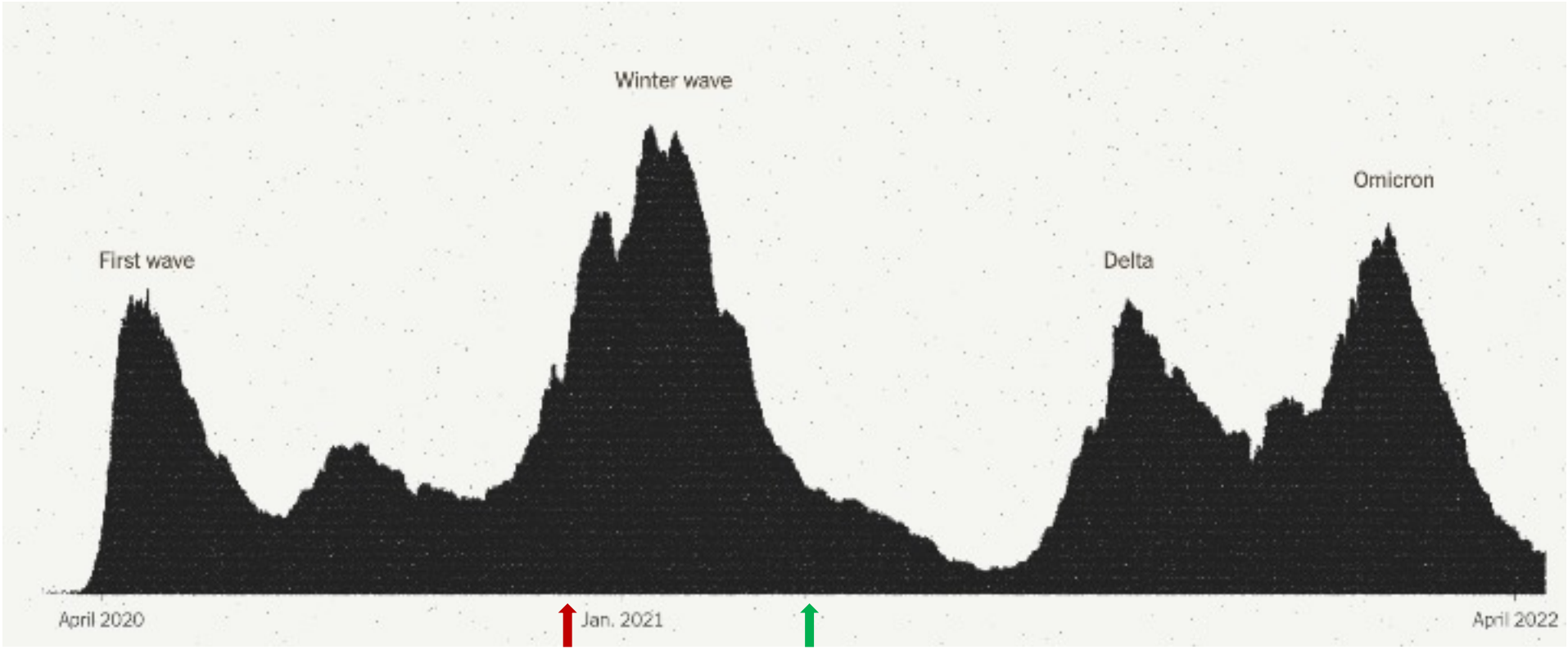


PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Does Not Require Hospitalization or Supplemental Oxygen	All patients should be offered symptomatic management **(AIII)**. For patients who are at high risk of progressing to severe COVID-19,[a] use 1 of the following treatment options: **Preferred Therapies** *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/

COVID Deaths (EEUU) = 1,000,000



https://www.nytimes.com/interactive/2022/05/13/us/covid-deaths-us-one-million.html

Treatment Updates

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).

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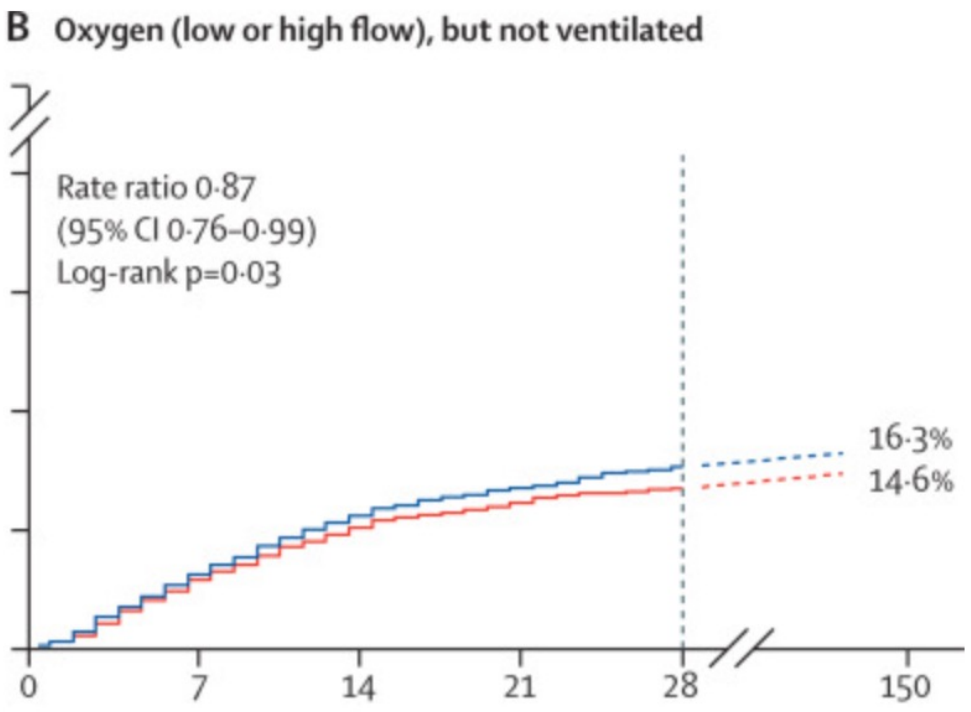


Death Outcome

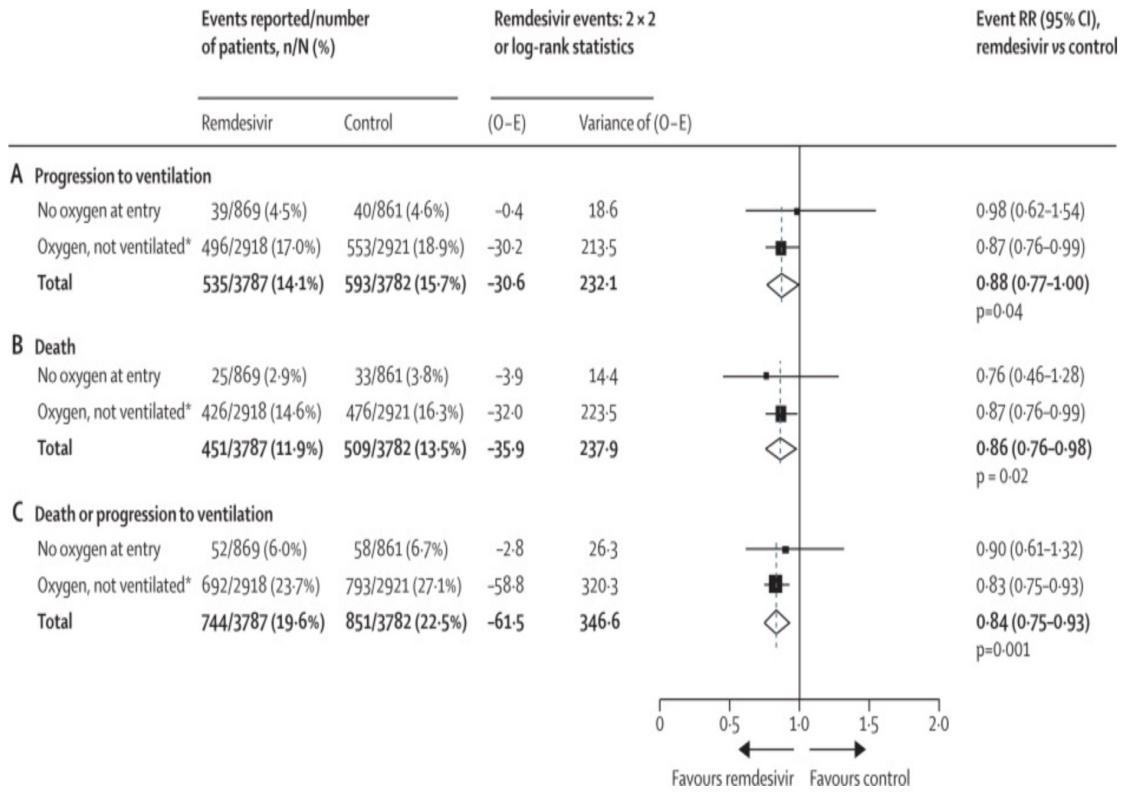


Figure 3 Secondary outcome of ventilation initiation for remdesivir *vs* its control in patients not already ventilated at study entry

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

- 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

Vaccine Update:
To Re-boost or not to Re-boost

Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. (Magen et al, NEJM. 4/13/2022)

- Analyzed 182,122 individuals in Israel, age > 60, re-boosted after 4 months
- Only had 30 days of follow up

Vaccine effectiveness during Omicron wave:

- 45% against PCR positive infection
- 55% against symptomatic COVID-19
- 74% against death

https://www.nejm.org/doi/full/10.1056/NEJMoa2201688

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.

Clinical Case # 2- January 2022

Male 72 yo AI/AN patient with a hx of HTN, DM and CAD presents to the urgent care

- Fever, chills, loss of taste and smell, and dry cough of 2 day duration

He just returned from visiting his family during Christmas in Arizona

Medical History:

- Acute myocardial infarction in 2018
- Type II DM
- CKD stage 3

Social History

- Works in a restaurant, drinks one beer per day, smoked tobacco for 10 years from age 25-35
- Lives with his wife

Medications

- Lisinopril, Metoprolol, Atorvastatin, aspirin, metformin, insulin QHS

COVID Vaccination:

- 1 dose of Johnson & Johnson (June 2021

Clinical Case # 2- January 2022

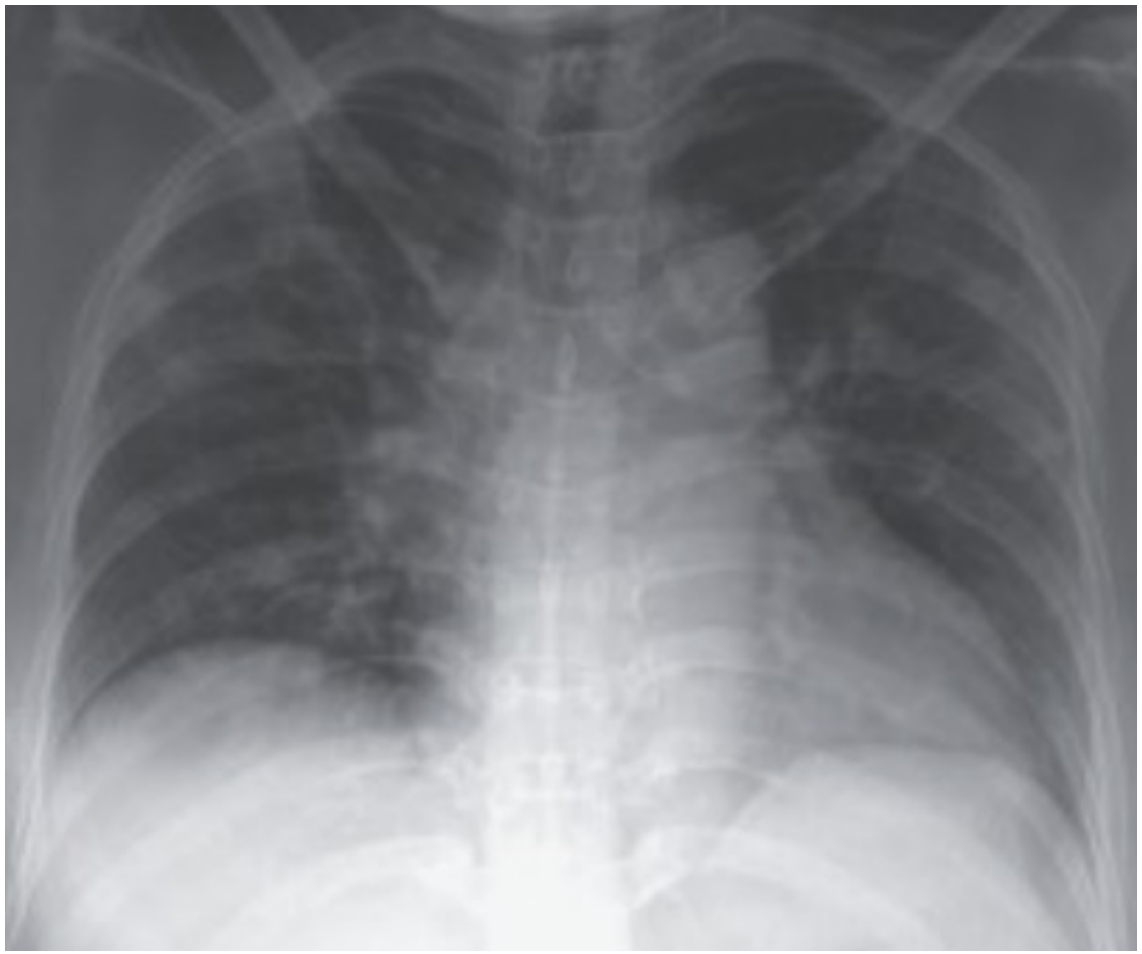
Physical Exam

- T 38.5, HR 115, BP 154/92, RR 22, SaO2 94%, BMI 37
- Alert and oriented, obese, coughing frequently
- CV: tachycardia, No murmurs
- Lungs: Bibasilar crackles

Labs

- Positive SARS-CoV-2 NAT test

Clinical Case # 2- September 2021
Radiology and Labs



Bilateral Ground Glass Opacities

- **CBC:**
  - WBC 17
  - Hgb 11.5
  - HCT 35
  - Plts 759,000
- **Influenza NAT:** negative
- Cr 1.9, **GFR** 50 ml/min
- **CRP** 29, ESR 75
- **AST/ALT:** 49/65
- **Pro-calcitonin** 0.05

Clinical Case # 2- January 2022

How would you classify his disease severity?

- Asymptomatic or pre-symptomatic infection
- Mild illness
- Moderate illness
- Severe illness
- Critical illness

¿What risk factors does he have for disease progression?

What pharmacological treatment do you recommend?

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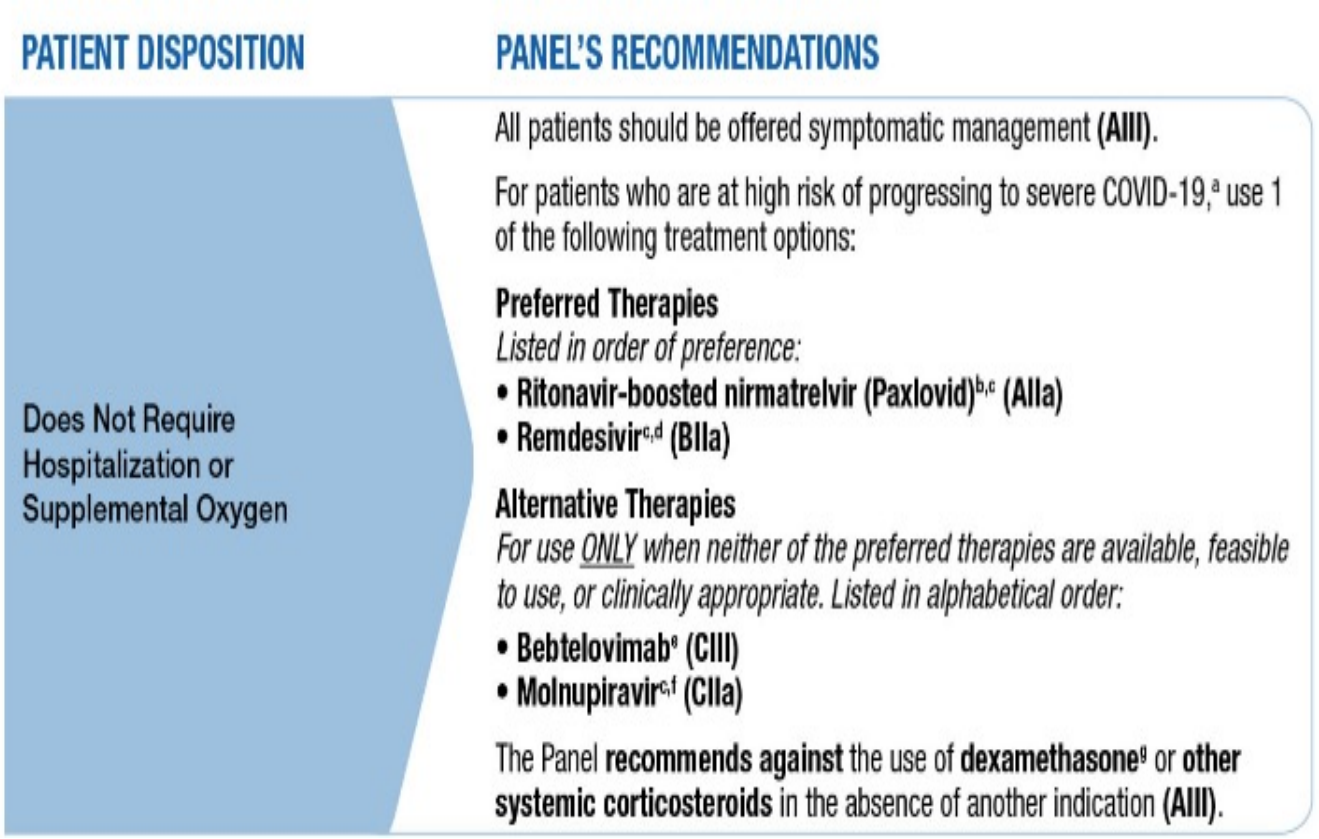
Slide credit: clinicaloptions.com

COVID-19 Treatment Recommendations for Symptomatic Outpatients Patients



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- **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/

Clinical Case # 1- September 2021

- How would you classify her disease severity?
  a) Asymptomatic or pre-symptomatic infection
  b) Mild illness
  c) Moderate illness
  d) Severe illness
  e) Critical illness

Clinical Case # 1- September 2021

- ¿What risk factors does she have for disease progression?
  a) None
  b) Being American Indian/Alaskan Native
  c) Age
  d) Marital status

Clinical Case # 1- September 2021

- What pharmacological treatment do you recommend?
  a) Dexamethasone 6 mg per day for 10 days
  b) None
  c) Remdesivir IV x 3 days
  d) Paxlovid x 5 days PO

Clinical Case # 2- January 2022

- How would you classify her disease severity?
  a) Asymptomatic or pre-symptomatic infection
  b) Mild illness
  c) Moderate illness
  d) Severe illness
  e) Critical illness

Clinical Case # 2- January 2022

- ¿What risk factors does she have for disease progression?
  a) Being American Indian/Alaskan Native
  b) Age
  c) Obesity
  d) Cardiovascular disease
  e) CKD
  f) All of the above are correct
  g) A, B and C are correct

Clinical Case # 2- January 2022

- What is the pharmacologic treatment of choice for this patient
  a) No treatment is indicated
  b) Dexamethasone 6 mg per day for 10 days
  c) Molnupiravir PO x 4 days
  d) Paxlovid x 5 days PO
  e) Bebtelovimab IV x 1