

# HHP/HPH COVID-19 Community Webinar Series

Thursday, January 13, 2022

5:30pm – 6:30pm

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HEALTH**

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# Moderator

**Andy Lee, MD**

Medical Director,  
Hawai'i Health Partners

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- Specific areas may not pertain directly to your clinical practice area and/or may not be applicable to your practice based on your existing workflows, infrastructure, software (e.g. EHR), and communications processes.

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- You have been automatically muted. You cannot unmute yourself.
- You will be able to submit questions via the Q&A section.
  - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

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- You should have completed a brief questionnaire before joining today's live webinar.

## 2. Step 2: HPH CME team will email you instructions

- Complete and submit evaluation survey that will be emailed to you within one week of the offering.
- Your CE certificate will be immediately available to you upon completion of your evaluation.
- Questions? Email [hphcontinuingeduc@hawaiiipacifichealth.org](mailto:hphcontinuingeduc@hawaiiipacifichealth.org)

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- Hawai'i Pacific Health designates this webinar activity for a maximum of 1.0 AMA PRA Category 1 Credit (s) <sup>TM</sup> for physicians. This activity is assigned 1.0 contact hour for attendance at the entire CE session.



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# Disclosures

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# Omicron – a new and rapidly spreading Variant of SARS-CoV-2

**Dr. rer. nat. Axel T. Lehrer, Associate Professor**

Department of Tropical Medicine, Medical Microbiology and Pharmacology,  
John A. Burns School of Medicine  
University of Hawai'i at Manoa  
Honolulu, Hawaii





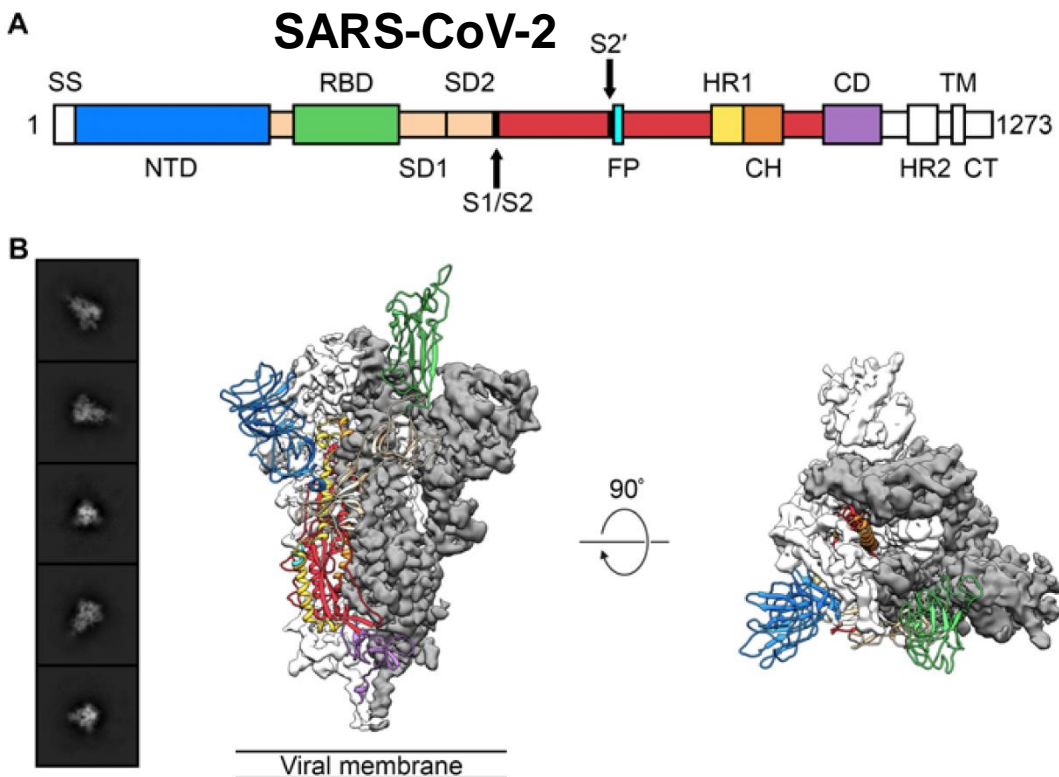


# A new variant rapidly emerges (B.1.1.529)



- First detected in South Africa in mid November 2021
- Described in an article in Nature on 25<sup>th</sup> November 2021
- Declared a variant of concern on November 26<sup>th</sup>, 2021 (WHO)
- **WHY?**
- More than 50 mutations, 30 in the spike protein





Wrapp and Wang et al. Science 2020

**Class I fusion glycoprotein on the surface of the virus responsible for to gain entry into host cells using the cell receptor human ACE2**

**The S protein is a trimeric protein that exists in a metastable prefusion**

**~180 kDa if fully glycosylated, 22 glycosylation sites**

**> Omicron carries significant modifications on the spike protein including in the furin cleavage site, NTD and may increase binding affinity to ACE2 (as seen with Delta)**

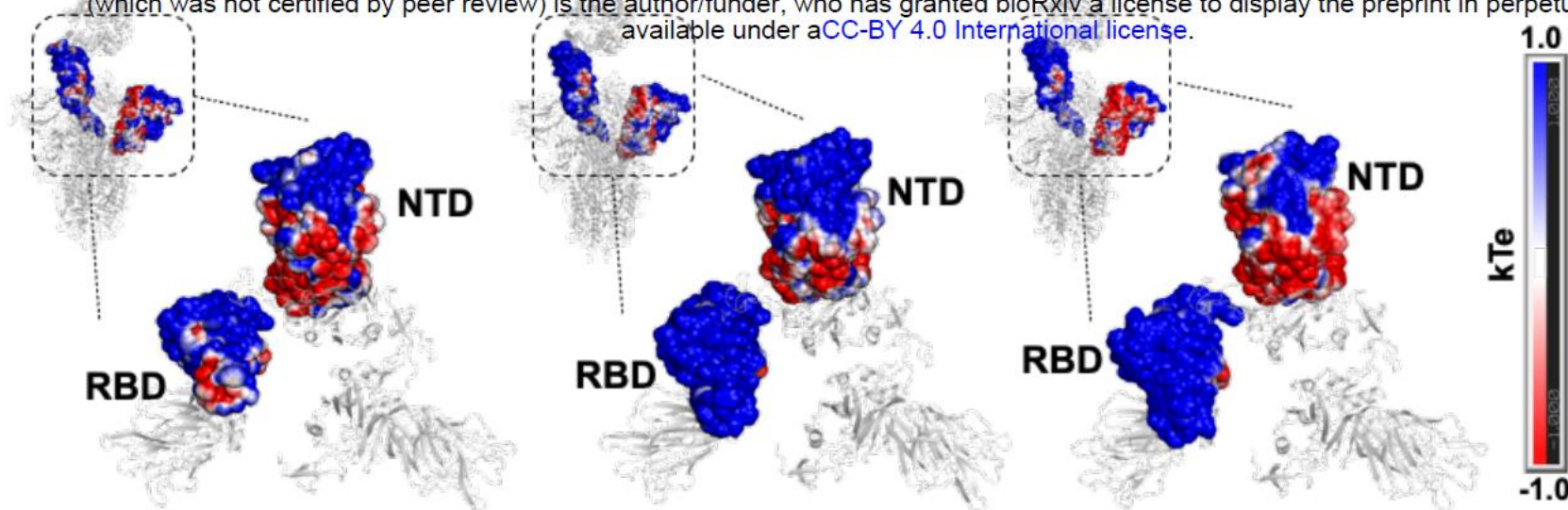




# Molecular dynamic simulation (PREPRINT)



**b.** bioRxiv preprint doi: <https://doi.org/10.1101/2021.12.17.473248>; this version posted December 22, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY 4.0 International license.

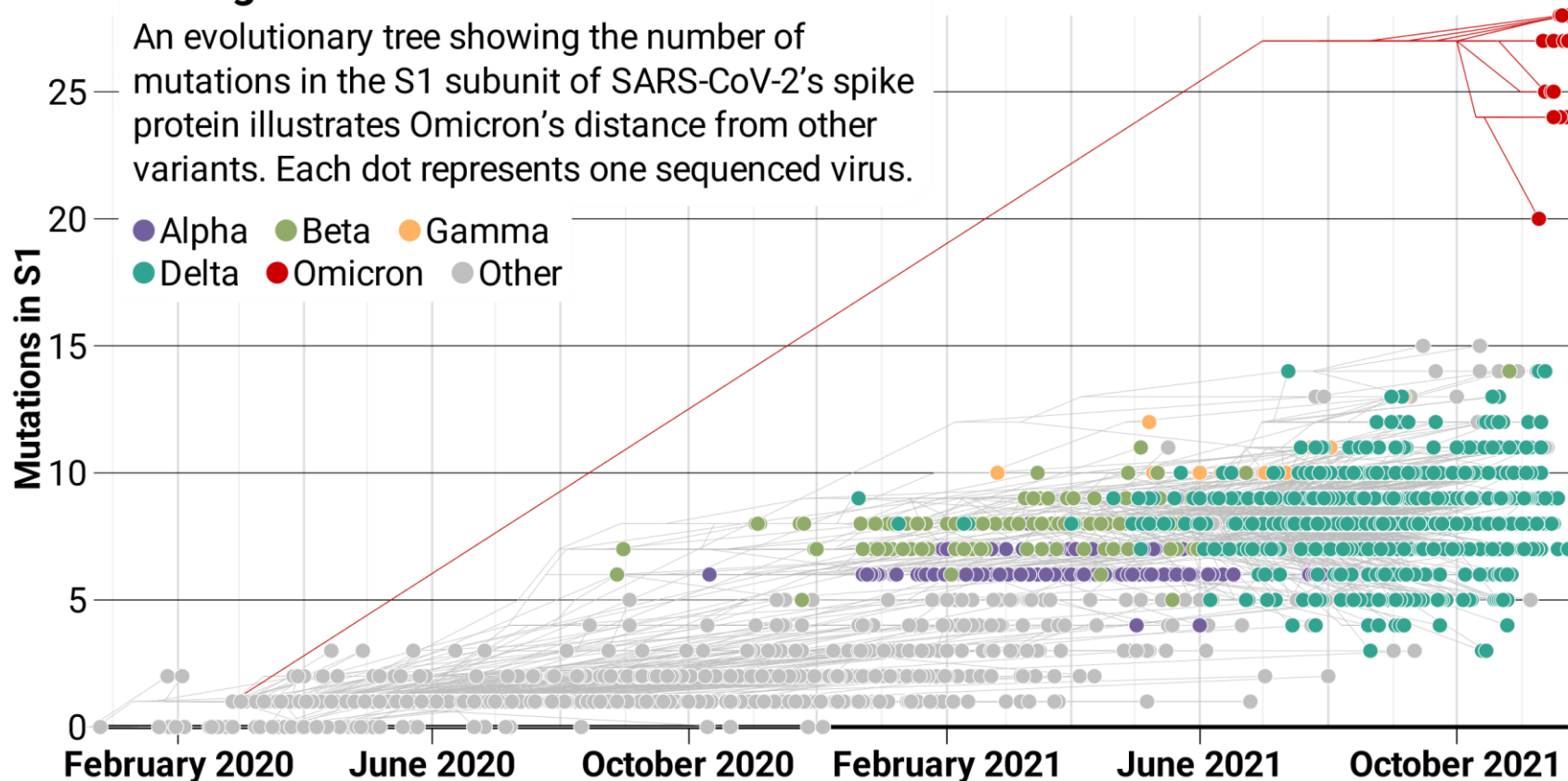




# Genetic Distance of Omicron to other Variants

## A long new branch

An evolutionary tree showing the number of mutations in the S1 subunit of SARS-CoV-2's spike protein illustrates Omicron's distance from other variants. Each dot represents one sequenced virus.



NEXTSTRAIN.ORG, ADAPTED BY N. DESAI/SCIENCE

Where did 'weird' Omicron come from? Kupferschmidt K. Science (2021); 374(6572):1179.





## OMICRON MAKES A FEEBLE ATTACK ON THE LUNGS

Animal studies suggest that the variant's inability to multiply in lung tissue could make it less dangerous.

By Max Kozlov

**E**arly indications from South Africa and the United Kingdom signal that the fast-spreading Omicron variant of the coronavirus SARS-CoV-2 is less dangerous than its predecessor Delta. Now, a series of laboratory studies offers a tantalizing explanation for the difference: Omicron does not infect cells deep in the lung as readily as it does those in the upper airways.

The observation "might explain what we see in patients", says Melanie Ott, a virologist at the Gladstone Institute of Virology in San Francisco, California. But she adds that Omicron's hyper-transmissibility means that hospitals are filling quickly – despite potential decreases in the severity of the disease it causes.

Authorities in South Africa announced on 30 December that the country had passed its Omicron peak without a major spike in deaths. And a 31 December UK government report said that people in England who were infected with Omicron were about half as likely to require hospitalization or emergency care as were those infected with Delta.

But the number of people who have gained immune protection against COVID-19 through

vaccination, infection or both has grown over time, making it difficult to determine whether Omicron intrinsically causes milder disease than do earlier variants. For answers, researchers have turned to the laboratory.

Michael Diamond, a virologist at Washington University in St. Louis, Missouri, and his colleagues infected rodents with Omicron and other variants to track disease progression. The differences were staggering: after a few days, the concentration of virus in the lungs of animals infected with Omicron was at least ten times lower than in rodents infected with other variants<sup>1</sup>. Other teams have also noted that, compared with previous variants, Omicron is found at reduced levels in lung tissue<sup>2,3</sup>.

Diamond was especially shocked to see that the Omicron-infected animals nearly maintained their body weight, whereas the others quickly lost weight – a sign that their infections were causing severe disease. The lungs are where the coronavirus does much of its damage, and lung infection can set off an inflammatory immune response that ravages both infected and uninfected cells. Fewer infected lung cells could mean milder illness.

Another group found that Omicron is much less successful than previous variants at infecting lung cells and miniature lung models called

might find it easy to hitch a ride on material expelled from the nose and mouth, allowing the virus to find new hosts, says Gupta.

The latest results could mean that "the virus establishes a very local infection in the upper airways and has less chance to go and wreak havoc in the lungs", Ott says. That would be welcome news – but a host's immune response plays an important part in disease severity, and scientists need more clinical data if they are to understand how Omicron's basic biology influences its disease progression in humans.

Omicron's course of infection could also have implications for children, says Audrey John, a specialist in paediatric infectious disease at the Children's Hospital of Philadelphia in Pennsylvania. Young children have relatively small nasal passages, and babies breathe only through their noses. Such factors can make upper respiratory conditions more serious for children than for adults, John says. But she adds that she has not seen data suggesting an uptick in the numbers of young children hospitalized for conditions that could indicate a severe infection of the upper respiratory tract.

Although there is still much to learn about the new variant, Gupta says that fears raised in late November by the multitude of mutations in Omicron's genome have not been completely borne out. He says the initial alarm offers a cautionary tale: it's difficult to predict how a virus will infect organisms from its genetic sequence alone.

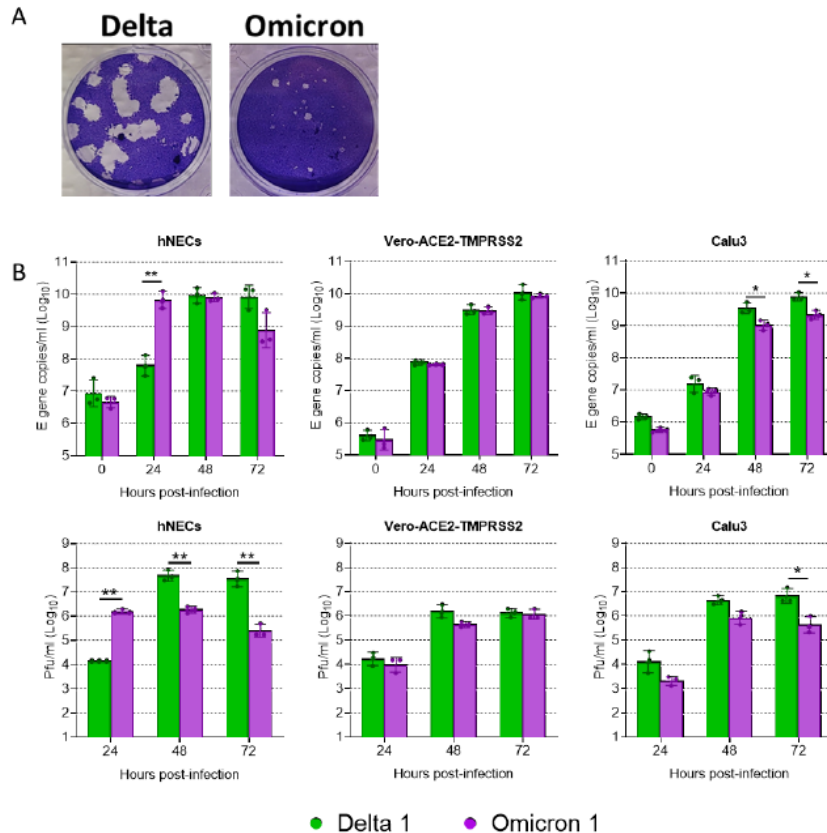
1. Diamond, M. *et al.* Preprint at Research Square <https://doi.org/10.21203/rs.3.rs-1211792/v1> (2021).
2. McMahan, K. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2022.01.02.474743> (2022).
3. Bentley, E. G. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.26.474085> (2021).
4. Meng, B. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.17.473248> (2021).
5. Peacock, T. P. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.31.474653> (2022).
6. Willett, B. J. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2022.01.03.21268111> (2022).

## All in Preprints...

1. Diamond, M. *et al.* Preprint at Research Square <https://doi.org/10.21203/rs.3.rs-1211792/v1> (2021).
2. McMahan, K. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2022.01.02.474743> (2022).
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# Viral Characteristics of Omicron



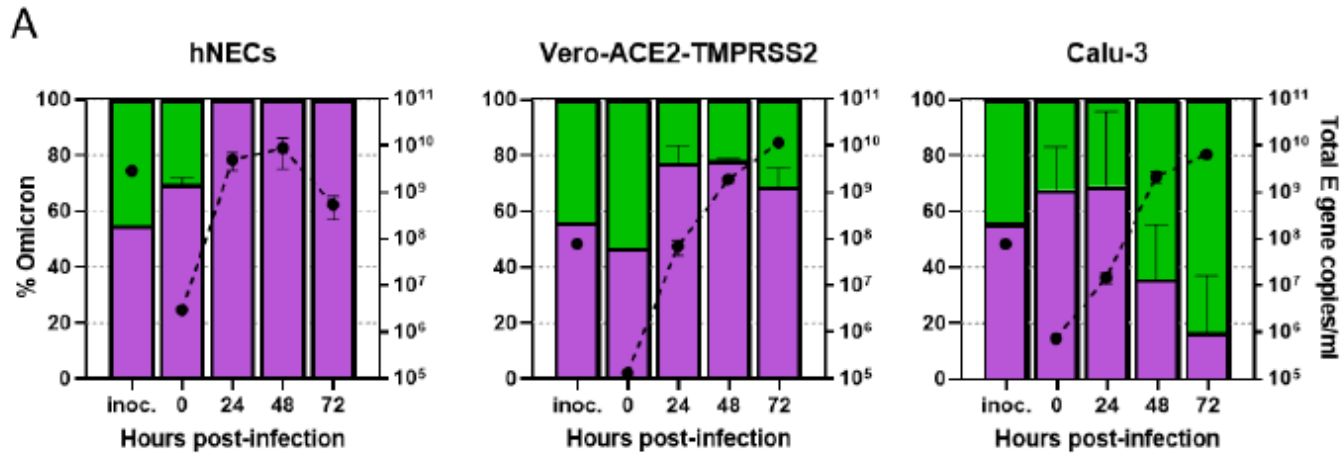
- Different plaque morphology = less induction of syncytia
- Different tissue tropism

Peacock, T. P. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.31.474653> (2022).





# Viral Characteristics of Omicron



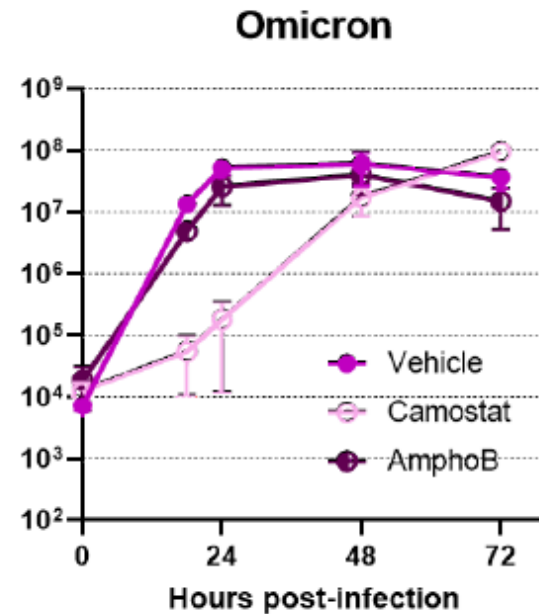
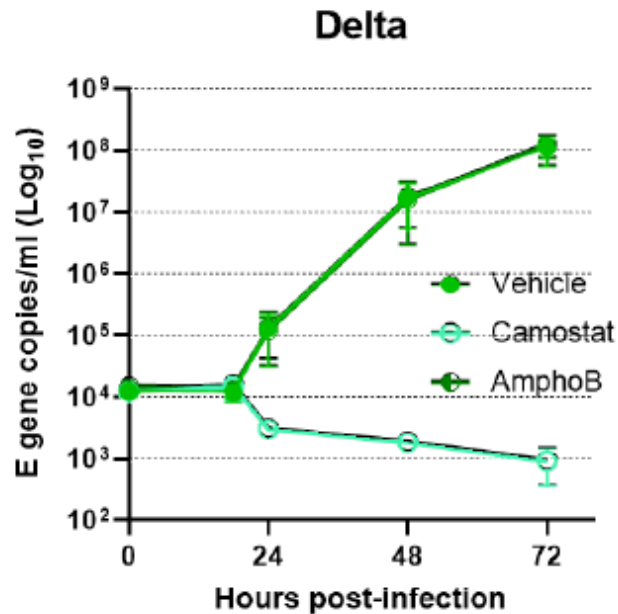
Peacock, T. P. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.31.474653> (2022).

When cultured 1:1 Delta and Omicron show different dominance in cells from upper and lower respiratory tract





# Viral Characteristics of Omicron



Delta variant is more dependent on functional proteases in the upper respiratory tract, Omicron develops Tolerance rapidly

Peacock, T. P. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.12.31.474653> (2022).



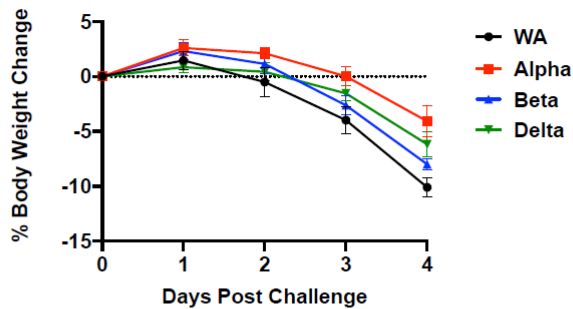




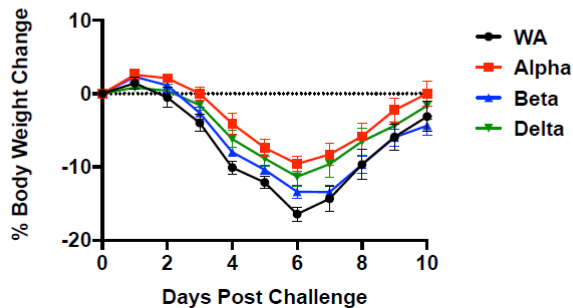
# Viral Characteristics – Pathology models



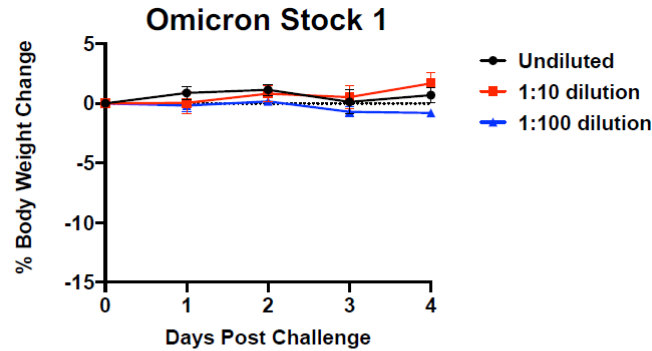
**a**



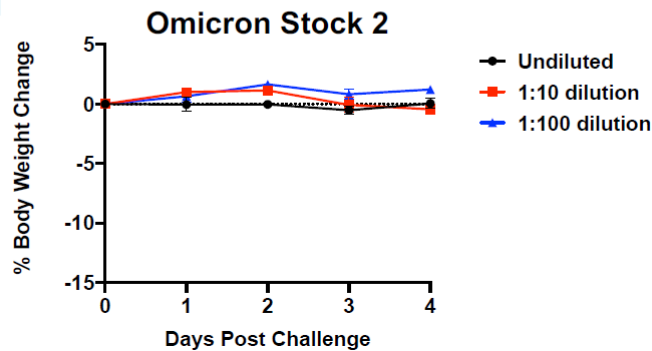
**b**



**c**



**d**



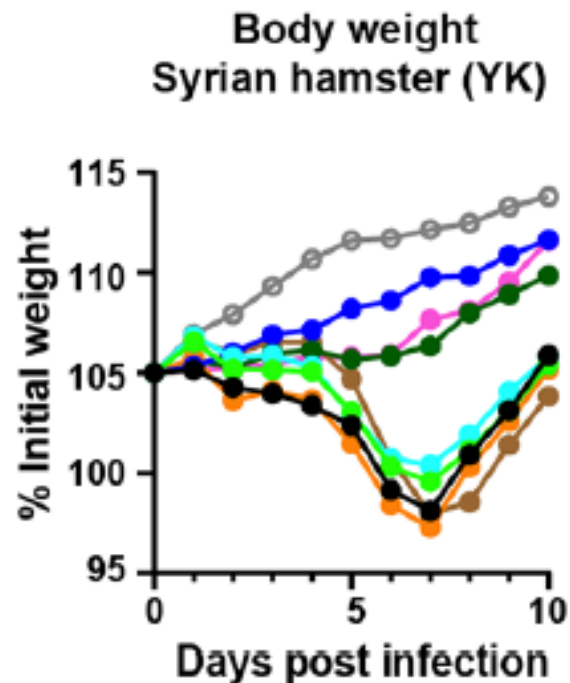
Pathology in Syrian golden hamsters is much reduced upon respiratory infection (no sign of weight loss) and is accompanied by reduced viral titers in lungs

McMahan, K. *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2022.01.02.474743> (2022).





# Viral Characteristics – Pathology models



- Mock
- 10<sup>5</sup> PFU Wuhan (NC002)
- 10<sup>5</sup> PFU Beta (HP01542)
- 10<sup>5</sup> PFU Delta (UW-5250)
- 10<sup>5</sup> PFU B.1.1.529
- 10<sup>5</sup> PFU Epsilon (VRLC009)
- 10<sup>5</sup> PFU Iota (PV26425)
- 10<sup>5</sup> PFU Mu (80384)
- 10<sup>5</sup> PFU Lambda (SEC0506)

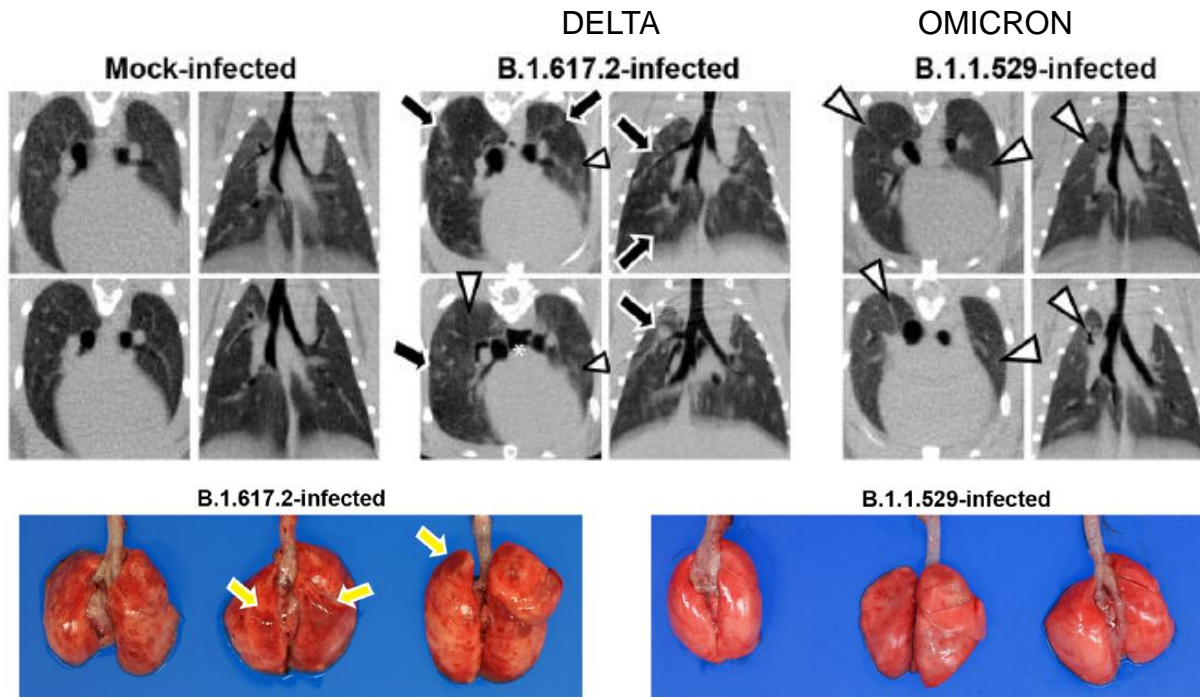
Reduced pathology is also seen in mouse models and replicated independently in a second hamster model (Michael Diamond lab)

Diamond, M. *et al.* Preprint at Research Square <https://doi.org/10.21203/rs.3.rs-1211792/v1> (2021).





# Viral Characteristics – Pathology models



Representative micro-CT axial and coronal images of the lungs of mock-infected (n = 3) or B.1.617.2- (n = 4) and B.1.1.529-infected (n = 4) hamsters on 7 dpi.

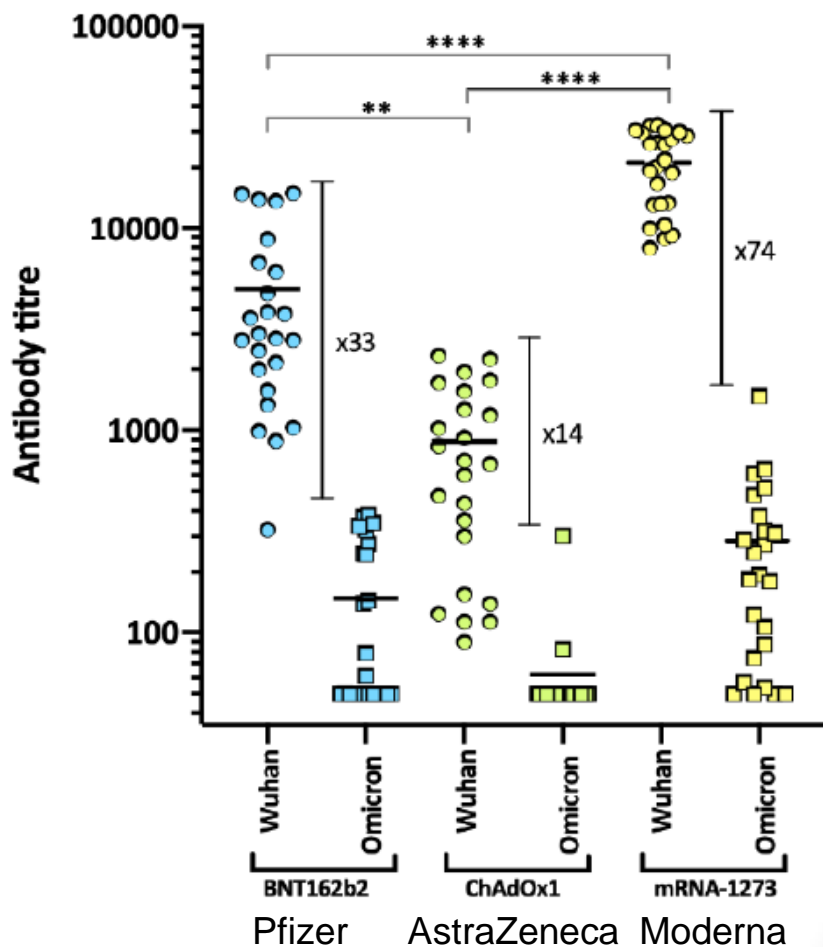
Lung abnormalities included **multifocal nodules (black arrows)**, **ground glass opacity (white arrowheads)**, and regions of lung consolidation (white arrows) that were peripheral, bilateral, and multilobar. Pneumomediastinum is indicated with white asterisks.

Diamond, M. *et al.* Preprint at Research Square <https://doi.org/10.21203/rs.3.rs-1211792/v1> (2021).





# Mutations in Omicron Spike cause reduced Neutralization



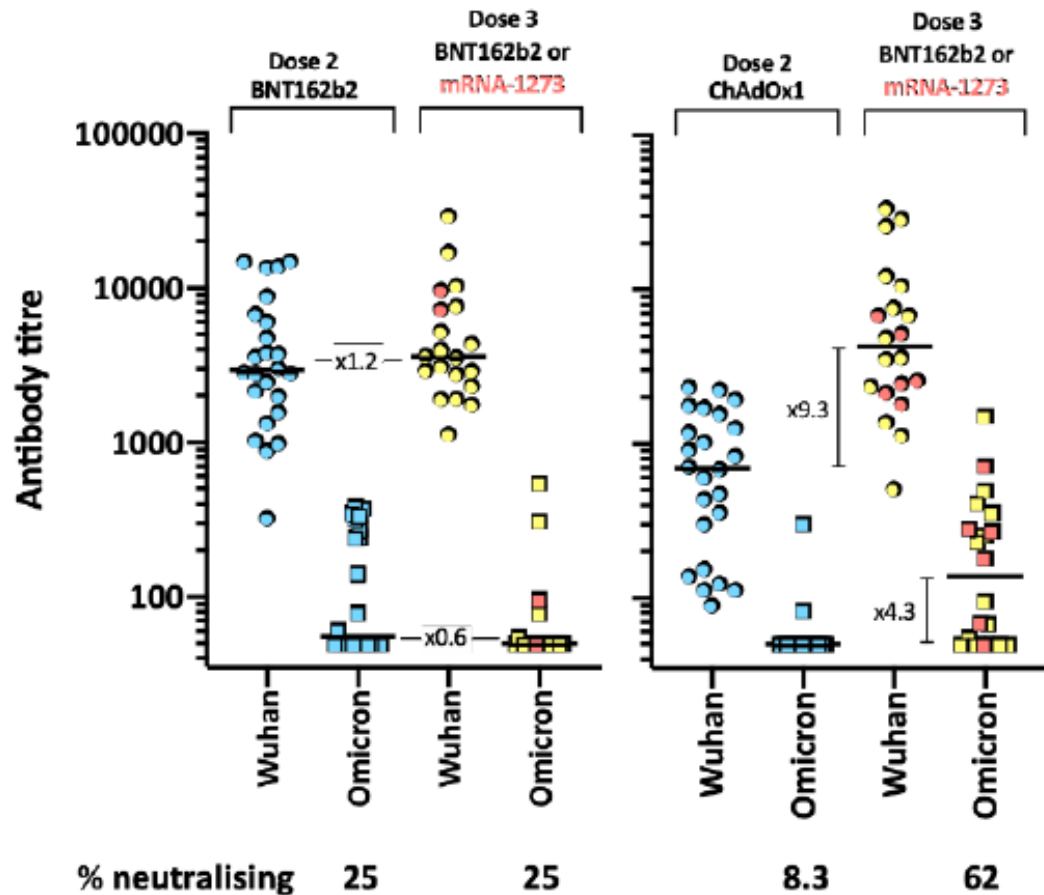
Significantly lower virus neutralization of Omicron variant is observed in vaccinees immunized with various vaccines

Willett, B. J. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2022.01.03.21268111> (2022).





# Mutations in Omicron Spike cause reduced Neutralization



mRNA as a booster increases neutralization, especially in individuals previously receiving an adenovirus-vectored vaccine

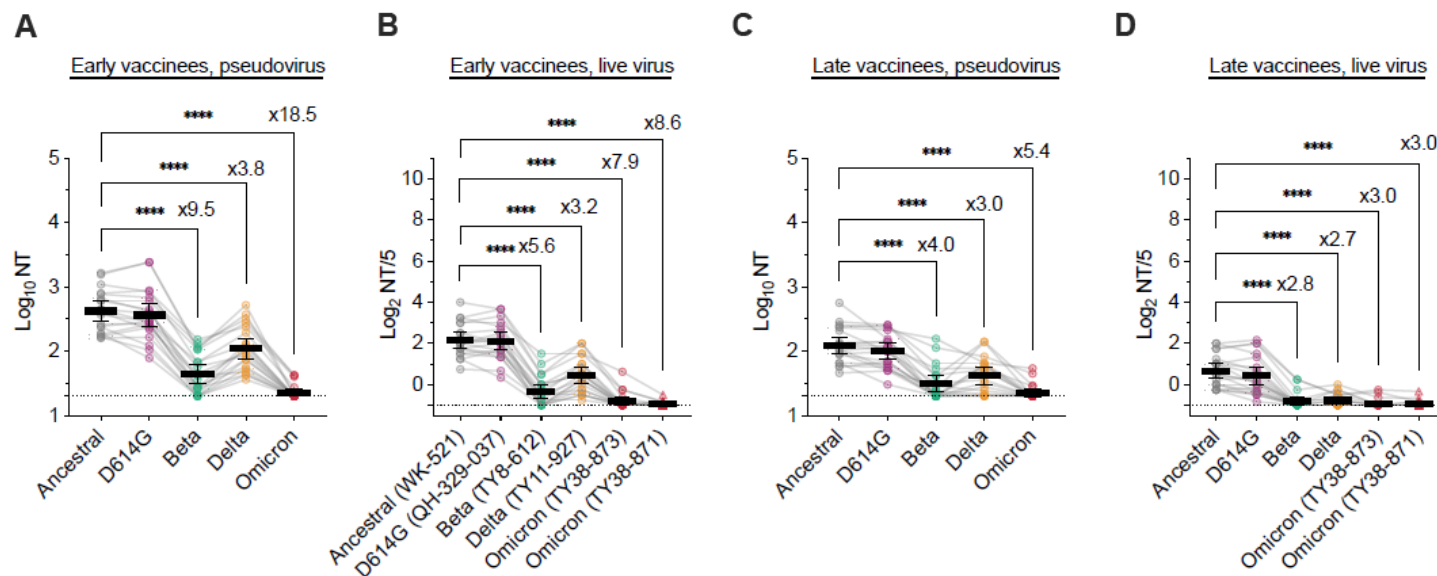
Willett, B. J. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2022.01.03.21268111> (2022).







# Temporal Aspects of Time since Vaccination



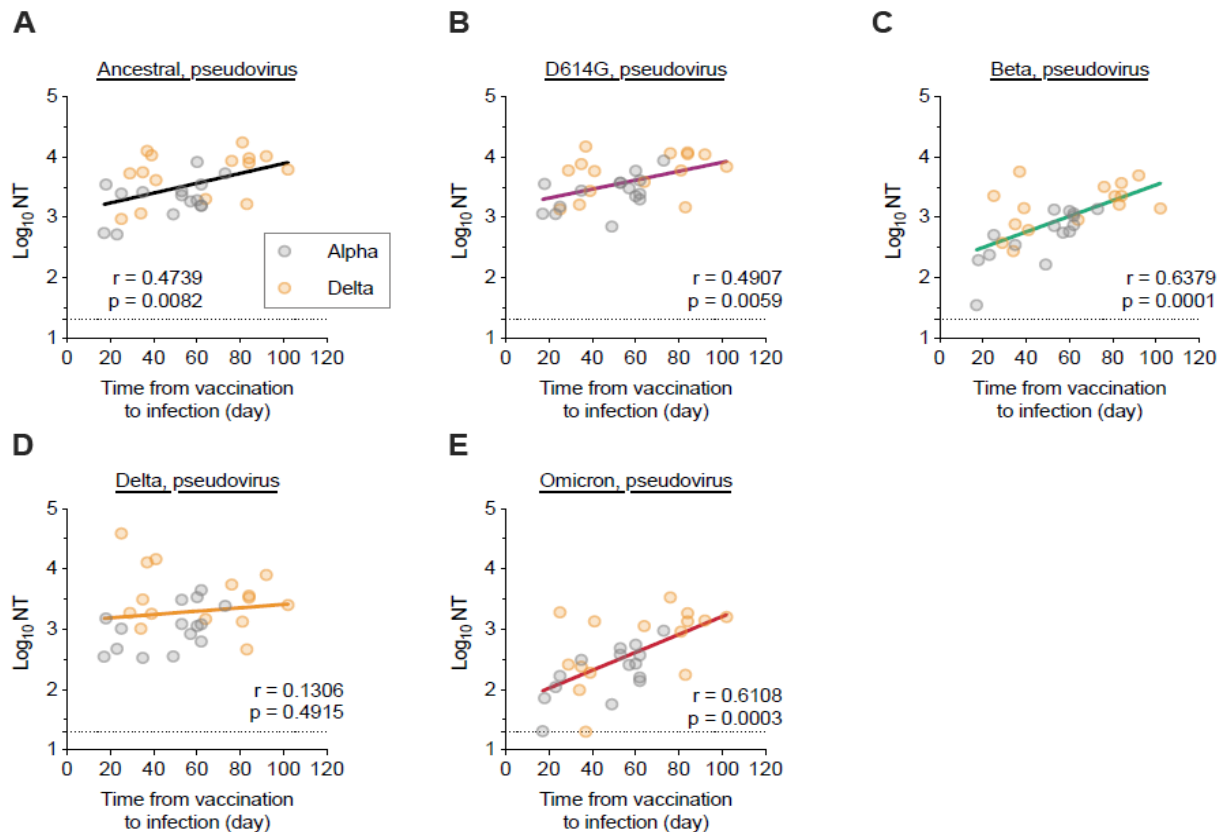
Japanese study (mRNA vaccines) – interval since vaccination matters

Miyamoto S. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2021.12.28.21268481> (2022).





# Temporal Aspects of Time since Vaccination



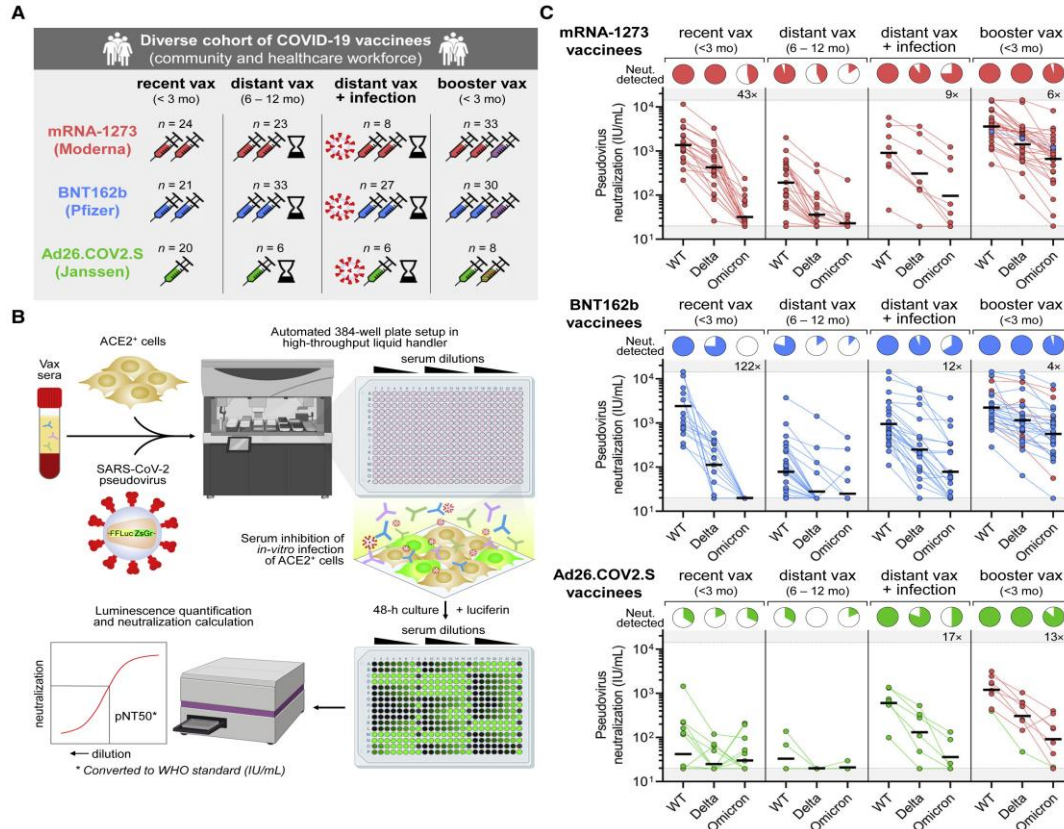
Especially titers to more distantly related Omicron variant increase over time (maturation)

Miyamoto S. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2021.12.28.21268481> (2022).





# Temporal Aspects of Boosters (homo- and heterologous)



All vaccinees show an improved response to vaccine boosters and a greater boost than subsequent COVID-19 infection

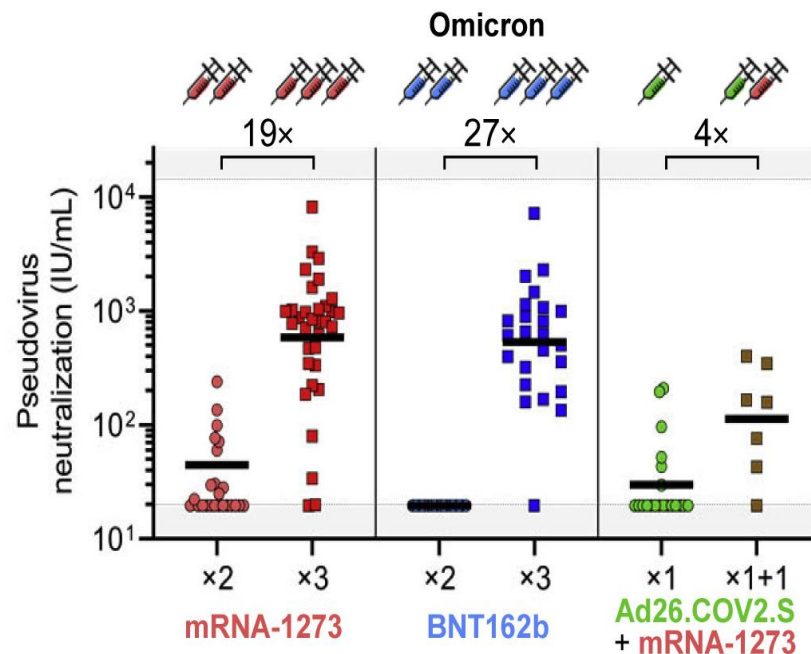
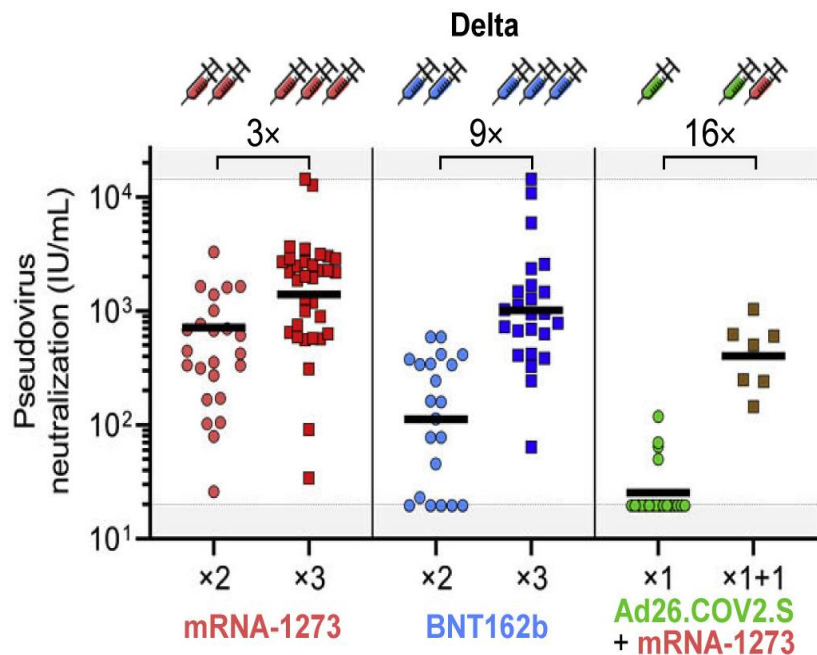
Garcia-Beltran, W.F. et al. *Cell*, in press (2022)  
DOI: 10.1016/j.cell.2021.12.033





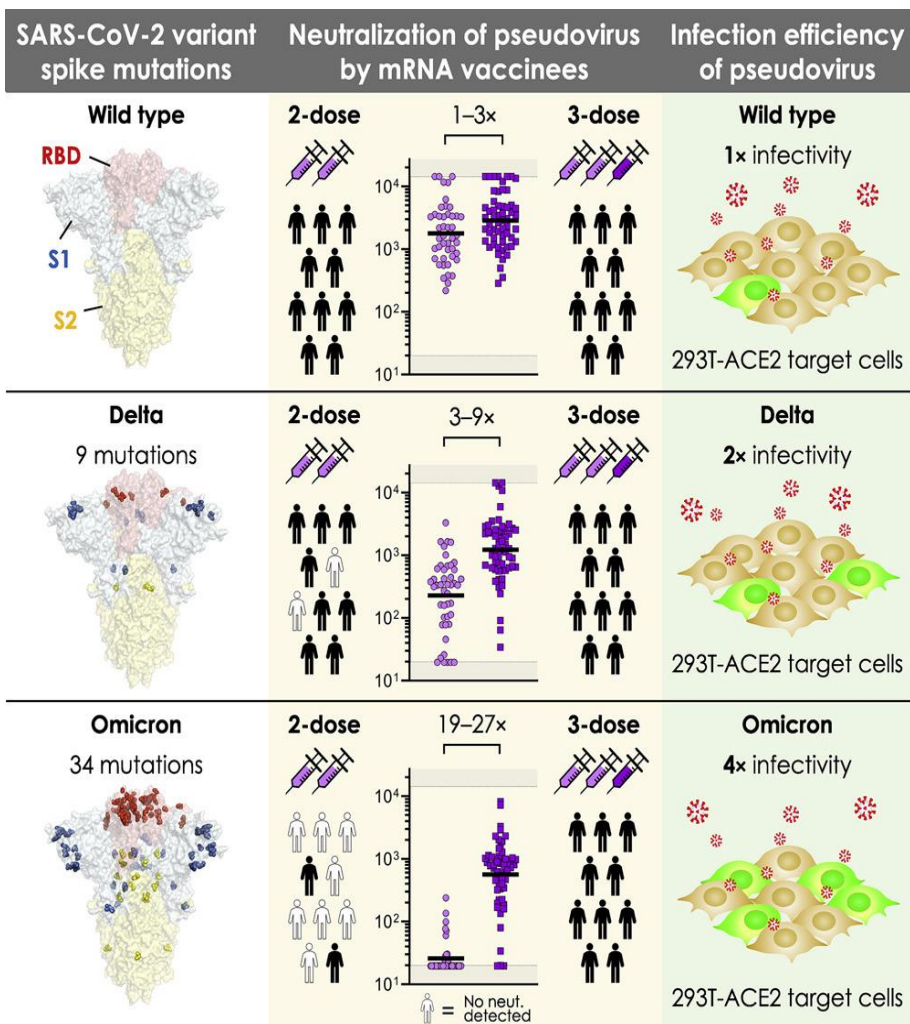


# Booster effect on Neutralization



Garcia-Beltran, W.F. et al. **Cell**, in press (2022)  
DOI: 10.1016/j.cell.2021.12.033





## mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant

Wilfredo F. Garcia-Beltran, Kerri J. St. Denis, Angelique Hoelzemer, Evan C. Lam, Adam D. Nitido, Maegan L. Sheehan, Cristhian Berrios, Onosereme Ofoman, Christina C. Chang, Blake M. Hauser, Jared Feldman, Alex L. Roederer, David J. Gregory, Mark C. Poznansky, Aaron G. Schmidt, A. John Iafrate, Vivek Naranbhai, Alejandro B. Balazs

Cell, in press (2022) DOI: 10.1016/j.cell.2021.12.033





# COVID-19 Treatment Updates

**Douglas Kwock, MD**

Vice President, Medical Staff Affairs

Hawai'i Pacific Health

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# Outpatient COVID-19 Therapeutic Options

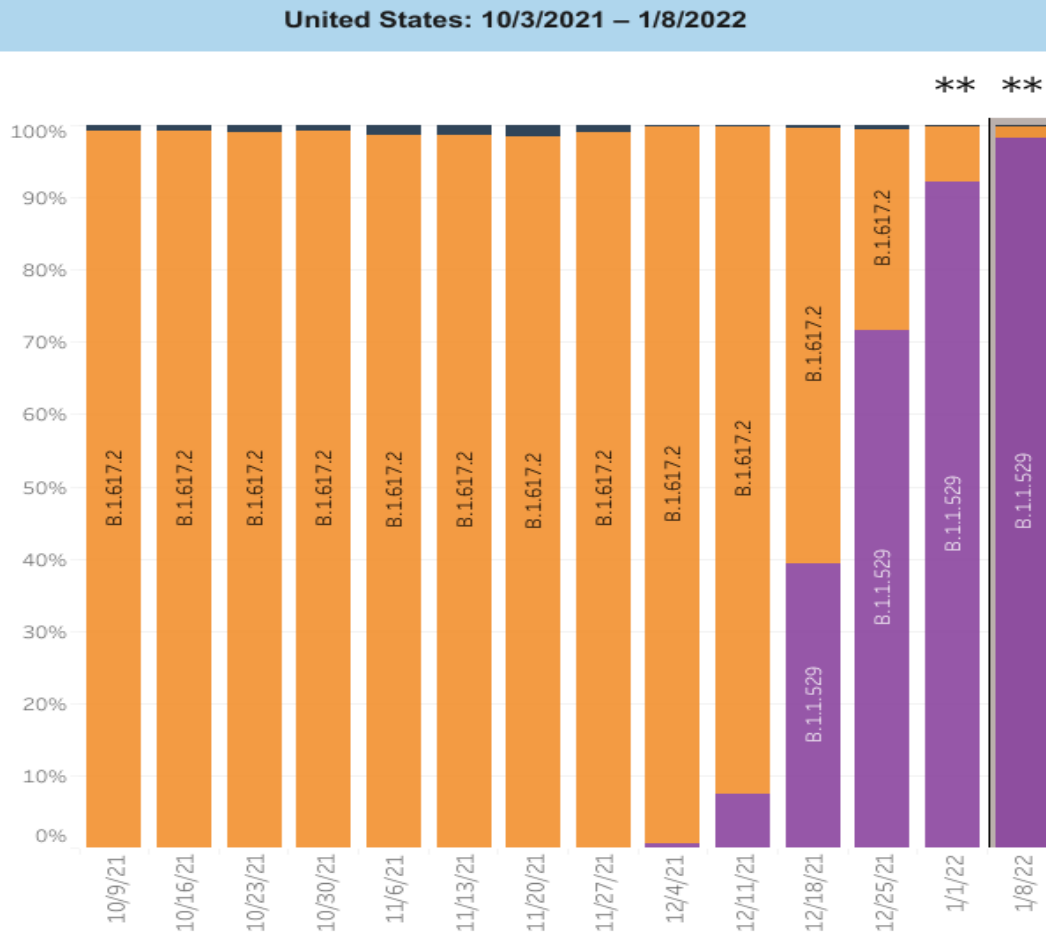
- Monoclonal antibodies
  - Sotrovimab
- Antiviral agents
  - Oral
    - Paxlovid
    - Molnupiravir
  - IV
    - Remdesivir

# Monoclonal Antibodies

- Bamlanivimab
- Bamlanivimab/Etesevimab
- Regen-CoV (Casarivimab/Imdevimab)

Omicron!

# Monoclonal Antibodies

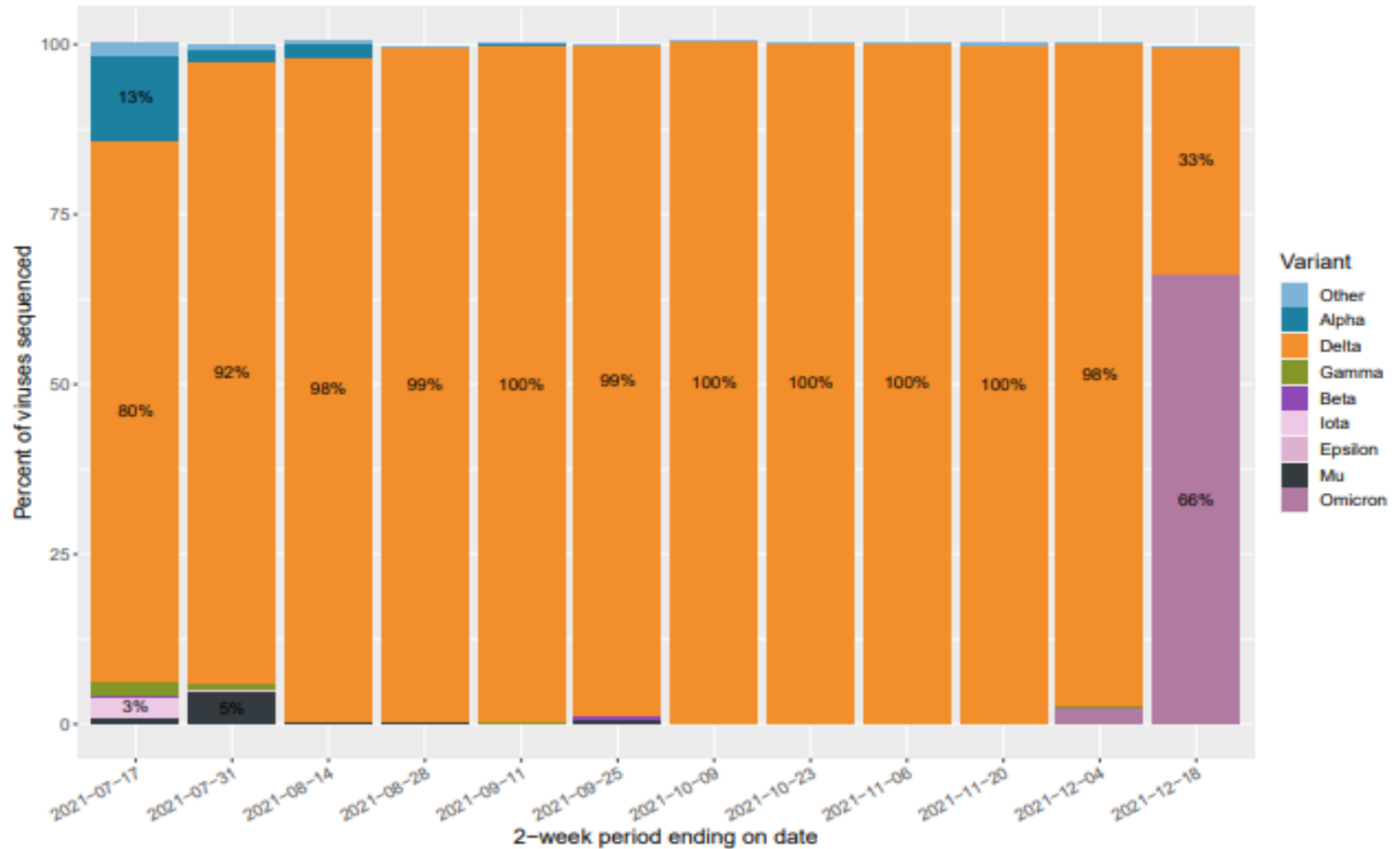


- 12/4/21: 0.6%
- 12/11/21: 7.5%
- 12/18/21: 39.4%
- 12/25/21: 71.6%
- 1/1/22: 92.3%
- 1/8/22: 98.3%

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

# Monoclonal Antibodies

Estimate of proportion of variants circulating in the State of Hawaii



State of Hawai'i sequencing and variant report for SARS-CoV-2, 2021-12-29

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# Monoclonal Antibodies

	BAM	ETE	BAM/ETE	CAS	IMD	CAS/IMD	CIL	TIX	CIL/TIX	SOT	REG
Alpha	1 <sub>13</sub>	16 <sub>11</sub>	1.2 <sub>4</sub>	1 <sub>19</sub>	0.7 <sub>19</sub>	1 <sub>8</sub>	1.0 <sub>8</sub>	1.7 <sub>7</sub>	0.8 <sub>5</sub>	2.3* <sub>15</sub>	2.6 <sub>2</sub>
Beta	>1000 <sub>15</sub>	313 <sub>13</sub>	>1000 <sub>5</sub>	76 <sub>23</sub>	0.6 <sub>22</sub>	1.3 <sub>11</sub>	1.1 <sub>7</sub>	6.3 <sub>7</sub>	1.3 <sub>5</sub>	1 <sub>14</sub>	33 <sub>3</sub>
Gamma	>1000 <sub>11</sub>	294 <sub>11</sub>	252	200 <sub>17</sub>	0.4 <sub>16</sub>	1 <sub>5</sub>	0.5 <sub>7</sub>	6.4 <sub>6</sub>	0.7 <sub>2</sub>	1.3 <sub>12</sub>	61 <sub>3</sub>
Delta	>1000 <sub>12</sub>	0.5 <sub>12</sub>	1 <sub>2</sub>	0.7 <sub>13</sub>	1.5 <sub>13</sub>	1 <sub>3</sub>	3.5 <sub>4</sub>	0.8 <sub>4</sub>	0.6 <sub>2</sub>	1.3 <sub>8</sub>	9.8 <sub>3</sub>
Omicron	>1000 <sub>12</sub>	294 <sub>11</sub>	501 <sub>4</sub>	>1000 <sub>13</sub>	500 <sub>13</sub>	>1000 <sub>6</sub>	336 <sub>12</sub>	735 <sub>12</sub>	100 <sub>7</sub>	4.9 <sub>12</sub>	>1000 <sub>5</sub>
Iota	>1000 <sub>5</sub>	1.4 <sub>5</sub>	21 <sub>2</sub>	11 <sub>4</sub>	1.2 <sub>4</sub>	1.2 <sub>2</sub>	0.9 <sub>2</sub>	8.1 <sub>2</sub>	-	0.8 <sub>4</sub>	-
Epsilon	>1000 <sub>4</sub>	1 <sub>4</sub>	10 <sub>2</sub>	1.3 <sub>2</sub>	1.7 <sub>2</sub>	1	3	-	-	0.7 <sub>3</sub>	43 <sub>4</sub>
Kappa	>1000 <sub>5</sub>	0.9 <sub>4</sub>	5.5 <sub>2</sub>	6 <sub>5</sub>	1.3 <sub>4</sub>	1 <sub>3</sub>	4.7	0.7	2	0.7 <sub>3</sub>	24
N501Y	1.1 <sub>5</sub>	3.1 <sub>8</sub>	1	1 <sub>9</sub>	0.8 <sub>9</sub>	0.8 <sub>3</sub>	1.1 <sub>5</sub>	1.3 <sub>4</sub>	1.0 <sub>2</sub>	1.7* <sub>8</sub>	5.5
E484K	>1000 <sub>4</sub>	2.9 <sub>7</sub>	24	13 <sub>13</sub>	1 <sub>13</sub>	1.9 <sub>7</sub>	1.5 <sub>4</sub>	4.6 <sub>4</sub>	3.2 <sub>2</sub>	0.4 <sub>7</sub>	8.7
K417N	0.5 <sub>4</sub>	761 <sub>9</sub>	-	7 <sub>9</sub>	0.7 <sub>9</sub>	1.3 <sub>4</sub>	0.6 <sub>5</sub>	0.4 <sub>4</sub>	0.4 <sub>2</sub>	0.6 <sub>7</sub>	-
L452R	>1000 <sub>2</sub>	1 <sub>5</sub>	5	1 <sub>5</sub>	2 <sub>6</sub>	2.5 <sub>4</sub>	-	-	-	0.6	35
T478K	1.7 <sub>2</sub>	0.8 <sub>2</sub>	-	1.9 <sub>2</sub>	1.5 <sub>2</sub>	2.6	1 <sub>2</sub>	1.5	-	1 <sub>3</sub>	1
N439K	1.3	0.4 <sub>3</sub>	-	0.8 <sub>5</sub>	28 <sub>6</sub>	1.8	-	-	-	1 <sub>3</sub>	-
Y453F	1.6 <sub>2</sub>	1.7 <sub>4</sub>	-	310 <sub>8</sub>	1.5 <sub>7</sub>	3.5	-	-	-	1.1	-
F490S	293 <sub>2</sub>	1.1 <sub>2</sub>	-	0.8 <sub>3</sub>	1.2 <sub>3</sub>	0.6 <sub>2</sub>	-	-	-	0.8 <sub>2</sub>	-
S494P	86 <sub>2</sub>	0.6 <sub>2</sub>	-	3.5 <sub>4</sub>	1.2 <sub>3</sub>	0.9	-	-	-	2 <sub>2</sub>	-

<https://covdb.stanford.edu/page/susceptibility-data/>



# Monoclonal Antibodies: Sotrovimab

- Emergency use authorization
  - Mild-to-moderate COVID-19
  - Patients  $\geq 12$  years of age and weighing  $\geq 40$ kg
  - Positive results of direct SARS-CoV-2 test
  - High risk for progression to severe COVID-19
  - Start within 10 days of symptoms onset
  - Administered IV, single dose
  - Not for:
    - Hospitalized for COVID-19
    - Require oxygen or an increase in baseline oxygen due to COVID-19

# Oral Antiviral Agents: Paxlovid & Molnupiravir

- Emergency use authorization
  - Mild-to-moderate COVID-19
  - Patients
    - Paxlovid: Patients  $\geq 12$  years of age and weighing  $\geq 40$  kg
    - Molnupiravir: Patients  $\geq 18$  years of age
  - Positive results of direct SARS-CoV-2 test
  - At high risk for progression to severe COVID-19
  - Start within 5 days of symptom onset
  - Not for:
    - Hospitalized for COVID-19
    - Pre-exposure or post-exposure prophylaxis
    - Use longer than 5 days

# Oral Antiviral Agents

Paxlovid	Molnupiravir
Pfizer	Merck
<p>Nirmatrelvir</p> <ul style="list-style-type: none"><li>• SARS-CoV-2 protease inhibitor</li><li>• 150mg tablet</li></ul> <p>Ritonavir</p> <ul style="list-style-type: none"><li>• HIV-1 protease inhibitor and CYP3A inhibitor</li><li>• 100mg tablet</li></ul>	<ul style="list-style-type: none"><li>• Nucleoside analog inhibits SARS-CoV-2 replication by viral mutagenesis</li><li>• 200mg capsules</li></ul>
88% reduction in hospitalization & death	30% reduction in hospitalization & death
Patients ≥ 12 years of age and weighing ≥ 40 kg	Patients ≥ 18 years of age
<ul style="list-style-type: none"><li>• 3 tablets (2 nirmatrelvir/1 ritonavir)</li><li>• Twice daily for 5 days</li></ul>	<ul style="list-style-type: none"><li>• 4 capsules</li><li>• Twice daily for 5 days</li></ul>

# Oral Antiviral Agents: Paxlovid

- Renal impairment
  - Mild renal (eGFR  $\geq 60$  to  $< 90$  mL/min)
    - No dosage adjustment
  - Moderate renal (eGFR  $\geq 30$  to  $< 60$  mL/min)
    - 150mg nirmatrelvir (1 tab) and 100mg ritonavir (1 tab)
    - Twice daily for 5 days
    - Prescriptions should specify the numeric dose of each active ingredient
  - Severe renal impairment (eGFR  $< 30$  mL/min)
    - NOT recommended

# Oral Antiviral Agents: Paxlovid

- Hepatic impairment
  - Mild (Child-Pugh Class A)
    - No dosage adjustment
  - Moderate (Child-Pugh Class B)
    - No dosage adjustment
  - Severe hepatic (Child-Pugh Class C)
    - NOT recommended

# Oral Antiviral Agents: Paxlovid

- Drug-Drug interactions
  - NIH Covid-19 Treatment Guidelines: Panel's Statement on Potential Drug-Drug Interactions Between ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications
    - [https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section\\_164.pdf](https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section_164.pdf)

Lots!

<p><b>Prescribe an alternative COVID-19 therapy for patients who are receiving any of the medications listed.</b></p>	<p><b>Before prescribing ritonavir-boosted nirmatrelvir (Paxlovid), determine whether the patient is receiving any of the medications listed.</b></p> <ul style="list-style-type: none"> <li>• If the patient is receiving any of these medications, withhold the medication if clinically appropriate.</li> <li>• If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.<sup>a</sup></li> </ul>
<ul style="list-style-type: none"> <li>• Amiodarone</li> <li>• Apalutamide</li> <li>• Bosentan</li> <li>• Carbamazepine</li> <li>• Cisapride</li> <li>• Clopidogrel</li> <li>• Clozapine</li> <li>• Colchicine in patients with renal and/or hepatic impairment</li> <li>• Disopyramide</li> <li>• Dofetilide</li> <li>• Dronedarone</li> <li>• Eplerenone</li> <li>• Ergot derivatives</li> <li>• Flecainide</li> <li>• Flibanserin</li> <li>• Glecaprevir/pibrentasvir</li> <li>• Ivabradine</li> <li>• Lumateperone</li> <li>• Lurasidone</li> <li>• Mexiletine</li> <li>• Phenobarbital</li> <li>• Phenytoin</li> <li>• Pimozide</li> <li>• Propafenone</li> <li>• Quinidine</li> <li>• Ranolazine</li> <li>• Rifampin</li> <li>• Rifapentine</li> <li>• Rivaroxaban</li> <li>• Sildenafil for pulmonary hypertension</li> <li>• St. John's wort</li> <li>• Tadalafil for pulmonary hypertension</li> <li>• Ticagrelor</li> <li>• Vorapaxar</li> </ul>	<ul style="list-style-type: none"> <li>• Alfuzosin</li> <li>• Alprazolam</li> <li>• Atorvastatin</li> <li>• Avanafil</li> <li>• Clonazepam</li> <li>• Codeine</li> <li>• Cyclosporine<sup>b</sup></li> <li>• Diazepam</li> <li>• Everolimus<sup>b</sup></li> <li>• Fentanyl</li> <li>• Hydrocodone</li> <li>• Lomitapide</li> <li>• Lovastatin</li> <li>• Meperidine (pethidine)</li> <li>• Midazolam (oral)</li> <li>• Oxycodone</li> <li>• Piroxicam</li> <li>• Propoxyphene</li> <li>• Rosuvastatin</li> <li>• Salmeterol</li> <li>• Sildenafil for erectile dysfunction</li> <li>• Silodosin</li> <li>• Simvastatin</li> <li>• Sirolimus<sup>b</sup></li> <li>• Suvorexant</li> <li>• Tacrolimus<sup>b</sup></li> <li>• Tadalafil for erectile dysfunction</li> <li>• Tamsulosin</li> <li>• Tramadol</li> <li>• Triazolam</li> <li>• Vardenafil</li> </ul>

# Oral Antiviral Agents: Molnupiravir

- May cause fetal harm
  - Pregnancy
    - NOT recommended
  - Childbearing potential
    - Effective contraception during treatment and for 4 days after the final dose
- May affect bone and cartilage growth
  - NOT for use in < 18 years of age



# IV Antiviral Agents: Remdesivir

- Approved on 10/22/2020
  - Patients  $\geq 12$  years of age and weighing  $\geq 40$  kg
  - Requiring hospitalization
- NIH recommendation
  - Off-label use for outpatient treatment
  - Start within 7 days of symptom onset
  - 200mg IV on day 1, 100mg IV on day 2 and 3

# Outpatient Treatment of COVID-19

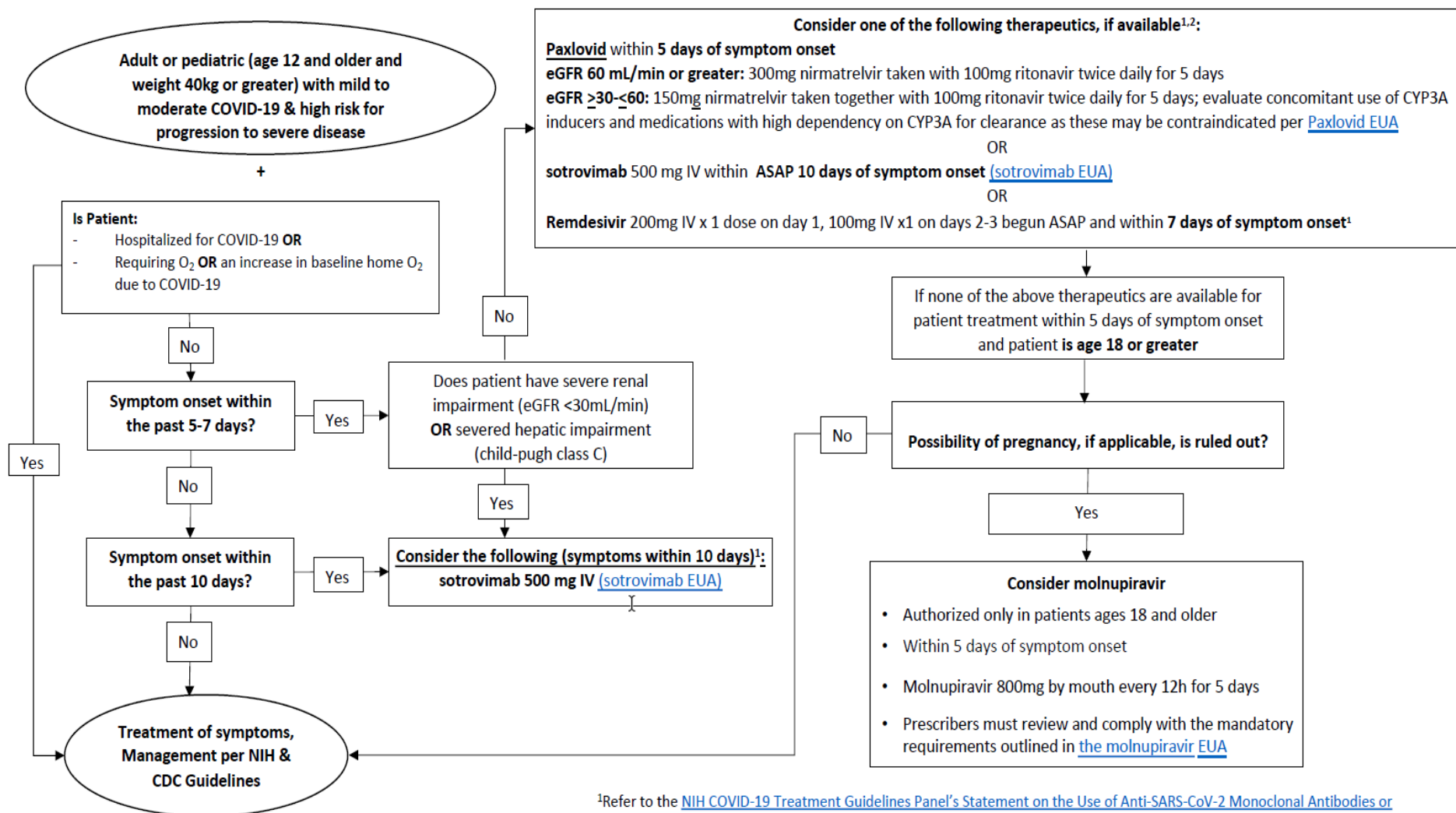
INTERIM  
Clinical Guidance on Therapeutics for  
Outpatient Treatment of COVID-19  
(updated January 7, 2022)



1

In order of preference

1. Paxlovid
2. Sotrovimab
3. Remdesivir
4. Molnupiravir



**Limited use of bamlanivimab/etesevimab and REGEN-COV as they are not expected to be active against the Omicron variant<sup>1</sup>**

<sup>1</sup>Refer to the [NIH COVID-19 Treatment Guidelines Panel's Statement on the Use of Anti-SARS-CoV-2 Monoclonal Antibodies or Remdesivir for the Treatment of Covid-19 in Nonhospitalized patients when Omicron is the Predominant Circulating Variant](#); Remdesivir is only approved for hospitalized individuals with COVID-19. Outpatient treatment is based on information from the literature ([Dec 22, 2021 Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients](#); DOI: 10.1056/NEJMoa2116846)

<sup>2</sup> COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies is authorized for the treatment of COVID-19 in patients with immunosuppressive disease in either the outpatient or inpatient setting ([COVID-19 Convalescent Plasma EUA](#))

# Outpatient Treatment of COVID-19

Tier	Risk Group
1	<ul style="list-style-type: none"><li>Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); or</li><li>Unvaccinated individuals at the highest risk of severe disease (anyone aged <math>\geq 75</math> years or anyone aged <math>\geq 65</math> years with additional risk factors).</li></ul>
2	<ul style="list-style-type: none"><li>Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> years with clinical risk factors)</li></ul>
3	<ul style="list-style-type: none"><li>Vaccinated individuals at high risk of severe disease (anyone aged <math>\geq 75</math> years or anyone aged <math>\geq 65</math> years with clinical risk factors)</li></ul> <p><b>Note:</b> Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.</p>
4	<ul style="list-style-type: none"><li>Vaccinated individuals at risk of severe disease (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> with clinical risk factors)</li></ul> <p><b>Note:</b> Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.</p>

**INTERIM**  
**Clinical Guidance on Therapeutics for**  
**Outpatient Treatment of COVID-19**  
(updated January 7, 2022)



1

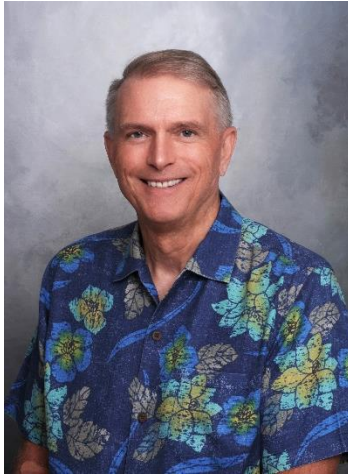
# Pre-Exposure Prophylaxis

- Evusheld
  - Monoclonal antibodies: Tixagevimab & Cilgavimab
  - Pre-exposure prophylaxis of COVID-19
    - Not currently infected with SARS-CoV-2
    - Have not had a known recent exposure
  - Patients  $\geq 12$  years of age and weighing  $\geq 40$  kg
  - Patients
    - Moderate to severe immune compromise and may not mount an adequate immune response to COVID-19 vaccination OR
    - Vaccination with any available COVID-19 vaccine is not recommended
  - Pre-exposure prophylaxis with Evusheld is NOT a substitute for vaccination

# Outpatient Treatment of COVID-19

- Resources will be uploaded to intranet and HHP website (COVID-19 Therapeutics folder)
  - EUAs
  - INTERIM Clinical Guidance on Therapeutics for Outpatient Treatment of COVID-19
  - Updated HPH COVID-19 Treatment Protocol

# HPH Facility Capacity & Cases



**David Underriner**

Executive Vice President of Oahu Operations  
Chief Executive Officer of Kapiolani Medical  
Center for Women & Children, Pali Momi  
Medical Center and Straub Medical Center,  
Hawaii Pacific Health



**Jen H. Chahanovich**

President & Chief Executive Officer  
of Wilcox Medical Center  
Chief Executive Officer of Kauai  
Medical Clinic

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# Monoclonal Antibodies (MOAB) and Respiratory Evaluation Clinic (REC)



## **Sandra Noon, DO**

*Primary Care Physician – Internal Medicine,*  
Mililani Family Health Center

*Chief of Primary Care*  
Hawai'i Pacific Health Medical Group

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# HPH Respiratory Evaluation Clinics

- **For COVID-19 Evaluation**
  - Patients who need in-person evaluation for COVID-19 symptoms, illness, etc.
  - Not to be used as a site for COVID-19 testing, unless your patient is at high risk of progressing to severe disease.
- **Straub Respiratory Evaluation Clinic**
  - Monday-Friday, 8:30 a.m.-4 p.m.
  - 826 S. King St., 2nd floor
  - 808-462-5100
- **Kaua'i Medical Clinic Respiratory Evaluation Clinic**
  - Monday-Friday, 8:30 a.m. to 4:30 p.m.
  - 3-3420 Kuhio Highway, Suite B
  - (Pediatric Isolation Room located between Wilcox Medical Center and Kaua'i Medical Clinic)
  - Lihu'e, HI 96766
  - 808-245-1504 or walk-in
- **HPH COVID-19 Virtual Clinic for Video and Phone Visits**
  - The HPH COVID-19 Virtual Clinic can be reached by calling 808-462-5430 (press option 3).
  - The hours of operation are 8 a.m. to 8 p.m. daily.

# Pediatric Options to Treat Patients with or Suspected to have COVID-19

- **Kapiʻolani Pediatric Outpatient Clinic**
  - HPH Medical Group pediatricians will see patients, newborns up to age 18, with viral symptoms when their PCP determines that an in-person visit is required. Hours of operation are Monday-Friday, 1:30 p.m.-5 p.m. This is located on the 3<sup>rd</sup> floor of the Diamond Head Tower in the Multidisciplinary Clinic. Providers with pediatric patient referrals should call 808-763-2888 to make an appointment. Please note, this clinic is not for testing only. COVID-19 testing should continue to be scheduled through the testing centers.
- **Kapiʻolani Pediatric After-Hours Clinic**
  - The Pediatric After-Hours Clinic at Kapiʻolani is open for in-person appointments, virtual appointments or walk-ins. Hours of operation are Monday-Friday, 5-8 p.m.; and Saturday-Sunday, Noon-7 p.m. It is located on the 1<sup>st</sup> floor in the Pediatric Outpatient Clinic. Children experiencing fever and respiratory symptoms (cough or difficulty breathing) or concerns associated with COVID-19 can walk-in with no appointment necessary to be seen by one of our pediatric health care professionals.
- For more information, or to schedule an appointment with either the Pediatric Outpatient Clinic or the Pediatric After-Hours Clinic, call 808-763-2888 from 8 a.m.-8 p.m.

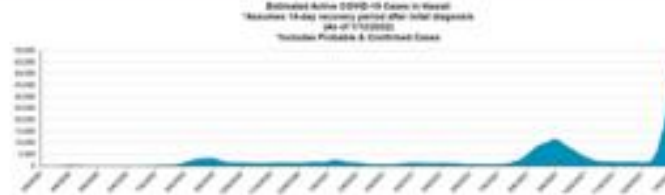
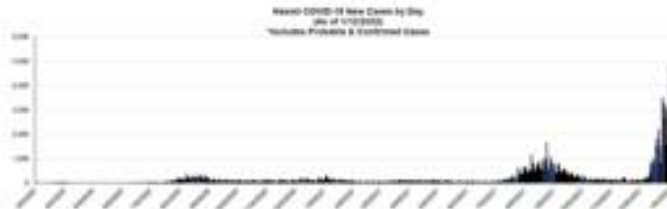
# Monoclonal Antibody (MoAb) - Sotrovimab

- HPH receives limited doses of the monoclonal antibody, sotrovimab, which is approved via EUA for treatment of active, mild/moderate COVID-19 infection (including the omicron variant).
- Priority is given to **Tier 1 and 2 Patients** (e.g. immunocompromised patients,  $\geq 75$ , or  $\geq 65$  with clinical risk factors). Patients should be 12 years or older and weigh at least 40kg. Patients who are hospitalized **OR** requiring oxygen therapy due to COVID-19 are *ineligible* to receive sotrovimab.
- Administration should be completed as soon as possible following a positive PCR/NAAT COVID-19 test **and** within 10 days of symptom onset.
- If your patient is experiencing mild/moderate COVID-19 symptoms **and** meets the criteria, please discuss the risks and benefits of sotrovimab therapy with your patient and document the discussion in patient's record.
- To place a referral:
  - From outside HHP, send an email to Dr. Sandra Noon ([sandra.noon@hphmg.org](mailto:sandra.noon@hphmg.org)) with the subject: **Sotrovimab Administration Request**.
  - From within HHP, please place a MoAb Treatment Request from the HHP intranet home page
- Please inform patients Sotrovimab is in limited supply and that we cannot guarantee they will receive it.

# Referrals for MoAb

HPH/HPH Community Webinar Series (CME ... 8/26/2021 12:00 PM  
& QPP/SSP Credit)

## COVID-19 UPDATES/ MEMOS



### COVID-19 Vaccination Requirement:

- Employee COVID Vaccine Policy November 2021
- COVID-19 Vaccine Requirement FAQs November 2021
- Testing Protocol October 2021
- COVID Vaccination and Testing Requirements Flowchart October 2021

### FAQs:

- COVID-19 Vaccine FAQs
- COVID-19 Vaccine FAQs for Managers
- COVID Convalescent Plasma (CCP) August 10, 2020
- Employee Health Reminders
- FAQs for HPH Employees
- FAQs for HPH Manager
- FAQs for Employees Working from Home
- FAQs – Patient Privacy Related to COVID-19
- HPH Travel Protocol Effective 10/20/21
- Return to Work January 7, 2022
- Working Together - Microsoft Teams and Q365

### Self-Care

### Leadership Resources

### For Patients:

- Multilingual Resources (scroll down in this DOH site for handouts)
- Stay Healthy And Informed With HPH
- What to do after you are tested for COVID-19

### COVID-19 Response Plan

### COVID-19 VACCINE – Patient Information for Providers and Employees:

### COVID-19 Testing/Vaccination Appointment Self-Scheduler

### Latest HPH COVID-19 Bulletins & Information (previous Bulletin is archived)

- MoAb Treatment Request
- Epic Infection/Isolation Banner and MyChart Home Monitoring Tip Sheet August 23, 2021
- DOH COVID-19 Update #20 – Quarantine Guidance for Vaccinated Persons Following Exposure Feb 11, 2021
- Bulletin #436 January 12, 2022
  - CLH COVID-19 Technical Bulletin – Molecular Revision May 19, 2020
  - Visitor Policy Update and Guidelines on Masks October 15, 2021
- COVID-19 Hawaii Cases January 12, 2022
- Beyond COVID-19: Concept Model & Indicators May 18, 2020
- Beyond COVID-19: Reopening Status Update
- HPH Surge Plan: KMCWC, PMMC, SMC, WMC

### Clinical/Workflow Algorithms and Specimen Collection:

- COVID-19 Algorithms:
- Specimen Collection:
- Ambulatory COVID Monitoring Program:
- Isolation Code Blue Process:

### Airway Management:

### Instrument/Medical Device Inspection Resources:

### PPE Guidelines:

### PPE Donning and Doffing:

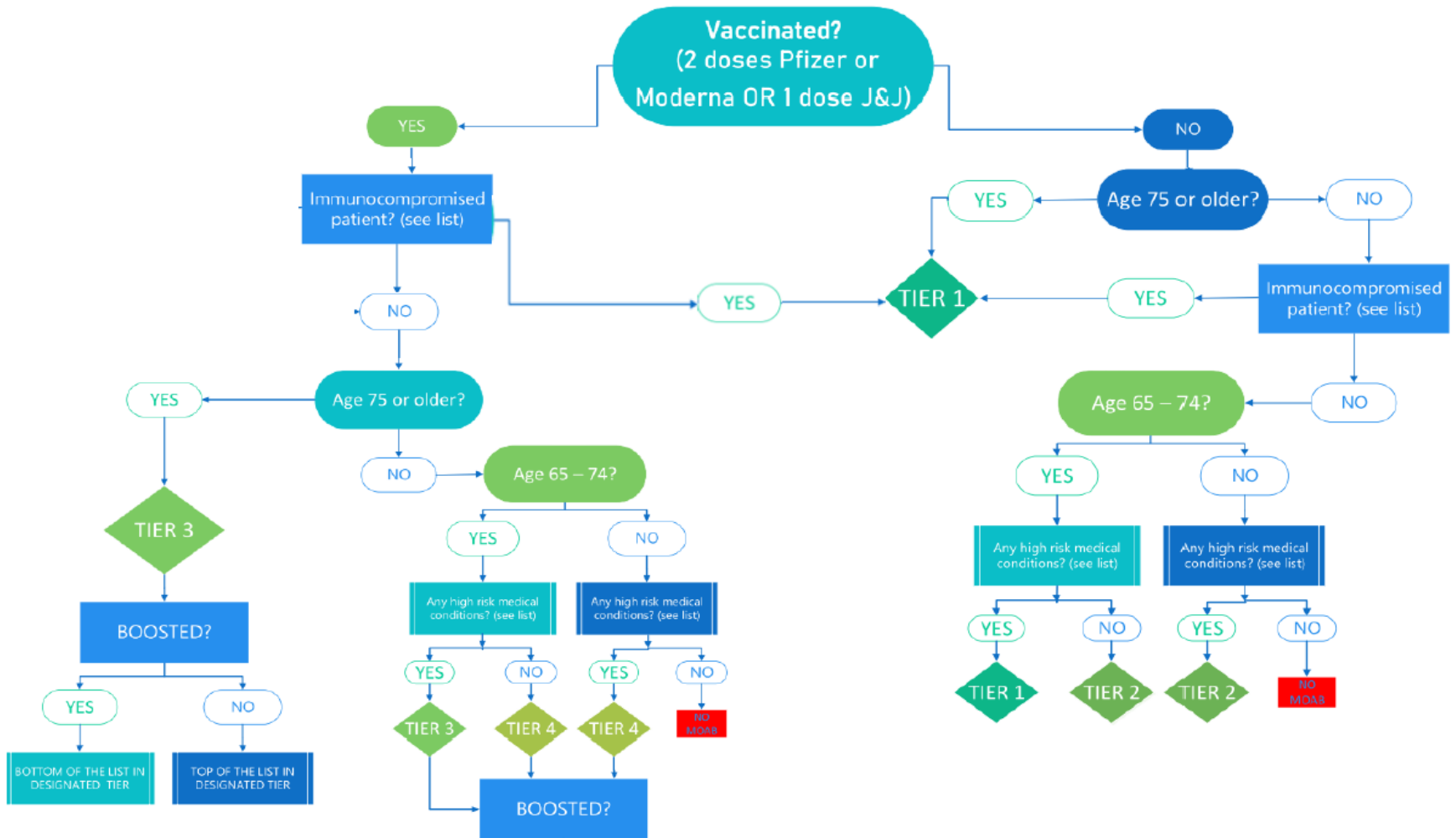
### PPE & Medical Equipment Cleaning and Conservation:

### COVID-19 Therapeutics (HPH):

### COVID-19 Inpatient Vaccination Resources:

### Advance Care Planning Scripting:

# Covid Treatment Tier Algorithm



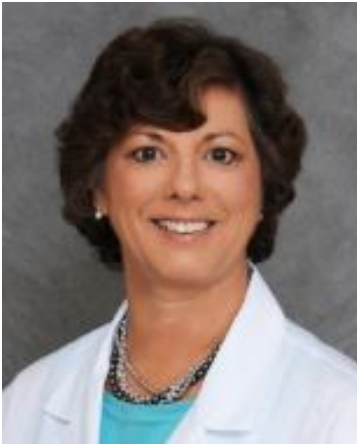
# Outpatient COVID-19 Treatment:

## Patient Risk Stratification - Criteria

- **Immunocompromised individuals**
  - Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
  - Patients receiving Bruton tyrosine kinase inhibitors
  - Chimeric antigen receptor T cell recipients
  - Post-hematopoietic cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
  - Patients with hematologic malignancies who are on active therapy
  - Lung transplant recipients
  - Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
  - Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
  - Patients with severe combined immunodeficiencies
  - Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm<sup>3</sup>
- **Medical conditions for high risk progression to severe COVID-19**
  - Adults with BMI >25 kg/m<sup>2</sup>, or if 12 to 17 years of age, have BMI ≥85th percentile for their age and gender based on CDC growth charts, [https://www.cdc.gov/growthcharts/clinical\\_charts.html](https://www.cdc.gov/growthcharts/clinical_charts.html))
  - Pregnancy
  - Chronic kidney disease III or higher
  - Diabetes
  - Cardiovascular disease (including congenital heart disease) or hypertension
  - Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
  - Sickle cell disease
  - Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
  - Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID 19])



# HPH Policies and Updates



**Melinda Ashton, MD**  
Executive Vice President and  
Chief Quality Officer  
Hawai'i Pacific Health



**Shilpa Patel, MD**  
Associate Chief Quality Office  
Hawai'i Pacific Health

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## Work Restrictions for HCP With SARS-CoV-2 Infection and Exposures

HCP are considered “boosted” if they have received all COVID-19 vaccine doses, including a booster dose, as recommended by CDC. HCP are considered “vaccinated” or “unvaccinated” if they have NOT received all COVID-19 vaccine doses, including a booster dose, as recommended by CDC.

For more details, including recommendations for healthcare personnel who are immunocompromised, refer to Interim Guidance for Managing Healthcare Personnel with SARS-CoV-2 Infection or Exposure to SARS-CoV-2 (conventional standards) and Strategies to Mitigate Healthcare Personnel Staffing Shortages (contingency and crisis standards).

### Work Restrictions for HCP With SARS-CoV-2 Infection

Vaccination Status	Conventional	Contingency	Crisis
Boosted, Vaccinated, or Unvaccinated	10 days OR 7 days with negative test <sup>†</sup> , if asymptomatic or mildly symptomatic (with improving symptoms)	5 days with/without negative test, if asymptomatic or mildly symptomatic (with improving symptoms)	No work restriction, with prioritization considerations (e.g., asymptomatic or mildly symptomatic)

### Work Restrictions for Asymptomatic HCP with Exposures

Vaccination Status	Conventional	Contingency	Crisis
Boosted	No work restrictions, with negative test on days 2 <sup>‡</sup> and 5–7	No work restrictions	No work restrictions
Vaccinated or Unvaccinated, even if within 90 days of prior infection	10 days OR 7 days with negative test	No work restriction with negative tests on days 1 <sup>‡</sup> , 2, 3, & 5–7	No work restrictions (test if possible)

<sup>†</sup>Negative test result within 48 hours before returning to work

<sup>‡</sup>For calculating day of test: 1) for those with infection consider day of symptom onset (or first positive test if asymptomatic) as day 0; 2) for those with exposure consider day of exposure as day 0



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[cdc.gov/coronavirus](https://cdc.gov/coronavirus)

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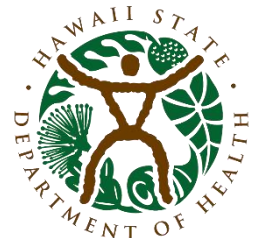
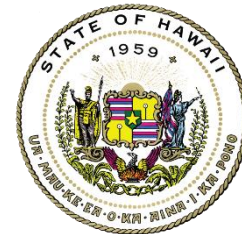


# Q&A

**Sarah Kemble, MD**

*State Epidemiologist,*

Hawai'i State Department of Health



# Q&A

CREATING A HEALTHIER HAWAI'I

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# Thank you!

- A recording of the meeting will be available afterwards.
- Unanswered question?
  - Contact us at [Covid19Bulletin@hawaiiipacifichealth.org](mailto:Covid19Bulletin@hawaiiipacifichealth.org)