Children's National and the Pediatric Health Network

Anti-Virals and Monoclonal Antibodies Treatments for COVID-19

January 20, 2022

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Introduction and Welcome

Ellie Hamburger, MD
Medical Director
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Notes About Today's Town Hall:

- All lines are muted throughout the presentation.
- Please use the Q&A to ask questions or make comments.
- We will be recording the session.
- Today's recordings and materials will be posted to the Children's National website and the Pediatric Health Network website following the presentation.
  --ChildrensNational.org
  --PediatricHealthNetwork.org

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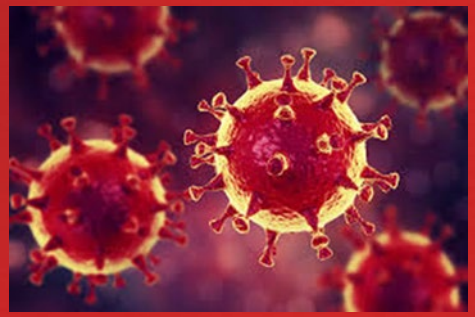
PLEASE NOTE
We've moved a few books around.
Travel is now in the Fantasy section, Sci-fi in current affairs and Epidemiology is in self help.

COVID Situation Update
January 18, 2021



Roberta L. DeBiasi, MD, MS

Chief, Division of Pediatric Infectious Diseases
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Professor of Pediatrics and Microbiology, Immunology and Tropical Medicine
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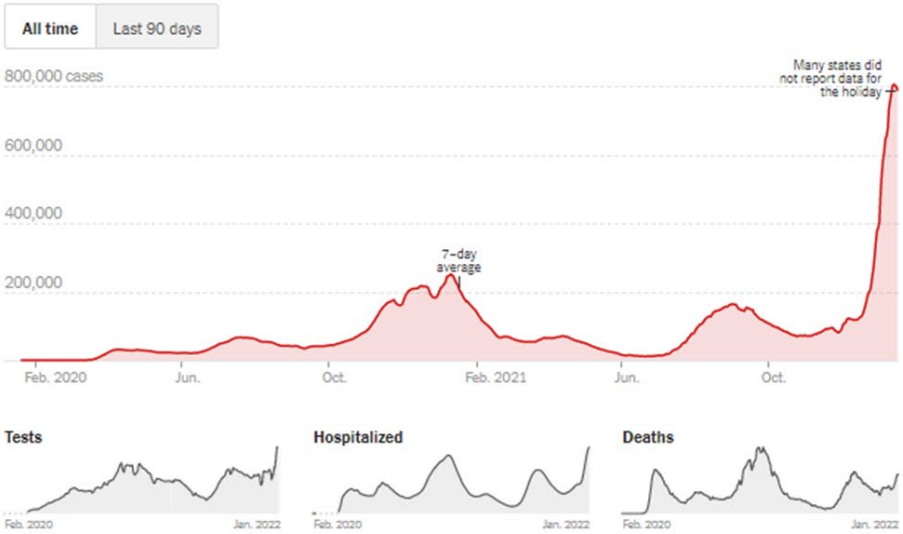
United States 14-Day New Case Trend – As of January 18, 2022

Coronavirus in the U.S.: Latest Map and Case Count

Updated Jan. 18, 2022

New reported cases



Vaccinations

	AT LEAST ONE DOSE	FULLY VACCINATED
All ages	75%	63%
12 and up	85%	72%
65 and up	95%	88%

See more details ›

About this data

State of the virus

Update for Jan. 14

- The Omicron variant has pushed the country's daily case reports to record levels, with more than 800,000 new infections being reported each day.

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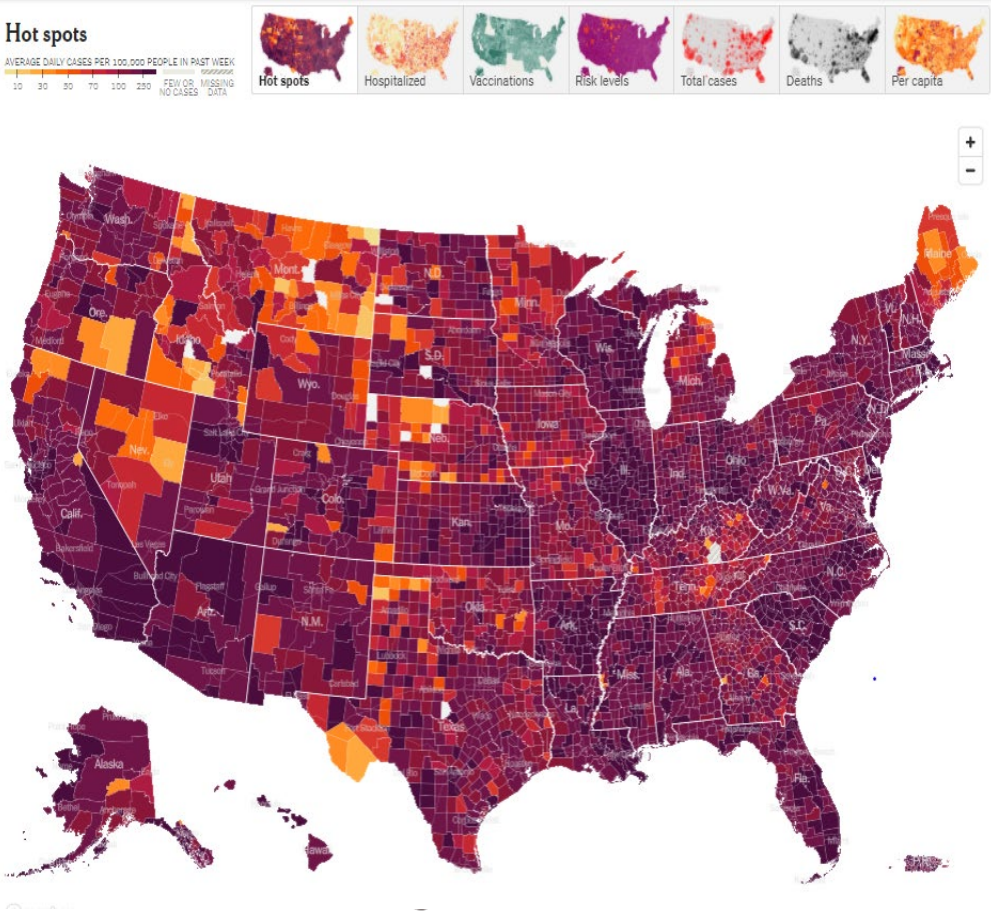
Global, National and Local as of January 18, 2022 – 7-day trend

	Global	US	DC/MD/VA	Greater DC Region Only
Total Cases	329,154,731	65,815,654	2,373,210	939,833
Percent Change (since last week)	14.1%	11.8%	-0.2%	-11.3%
Total Hospitalizations		3,919,141	153,513	
Percent Change (since last week)		18.7%	0.1%	
Total Deaths	5,559,322	849,980	29,724	9,217
Percent Change (since last week)	9.5%	16.3%	50.9%	90.9%
Case Fatality Rate (7 day average)	0.2%	0.2%	0.3%	0.2%
New Cases Per 100K (7 day average)	36.2	246.2	196.2	220.0
Test Positive Rate (7 day average)		28.4	33.6	24.8

US Hotspots – as of January 18, 2022



US Overall Case Rate per 100K

- **238 (61% increase)**

Highest Case Rate States (per 100K)

- **Rhode Island = 457**
- **Wisconsin = 396**
- **Vermont = 320**

Still High but Falling

- **New York = 249 (-27%)**
- **DC = 239 (-20%)**

Other Local Case Rates

- Maryland = 155 (-21%)
  - almost lowest in US only 3 states lower!
- Virginia = 198 (+28%)

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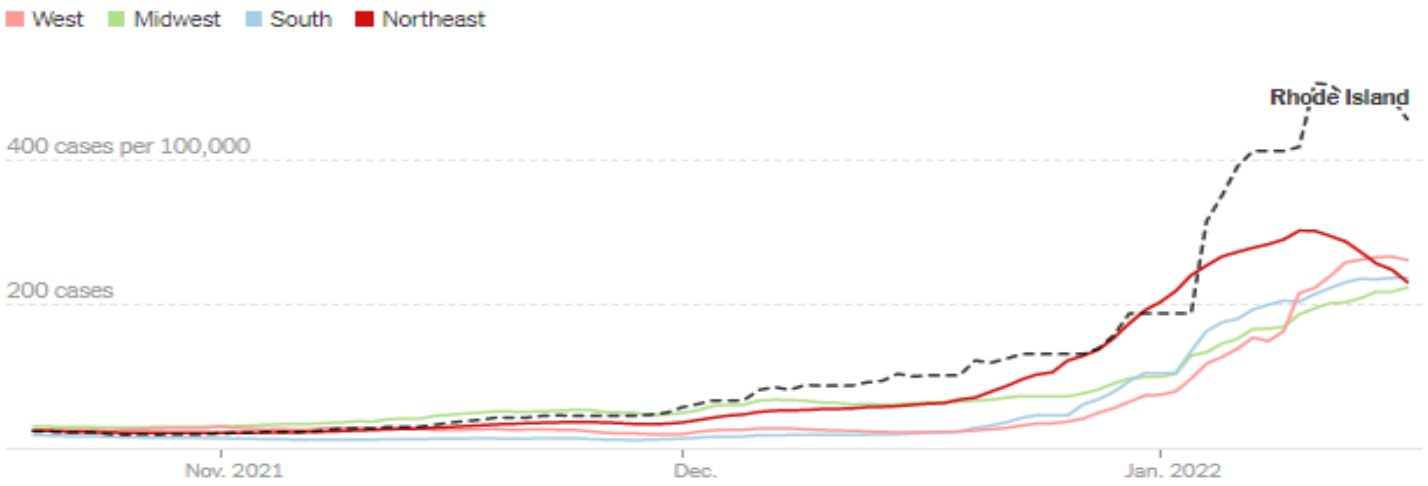
Transmission by US Region – As of Jan 18: Northeast declining now

Cases by region

This chart shows how average daily cases per capita have changed in different parts of the country. The state with the highest recent average cases per capita is shown.

All time | **Last 90 days**



About this data

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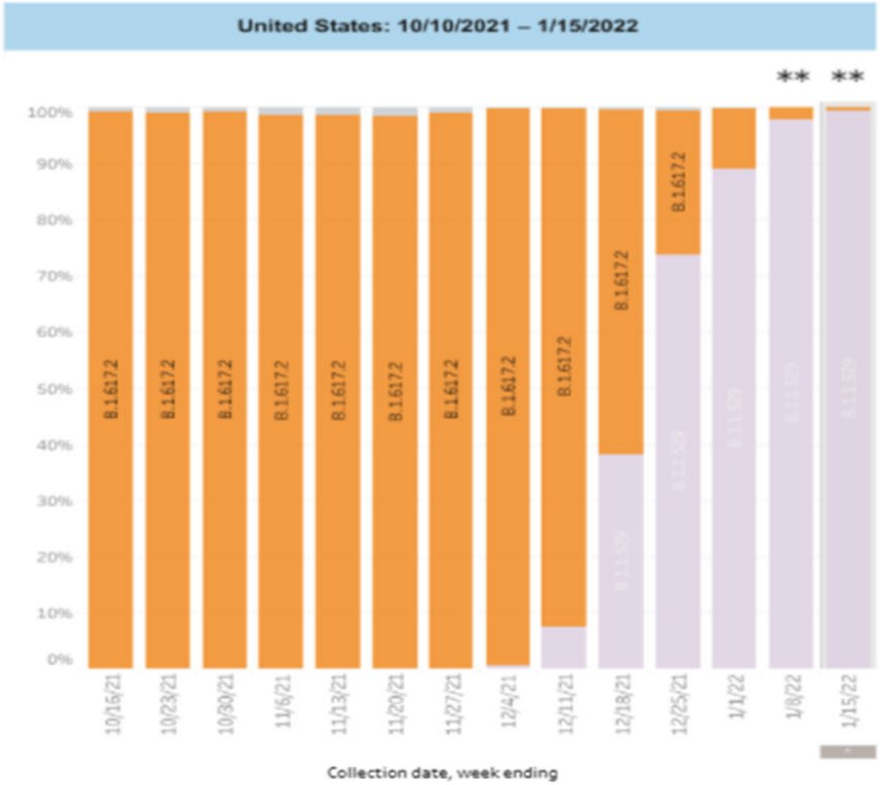
SARS-CoV-2 Variant Proportions in US through Jan 15, 2022: Omicron now 99% of Isolates



United States: 1/9/2022 – 1/15/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	99.5%	99.3-99.7%
Delta	B.1.617.2	VOC	0.5%	0.3-0.7%
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.127 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

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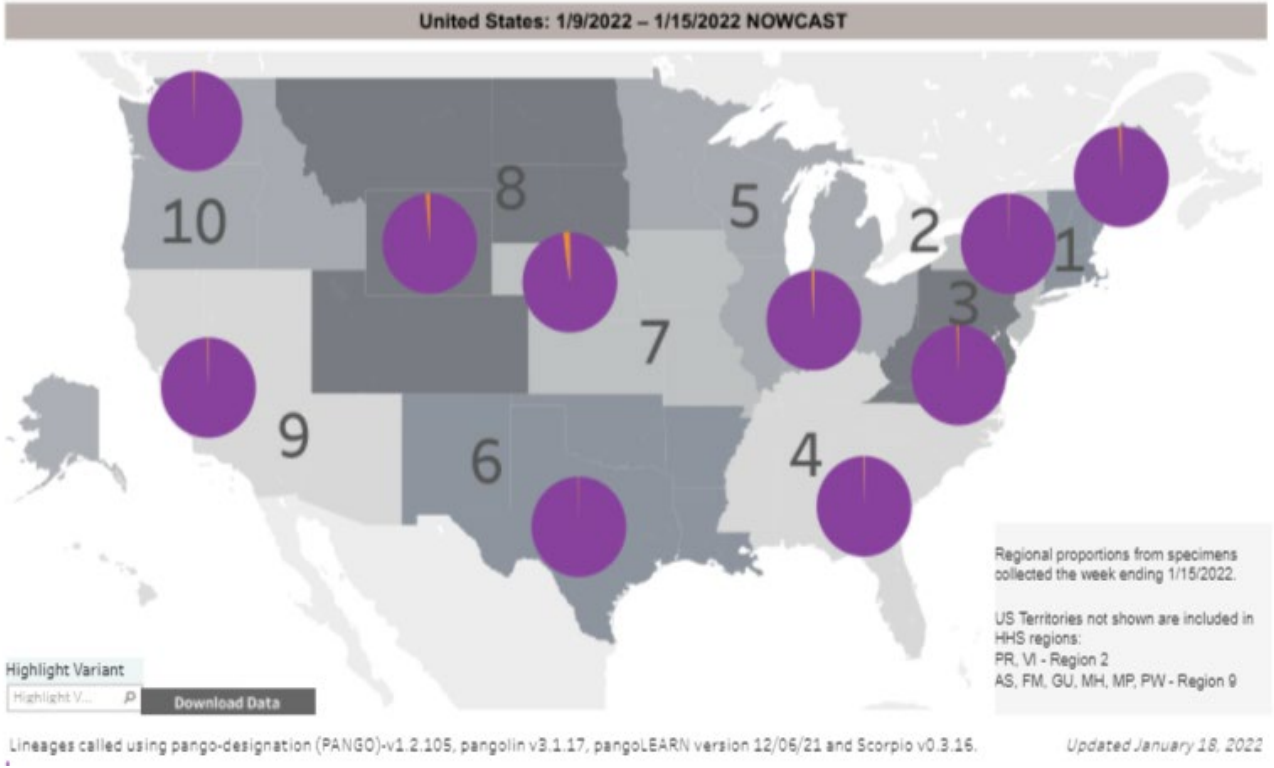
Omicron Proportions by US Region through Jan 15, 2022



Children and COVID: AAP/CHA data as of January 13, 2022 (Including Omicron)

- Cases
  - 9.5million cumulative child COVID-19 cases reported
    - Nearly 1 million added in last 1 week (20% increase)
  - Children represent **17.8%** of all cases cumulatively
  - Down from **25.1%** of all cases 2 weeks ago

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

CHILDREN'S HOSPITAL ASSOCIATION

- **Hospitalizations:**
  - **Children still represent only up to 4.5 % of all COVID hospitalizations**
  - **0.1-1.6% of pediatric cases resulted in hospitalization**
- Deaths
  - <0.25% of COVID deaths are in children
  - <0.05% of COVID cases in children result in death

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Children's National COVID-19 and MIS-C: March 15, 2020 - January 17, 2022

COVID

- Cumulative **7821** COVID+ symptomatic patients

- **25-50** new COVID+ symptomatic patient tests per day (**Marked decrease from 200/day**)
  - Test positive percentage – **26%** (**Marked decrease from peak of 48% positive)**
- **Daily** new COVID+ admissions decreased to as low as **8 per day (down from peak 24/day)**

- Cumulative **1258** COVID+ patients admitted
  - 368(29%) critical care (324 PICU, 44 NICU)
  - 890 (71%) acute care

- Current census COVID+ = **47** (2 NICU, 10 PICU, 35Acute) - **Down from Peak 67 on 1.9.22**

MIS-C:

- 219 cumulative
  - Omicron-related MISC surge- (14 admits since 12.13. 22)

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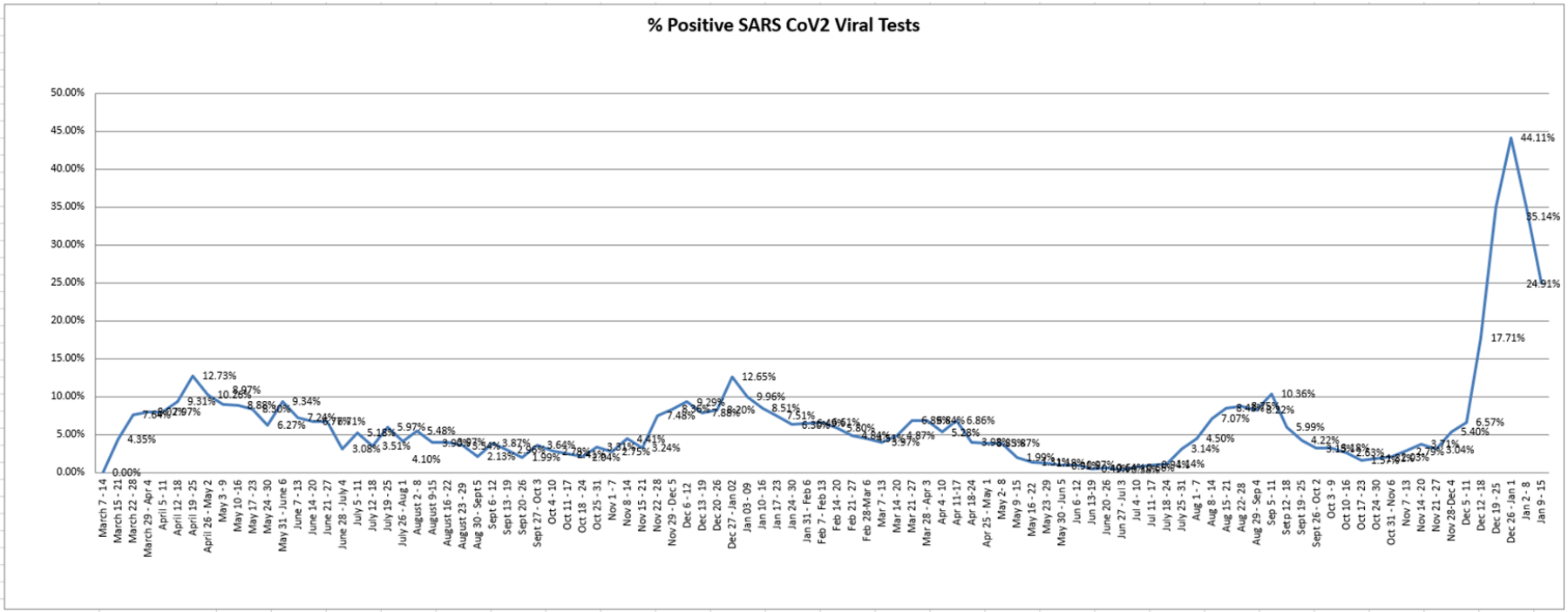
Weekly SARS-CoV-2 Percent Positive Tests – CNH Laboratory

Data Courtesy of Dr. Meghan Delaney and Lab Medicine Team



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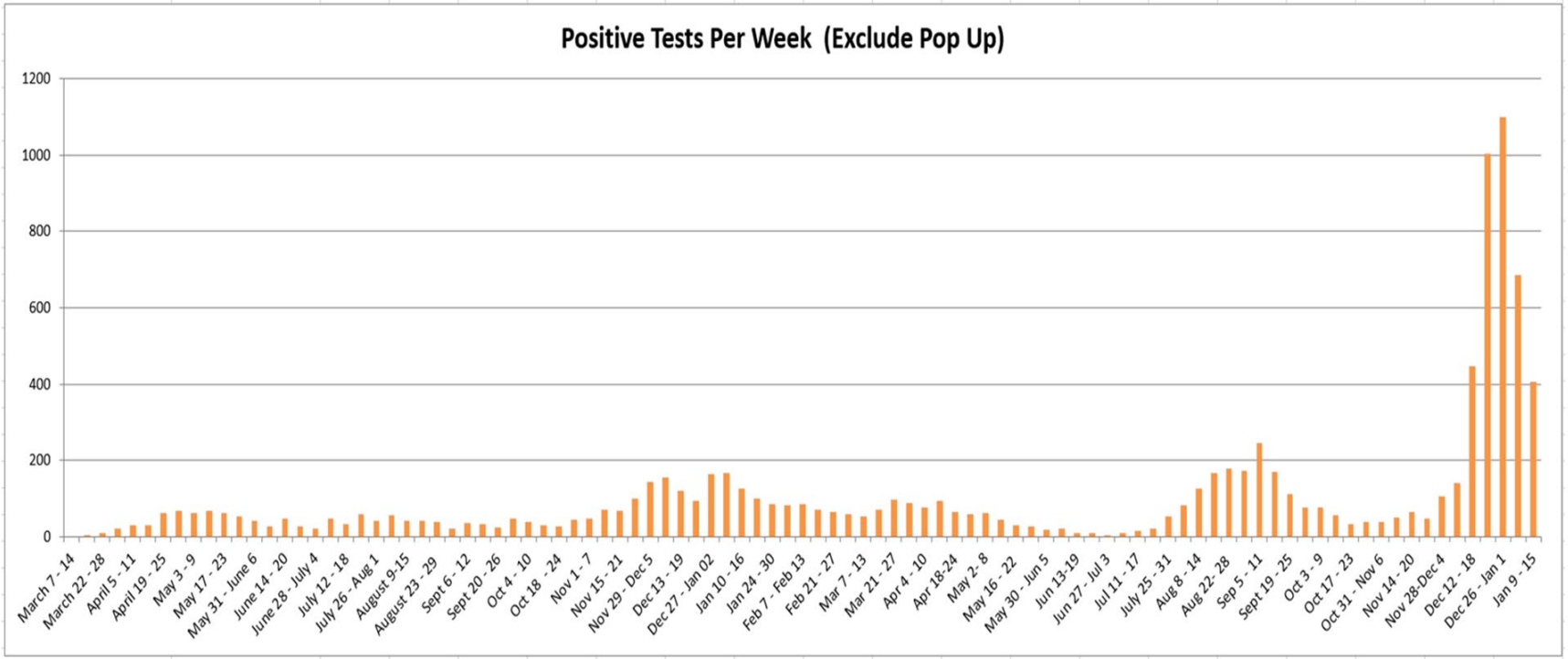
Weekly SARS-CoV-2 Positive Tests– CNH Laboratory

Data Courtesy of Dr. Meghan Delaney and Lab Medicine Team



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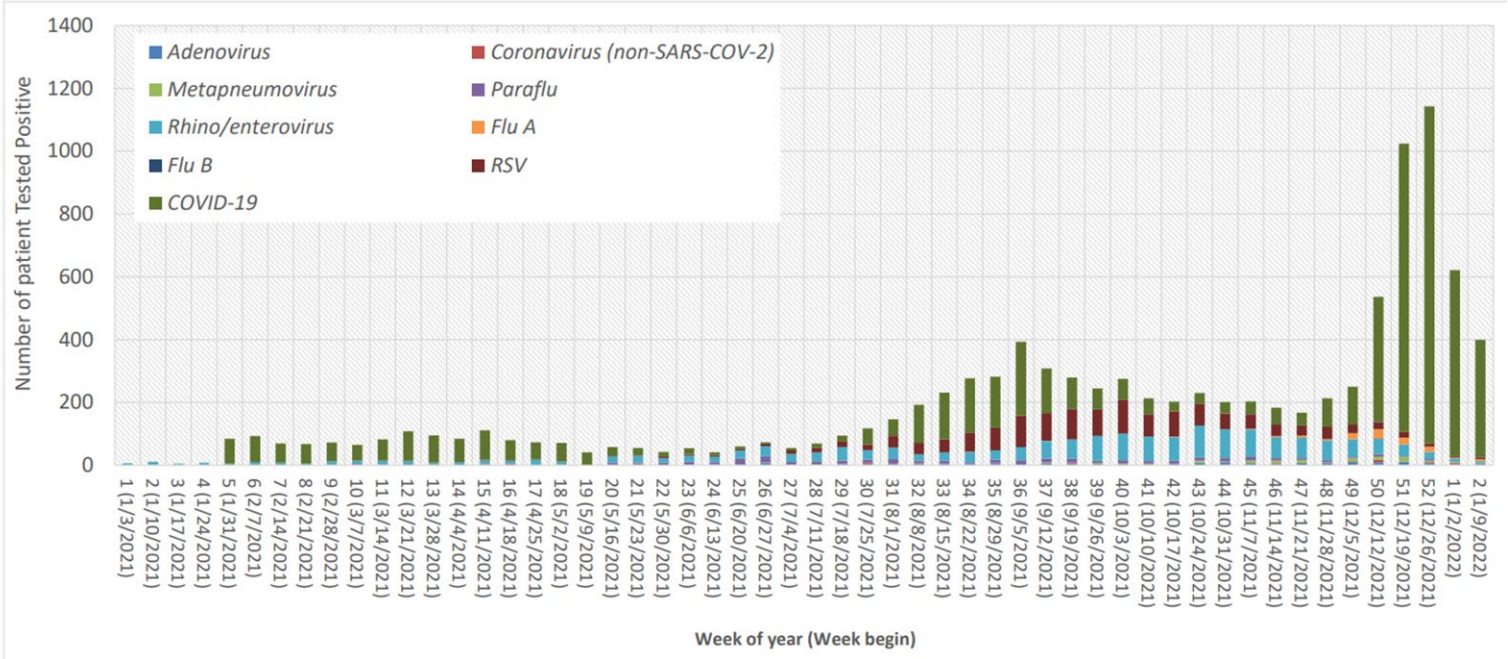
CNH Lab-confirmed Seasonal Respiratory Viral Infections and COVID-19*

Virus- Specific, 1/3/2021 – 1/15/2022



Data Courtesy of Dr. Xiaoyan Song; Epidemiology and Infection Control Team

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Comparing Omicron (6 weeks and ongoing) to Delta (5 months)

	Delta	Omicron
Total	1831	3165
Outpatient Visits	1602	2915
Admissions	229	260
ICU Admissions	77	73
LOS	1817	1564

Data Courtesy of Dr. Song, Chief, Infection Control and Epidemiology

COVID-19 Therapeutics: Monoclonal Antibodies and Oral Antivirals

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COVID-19 Therapeutics

- Emergency Use Authorization (EUA) for prevention or treatment of patients not hospitalized for COVID-19 at **high-risk*** for progression to severe disease (including hospitalization and death)
  - **Monoclonal antibodies (mAbs):**
    - Administered to provide passive immunity
    - Adhere to viral surface and prevent from attaching to cellular target
    - **Currently available at CNH based on inventory allocation**
  - **Oral antivirals:**
    - Interfere with viral replication - prevents virus from proliferating
    - **Not currently available at CNH**

*Which patients are **“high risk”** for progression to severe disease?

- Specific conditions outlined within each product’s EUA
- Current CNH criteria include, *but not limited to:*
  - Immunosuppressive disease or treatment
  - Non-asthma chronic respiratory disease
  - Congenital or acquired heart disease
  - Chronic kidney disease
  - Diabetes mellitus
  - Obesity (BMI ≥95th percentile for age)
  - Sickle cell disease
  - Neurodevelopmental disorder
- Additional conditions outlined by CDC

COVID-19 Therapeutics

- Helpful links
  - COVID-19 Therapeutics | HHS/ASPR
  - Side-by-Side Overview of Therapies Authorized for the Treatment of Mild-Moderate COVID-19 (phe.gov)
  - DHHS Therapeutics locator

COVID-19 Monoclonal Antibodies (mAbs)

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COVID-19 Treatment Monoclonal Antibodies (mAbs)

	REGEN-COV™ (Casirivimab/ Imdevimab)	Bamlanivimab/ Etesevimab	Sotrovimab
EUA eligibility	≥12 years old AND ≥40 kg	Adult and pediatric (including neonates)	≥12 years old AND ≥40 kg
Indication(s)	Treatment, PEP	Treatment, PEP	Treatment
Treatment efficacy[1]	70% reduction in hospitalizations/deaths	87% reduction in hospitalizations/deaths	79% reduction in hospitalizations/deaths
SARS-CoV-2 variant activity[2]	Delta variant: Active **Omicron variant: Unlikely**	Delta variant: Active **Omicron variant: Unlikely**	Delta variant: Active **Omicron variant: Likely active**
Product availability	Variable by jurisdiction and healthcare facility; weekly allocation to CNH through DC DOH. Call **202-476-5000** and ask to speak to the ID doctor on-call to discuss availability.		

1. For more details on clinical trial results, see Section 18 of each respective product's Fact Sheet for Health Care Providers.
2. See section 15 of respective product's Fact Sheet for Health Care Providers.

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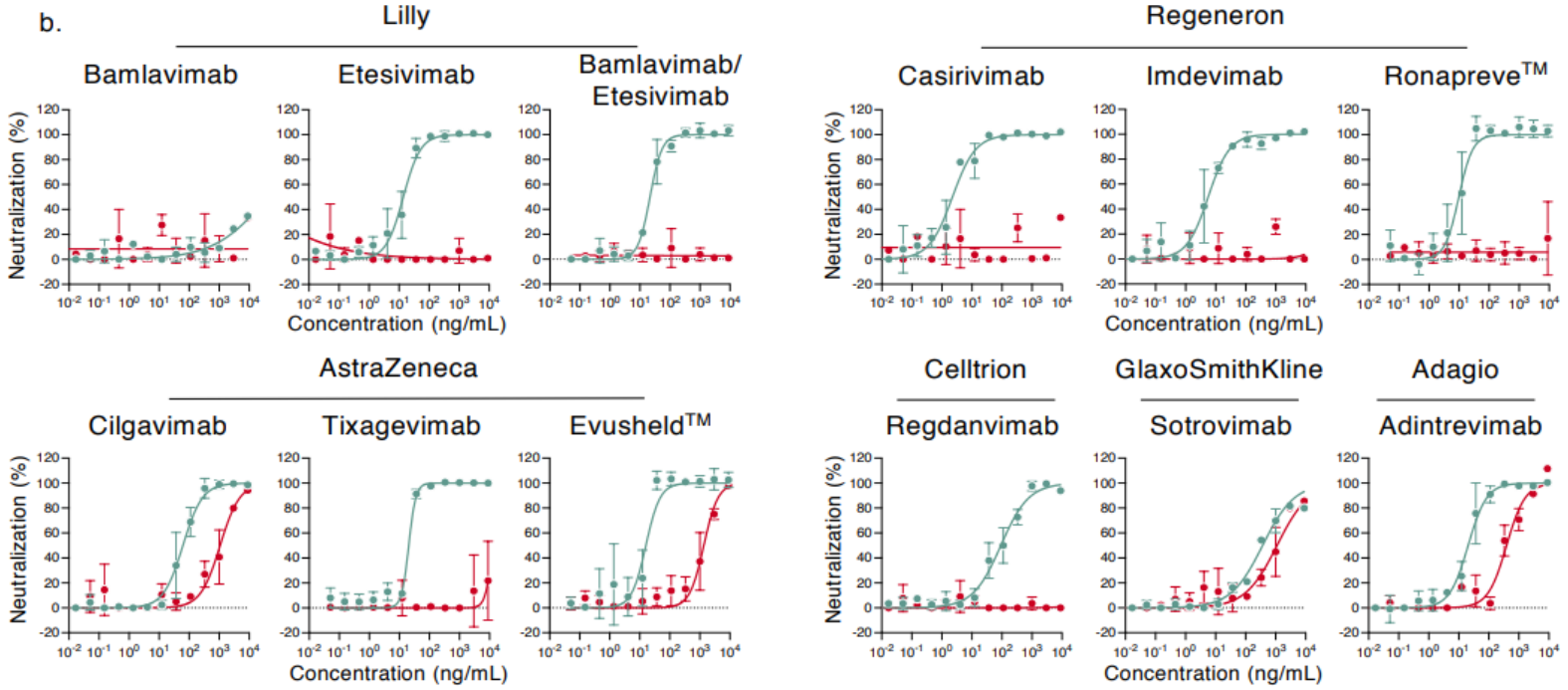
Susceptibility to mAbs seemingly lower for **Omicron** than **Delta**



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Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization (biorxiv.org)

Current SARS-CoV-2 Monoclonal Antibody Recommendations

- **Not recommended** in setting of Omicron:
  - REGEN-COV™ (casirivimab/imdevimab)
  - Bamlanivimab/Etesevimab
- **Recommended** in setting of Omicron:
  - Sotrovimab for treatment
  - Evusheld™ (tixagevimab and cilgavimab) for pre-exposure prophylaxis

Sotrovimab

- Mechanism of action (MOA): blocks spike protein viral entry to host cell

- **Eligibility**: patients ≥12 years old AND ≥40 kg, with mild-moderate COVID-19 at high risk of progression to severe COVID-19
  - **Treatment only**
  - Within 10 days of symptom onset (ideally 5)

Sotrovimab

- Dosing
  - **Treatment**: sotrovimab 500 mg as single IV infusion
- Risk of infusion-related reactions, monitor for 1 hour
  - Pyrexia, chills, dizziness, dyspnea, pruritis, rash
- Helpful links
  - Fact Sheet for Health Care Providers
  - Fact Sheet for Patients, Parents, and Caregivers (English)
  - Fact Sheet for Patients, Parents, and Caregivers (Spanish)

Evusheld™ (Tixagevimab and Cilgavimab)

- MOA: bind to non-overlapping regions of SARS-CoV-2 spike protein to block binding to host receptor

- **Eligibility**: patients ≥12 years old AND ≥40 kg, **NOT** currently infected with SARS-CoV-2
  - **Have NOT** had a known exposure
  - Have moderate-severe immune compromise AND
  - May not mount an adequate vaccine response OR for whom vaccination is not recommended
  - **Pre-exposure prophylaxis (PrEP) only**

Evusheld™ (Tixagevimab and Cilgavimab)

- Dosing:
  - Tixagevimab 150 mg IM PLUS cilgavimab 150 mg IM
  - **Two separate, consecutive IM injections**
    - Preferably one in each gluteal muscle
  - Administer two weeks after COVID-19 vaccination
- Risk of hypersensitivity, monitor for 1 hour
  - Caution: thrombocytopenia, coagulation disorder
  - Increased risk of cardiovascular events (seen in patients with cardiovascular disease)
- Helpful links
  - Fact Sheet for Health Care Providers
  - Fact Sheet for Patients, Parents, and Caregivers (English)
  - Fact Sheet for Patients, Parents, and Caregivers (Spanish)

Logistics of Monoclonal Antibody Administration

- To inquire regarding eligibility for monoclonal antibody therapy contact Infectious Diseases COVID on call **202-476-5000**

- If approved, institutional protocol in effect for administration
  - Referral to ED for treatment infusion (sotrovimab)
    - Coordinate patient arrival time with ED by calling ECIC: **202-476-5433**
  - Provide Fact Sheet for Patients, Parents and Caregivers
  - Counsel patient/caregiver: no alternative therapies, not FDA approved

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Product Availability: Additional Infusion Locations

- Provider referrals:
  - Johns Hopkins Sibley Memorial Hospital
  - MedStar Health
  - Inova

- Patient self-referrals:
  - University of Maryland Medical System
  - Inova

COVID-19 Oral Antivirals

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COVID-19 Oral Antivirals

	Paxlovid™ (Nirmatrelvir/Ritonavir)	Molnupiravir
EUA eligibility	≥12 years old AND ≥40 kg	≥18 years old
Indication(s)	Treatment	Treatment
Treatment efficacy[1]	88% reduction in hospitalizations/deaths	30% reduction in hospitalizations/deaths
SARS-CoV-2 variant activity[2]	Delta variant: Active **Omicron variant: Data pending**	Delta variant: Active **Omicron variant: Data pending**
Product availability	**https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator**	

1. For more details on clinical trial results, see Section 18 of each respective product's Fact Sheet for Health Care Providers.
2. See section 12.4 of respective product's Fact Sheet for Health Care Providers.

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Paxlovid™ (Nirmatrelvir/Ritonavir)

- MOA: viral protease inhibitor that inhibits viral replication
  - Combination Therapy
    - Nirmatrelvir – active component
    - Ritonavir: CYP3A inhibitor that increases nirmatrelvir plasma levels; no SARS-CoV-2 antiviral activity
- **Eligibility**: patients ≥12 years old AND ≥40 kg
  - With mild-moderate COVID-19
  - At high risk of progression to severe COVID-19
- **Treatment only**
  - Within 5 days of symptom onset

Efficacy Results in Non-Hospitalized Adults with COVID-19 Dosed within 5 Days of Symptom Onset who Did Not Receive COVID-19 mAb Treatment at Baseline

	PAXLOVID™ (N=1,039)	PLACEBO (N=1,046)
Primary endpoint: COVID-19 related hospitalization or death from any cause through Day 28, n(%)	8 (.08%)	66 (6.3%)
Reduction relative to placebo for primary endpoint[a] [95%, CI], %	-5.62 (-7.21,-4.03)	
All-cause mortality through Day 28, %	0	12 (1.1%)

a. Estimated cumulative proportion of participants with COVID-19 related hospitalization or death from any cause through Day 28 was calculated for each treatment group using Kaplan-Meier method, where subjects without hospitalization and death status through Day 28 were censored at the time of study discontinuation

- **88% (95% CI: 75%, 94%)** relative risk reduction for the primary endpoint (proportion of subjects with COVID-19 related hospitalization or death from any cause through Day 28)
- Treatment effect was generally consistent across subgroups, including baseline serology status.

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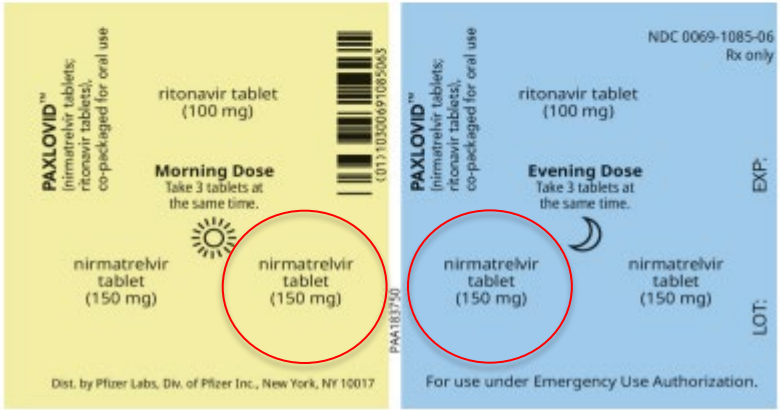
Slide from January 12, 2022 Clinician Outreach and Communication Activity Call

Paxlovid™ (Nirmatrelvir/Ritonavir)

- Dosing: nirmatrelvir 300 mg (2 x 150 mg tabs) + ritonavir 100 mg PO BID x 5 days
  - Take with or without food
  - **Moderate renal impairment:**
    - Nirmatrelvir 150 mg + ritonavir 100 mg PO BID x 5 days
  - **Not recommended:**
    - Severe renal or severe hepatic impairment



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Clean_EUA-105-mitigation-plan-for-moderate-renal-impairment-01-11-22.pdf (covid19oralrx-hcp.com)

Paxlovid™ (Nirmatrelvir/Ritonavir)

- **Significant** drug interactions!
  - Potent **CYP3A inhibitor** → may increase plasma concentrations of concurrent CYP3A medications
  - **CYP3A substrate** → may be increased / decreased by concurrent medications that inhibit / induce CYP3A
  - See section 7.3 of Fact Sheet for Health Care Providers
  - NIH Statement on Paxlovid™ interactions
- Based on the interaction, may need to hold, change, or dose-reduce other medications while on Paxlovid™
  - **American Society of Transplantation recommends against use in transplant patients in light of interactions**

Paxlovid™ (Nirmatrelvir/Ritonavir)

- Risk of dysgeusia, diarrhea, hypertension, myalgia

- Helpful links
  - Fact Sheet for Health Care Providers
  - Fact Sheet for Patients, Parents, and Caregivers (English)
  - Fact Sheet for Patients, Parents, and Caregivers (Spanish)

Molnupiravir

- Mechanism of Action
  - Nucleoside analog, inhibits viral replication via viral mutagenesis
- **Eligibility**: patients ≥18 years old with
  - Mild-moderate COVID-19
  - At high risk of progression to severe COVID-19
  - **For whom alternative COVID-19 treatment options are not accessible or clinically appropriate**
- **Treatment only**
  - Within 5 days of symptom onset

Molnupiravir Efficacy: MOVe-OUT

	Molnupiravir (N=709) n(%)	Placebo (N=699) n(%)	Adjusted Risk Difference % (95%CI)
All-cause hospitalization ≥24 hours for acute care or death through Day 29	48 (6.8%)	68 (9.7%)	-3.0 (-5.9%, -0.1%)
All-cause mortality through Day 29	1 (0.1%)	9 (1.3%)	

*The determination of primary efficacy was based on a planned interim analysis of 762 subjects. At the interim analysis, 7.3% of participants who received molnupiravir were either hospitalized or died through Day 29 (28/385), compared with 14.1% of placebo-treated participants (53/377). The adjusted risk difference was -6.8% with a 95% CI of (-11.3%, -2.4%) and 2-sided p-value = 0.0024.

Adjusted relative risk reduction of molnupiravir compared to placebo for all randomized participants was 30% (95% CI: 1%, 51%).

Molnupiravir

- Dosing:
  - Molnupiravir 800 mg (4 x 200 mg capsules) PO q12h x 5 days
  - Take with or without food
- Not recommended in:
  - Pregnancy - risk of fetal harm; counsel on contraception x 3 months after
  - Breastfeeding – for treatment, and 4 days after
  - < 18 years - may affect bone and cartilage growth
- Risk of diarrhea, nausea, dizziness
- Helpful links
  - Fact Sheet for Health Care Providers
  - Fact Sheet for Patients, Parents, and Caregivers (English)
  - Fact Sheet for Patients, Parents, and Caregivers (Spanish)

Oral Antivirals for COVID-19 in Washington, DC

- Limited availability as of early January 2022

- DC Health **limiting use to persons most likely to benefit** based on age, comorbidities, and/or presence of immune deficiency

*For the purposes of eligibility for prescription of these oral therapeutics, DC Health considers persons to be at high risk of progression to severe COVID-19 illness if they meet any the following combinations of age and pre-existing medical conditions.

- **Age ≥ 75**, or
- **Age 65 – 74 and having any of the following conditions**:
  - Cancer
  - Chronic kidney disease
  - Chronic obstructive pulmonary disease
  - Obesity
  - Heart conditions
  - Smoker (current)
  - Sickle cell disease
  - Type 2 diabetes mellitus
- **Age > 12 (for Paxlovid) or >18 (for Molnupiravir) and severely immunocompromised,** such as persons:
  - Actively receiving cancer chemotherapy
  - On immunosuppressive treatment for organ transplant
  - With untreated HIV infection **and** CD4 counts below 50 cells/mm^3
  - With severe combined immunodeficiency syndrome

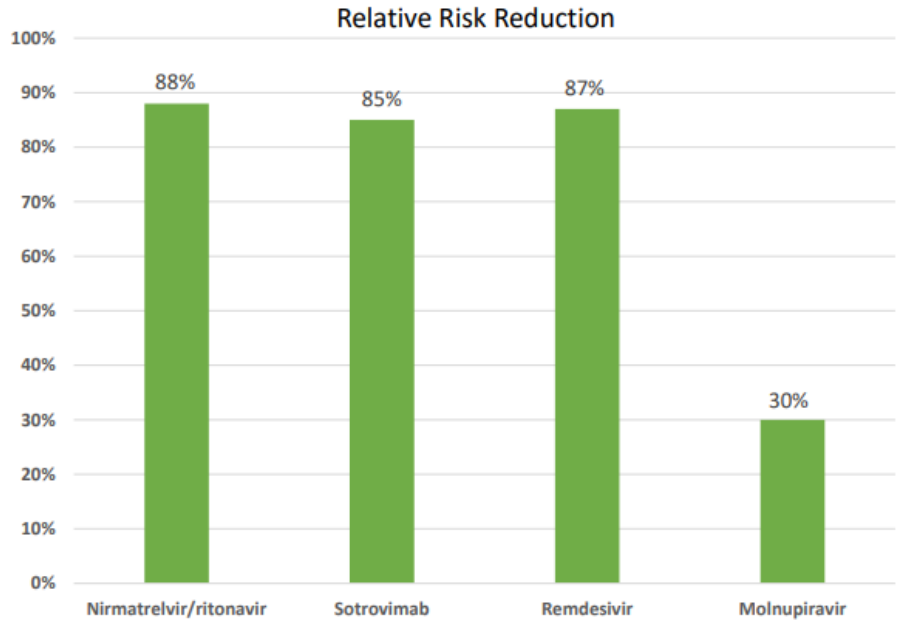
Product Availability: Publicly Available Therapeutics

- As of early January 2020, DC Health allocation to select Safeway pharmacy locations:

Store Name	Address	Phone Number
Safeway #2912	1855 Wisconsin Ave, NW, Washington DC 20007	(202) 333-6048
Safeway #3217	415 14th Street SE, Washington DC 20003	(202) 920-5875
Safeway #4270	1601 Maryland Ave., NE, Washington DC 20002	(202) 398-6900

- HealthData.gov
  - Locations of publicly available Evusheld™, Paxlovid™, and molnupiravir
  - Filter by location, courses available, etc.

Clinical Efficacy Comparison



Events* (%) Drug vs. placebo	0.8% vs. 6.3%	1% vs. 7%	0.7% vs. 5.3%	6.8% vs. 9.7%

*Events = hospitalizations or deaths

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Listed in Order of Preference

Comparisons of Recommended Outpatient Therapies

	Paxlovid™ (1)	Sotrovimab (2)	Remdesivir (3)	Molnupiravir (4)
Age allowed for use	≥ 12 yr	≥ 12 yr	≥ 12 yr	≥18 yr
Initiate within # days of symptom onset	< 5 days	< 10 days	< 7 days	< 5 days
Route of Administration	PO	IV	IV	PO
Duration of Therapy	5 days	1 time	3 days	5 days
Pros	-High efficacy -Oral	-High efficacy -Single IV infusion	-High efficacy -Greater experience	-Oral -No drug-drug interaction concerns
Cons	Ritonavir-related drug-drug interactions	Requires IV infusion	-Requires 3 days of IV infusion -Not FDA approved for outpatient	-Low efficacy -Not authorized for age 12-17 years -Not approved for pregnancy -Concerns for mutagenciity
Supply Availability	Limited supply	Limited supply	Commercially available	More supply than Paxlovid™ & Sotrovimab

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Slide from January 12, 2022 Clinician Outreach and Communication Activity Call

We welcome your questions, feedback, suggestions:

phn@childrensnational.org

THANK YOU!

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