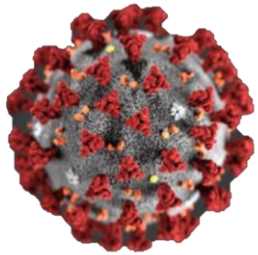


New Hampshire Coronavirus Disease 2019 Weekly Partner Call

November 18, 2021

Ben Chan
Elizabeth Talbot
Beth Daly
Lindsay Pierce

Thursday noon-time partner calls will focus on science, medical, and vaccine updates with time for Q&A

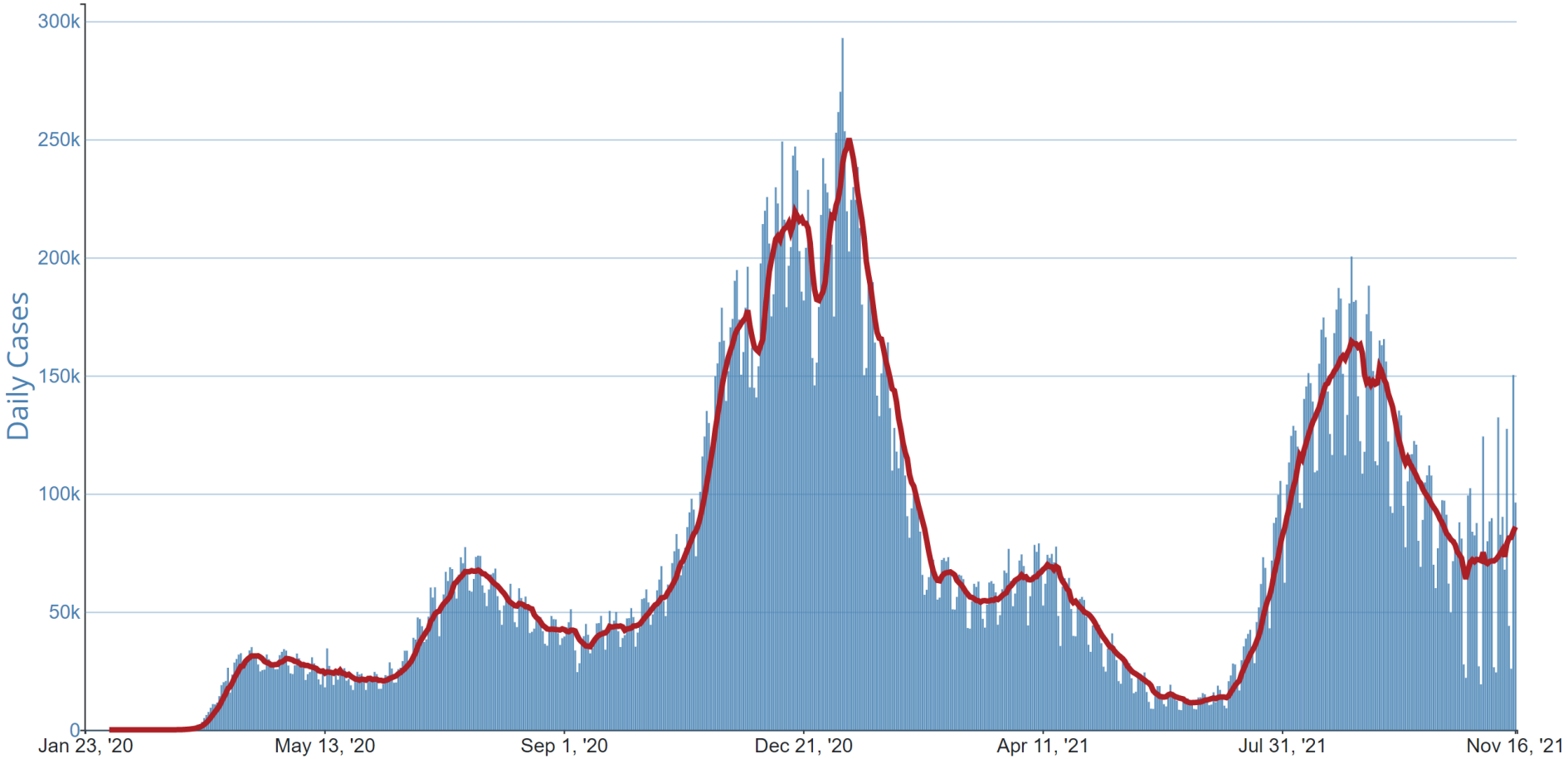
NH DIVISION OF Public Health Services
Department of Health and Human Services

Agenda

- Epidemiology Update
- SARS-CoV-2 antiviral medications
- CDC's Updated Recommendations for Use of COVID-19 Vaccines
- Questions & Answers (Q&A)

Epidemiology Update

U.S. National Daily Incidence of COVID-19



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases

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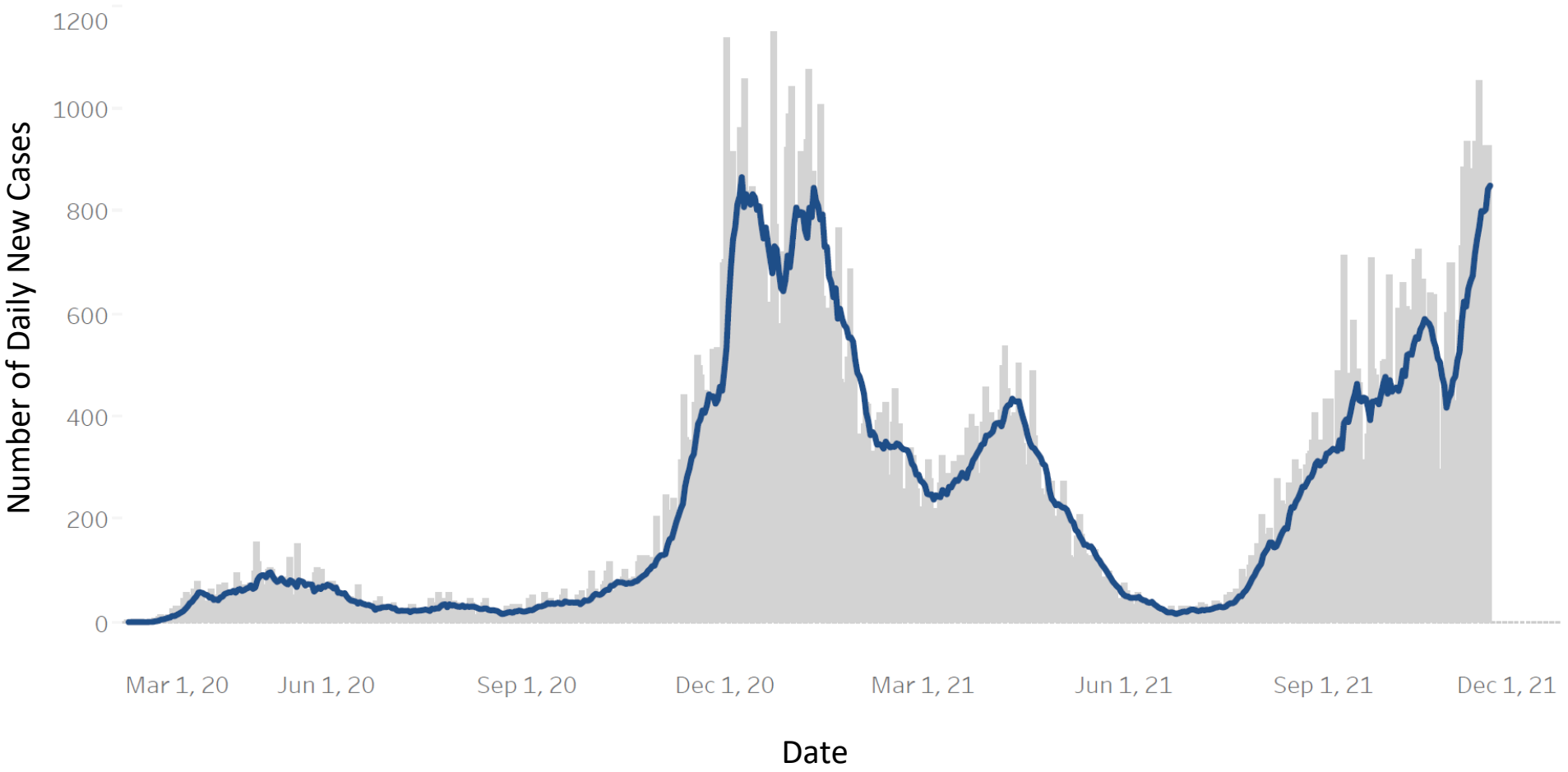
Number of New COVID-19 Cases per Day in NH (All Ages)



https://www.nh.gov/covid19/dashboard/overview.htm#dash

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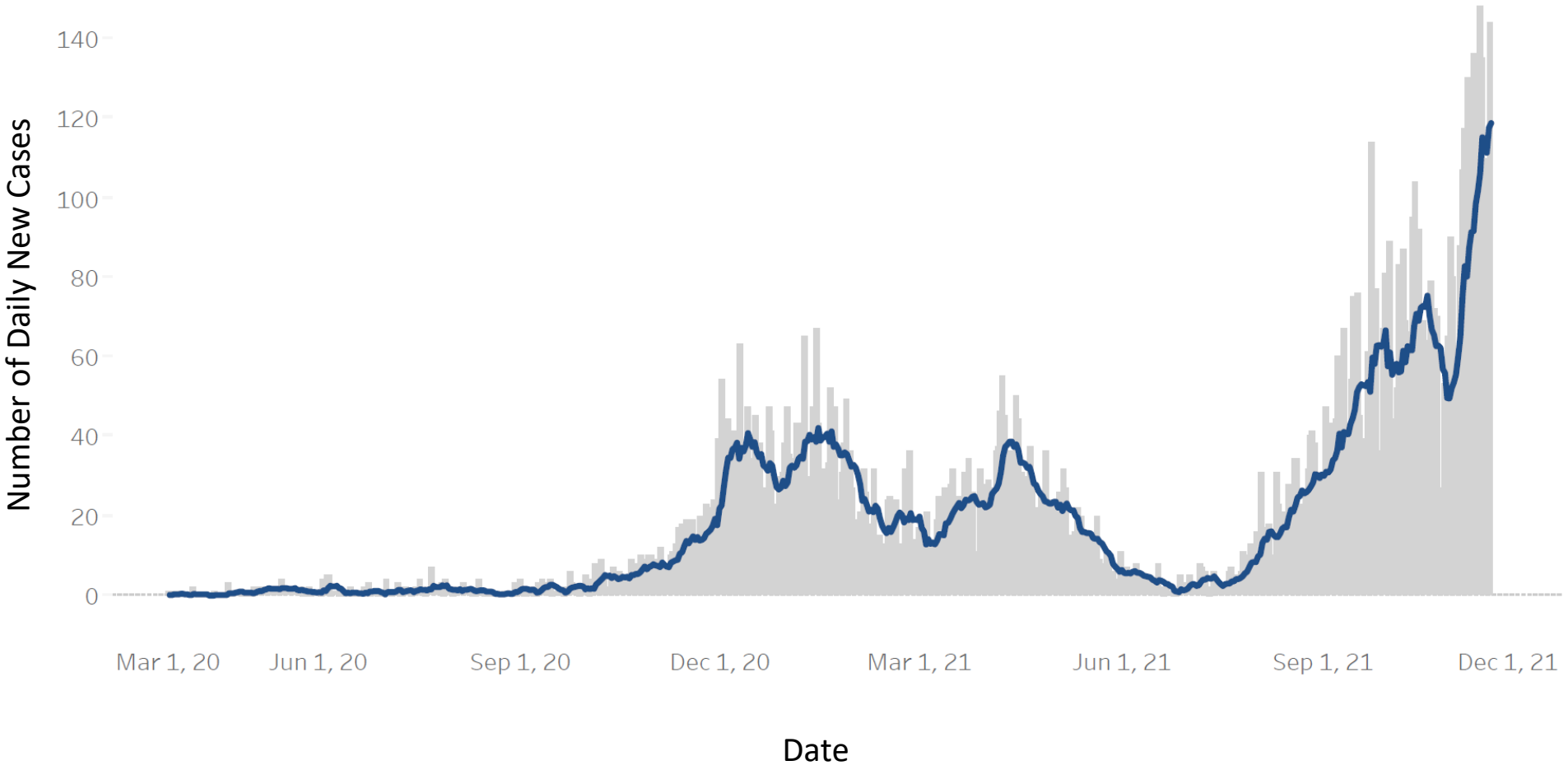
Number of New COVID-19 Cases per Day in NH (0-9 Year Olds)



https://www.nh.gov/covid19/dashboard/overview.htm#dash

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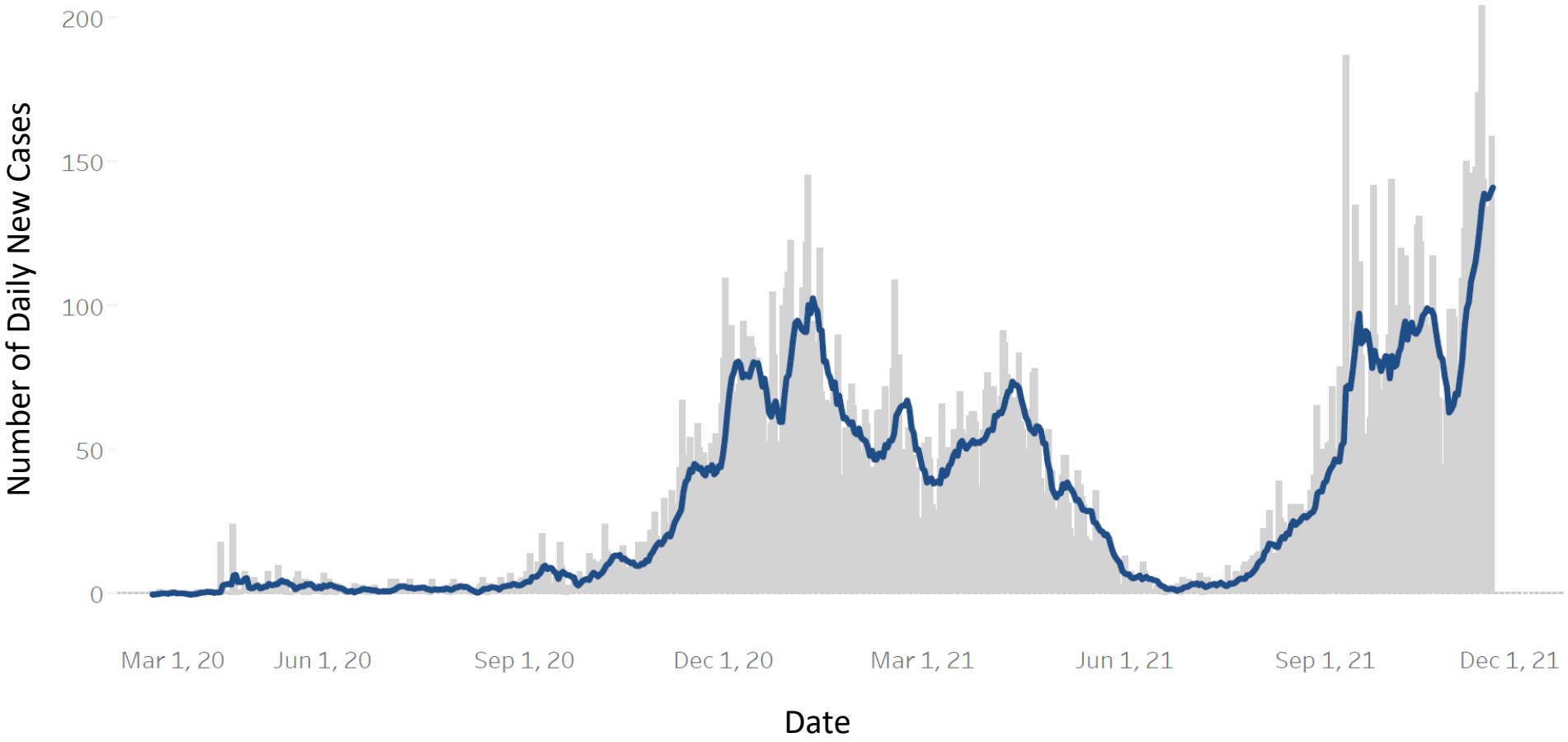
Number of New COVID-19 Cases per Day in NH (10-19 Year Olds)



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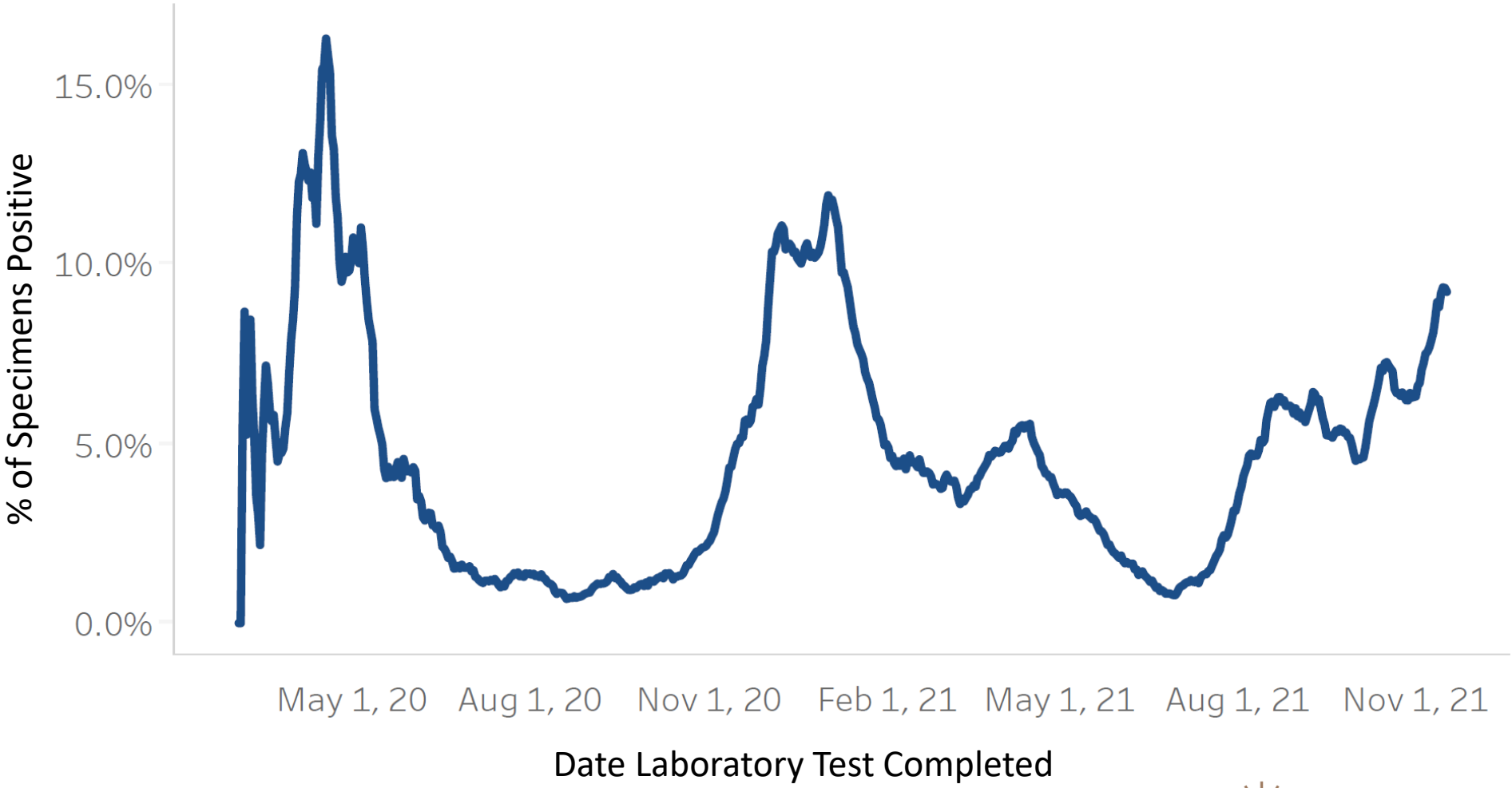
% of Tests (Antigen and PCR) Positive for COVID-19 (7-Day Average)



https://www.nh.gov/covid19/dashboard/overview.htm#dash

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Level of Community Transmission in NH

Statewide Level of Transmission

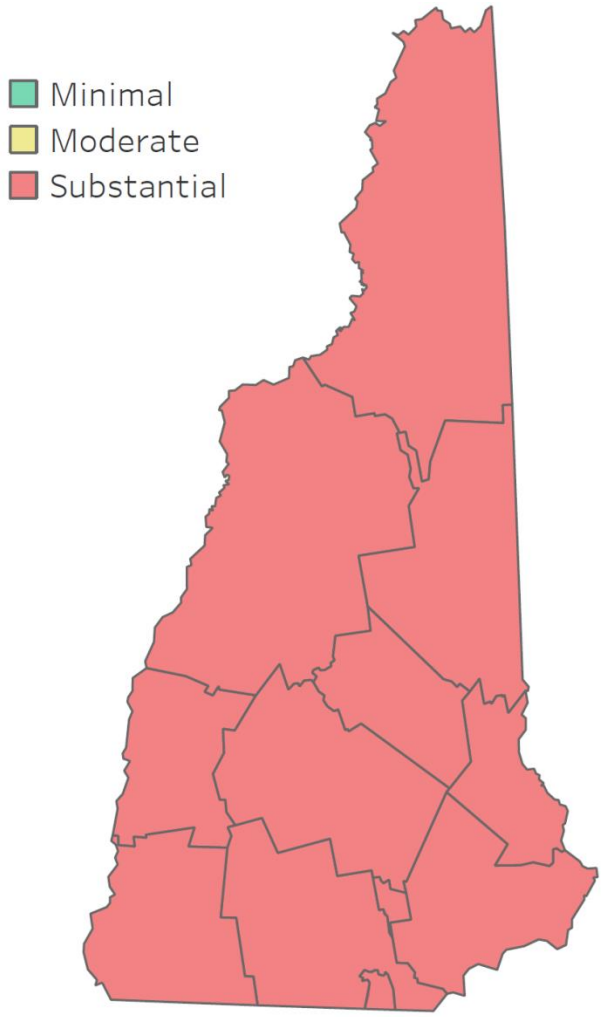
Substantial

New Cases per 100k over 14 days

807.5

7-Day Total Test Positivity Rate

9.3%



Data as of: 11/17/2021

https://www.covid19.nh.gov/dashboard/schools

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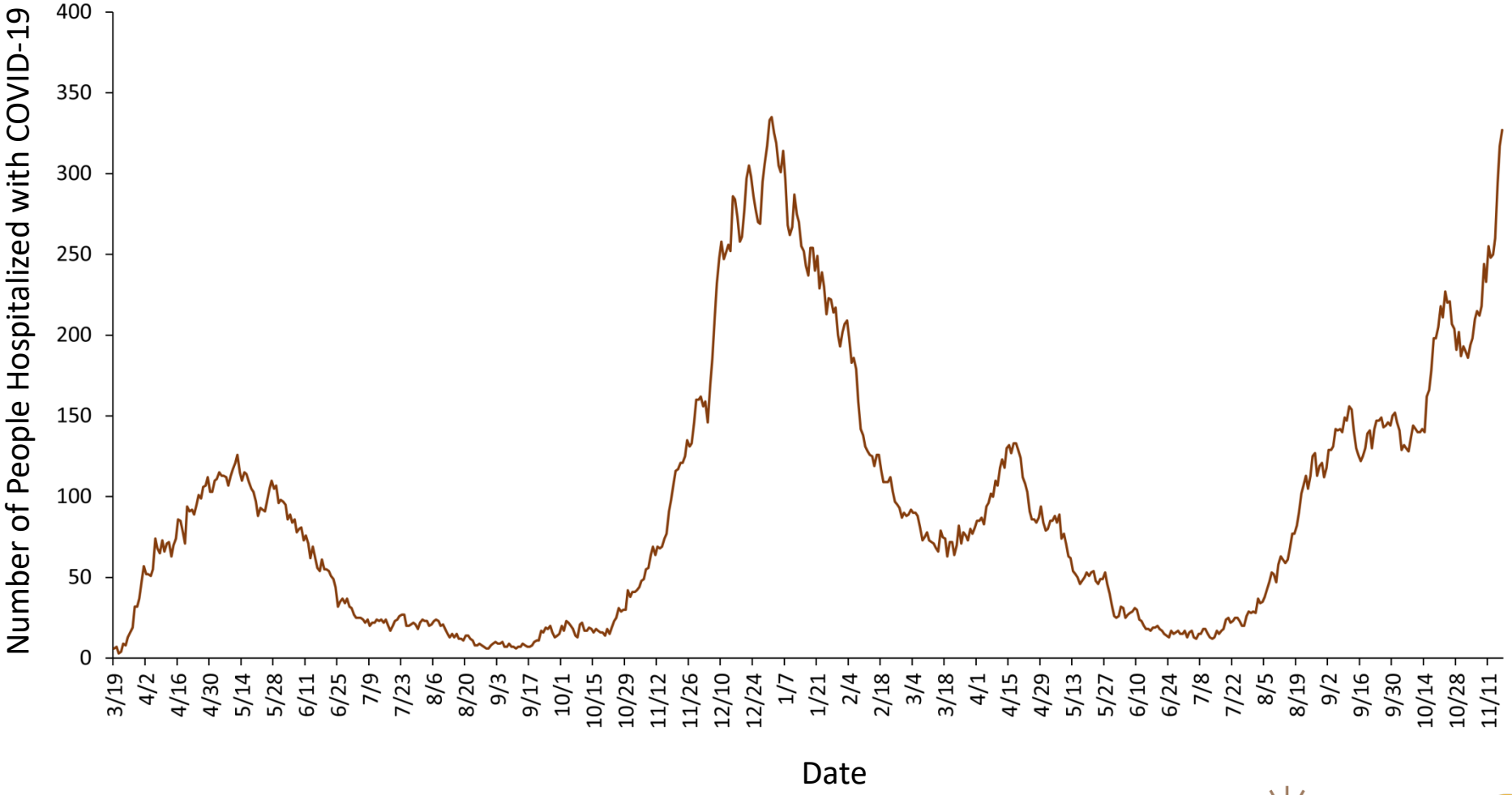
Number of People Hospitalized with COVID-19 Each Day in NH (Hospital Census)



https://www.nh.gov/covid19/dashboard/overview.htm#dash

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Average Number of COVID-19 Deaths per Day in NH (Based on Date of Death)

https://www.nh.gov/covid19/dashboard/overview.htm#dash

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SARS-CoV-2 Antiviral Medications: Molnupiravir & Paxlovid

COVID-19 Treatment: Preliminary Info on 2 Antivirals

1. Molnupiravir
2. Paxlovid

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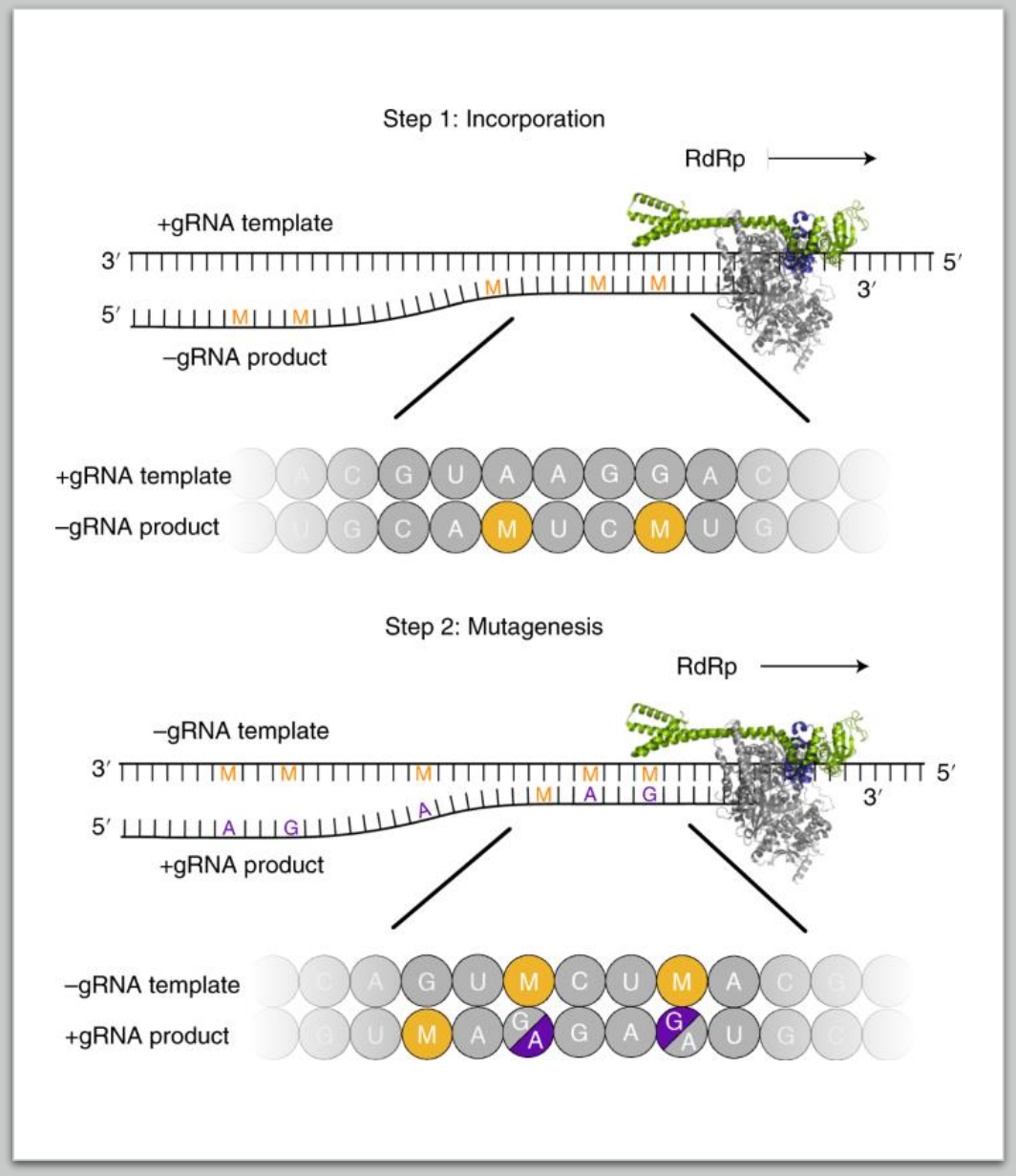
Molnupiravir

Oral, 5-day course of nucleoside analogue invented by Emory, licensed by Ridgeback, jointly developed by Merck

Mechanism of Action

- Developed as flu drug
- Targets viral polymerases
- “Lethal mutagenesis” increases frequency of viral RNA mutations and impairs SARS-CoV-2 replication
- Works for various viral polymerases, resulting in broad-spectrum antiviral activity



Kabinger, F., *et al.* Mechanism of molnupiravir-induced SARS-CoV-2 mutagenesis. *Nat Struct Mol Biol* **28,** 740–746 (2021). https://doi.org/10.1038/s41594-021-00651-0

Molnupiravir: Ph 3 MOVe-OUT Study

Merck and Ridgeback Press Release

Planned analysis of 775 of 1550 intended outpatients in 170 sites who had confirmed mild-mod COVID-19, within 5 days of onset, at risk for progression to severe disease

- Most common obesity, >60 years, diabetes mellitus, CVD

Significantly reduced the risk of hospitalization or death by ~50%. At 29d post randomization:

- 7.3% of 385 in molnupiravir group (28 hospitalized, 0 deaths)
- 14.1% of 377 in placebo (8 deaths)

Incidence of AEs comparable in molnupiravir and placebo groups

- Any AE 35% and 40%
- Drug-related AE 12% and 11%
- AEs leading to discontinuation of therapy 1.3% and 3.4%

Molnupiravir Updates

- Oct 11 EUA application
- Brand name Lagevrio
- Nov 4 UK first country to approve
- USG purchased 1.7M courses, pending EUA
- MOVe-AHEAD underway: global RCT of efficacy and safety of molnupiravir of PEP to prevent spread of COVID-19 among household contacts
- Investigate capacity for off-target effects, since molnupiravir is substrate for host mitochondrial RNA polymerase
    - Studies do not show host mitochondrial function over 14 days was inhibited

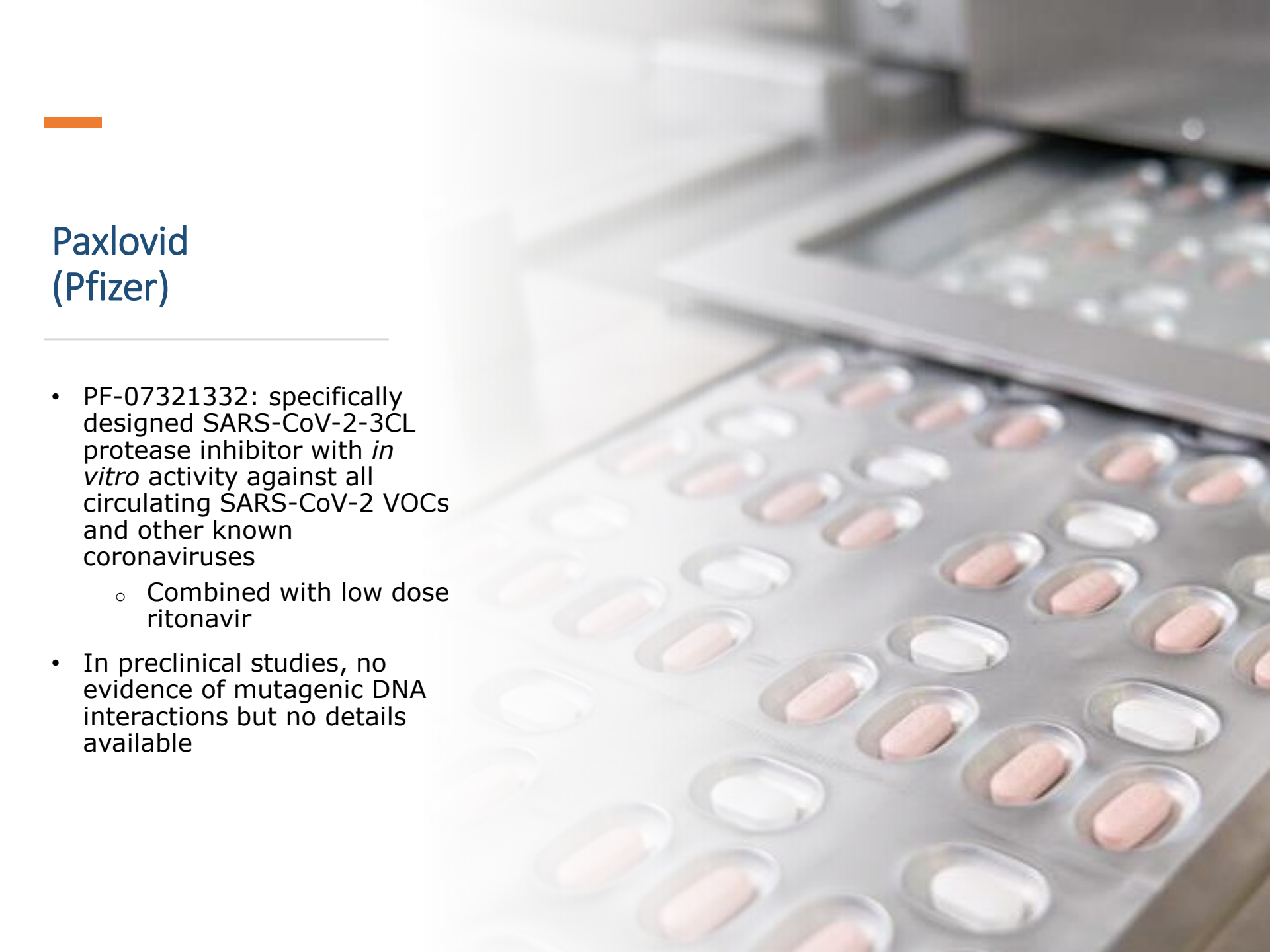
Credit: Merck & Co via Reuters

PAXLOVID™

Protease inhibitor given with ritonavir to prevent liver from breaking it down

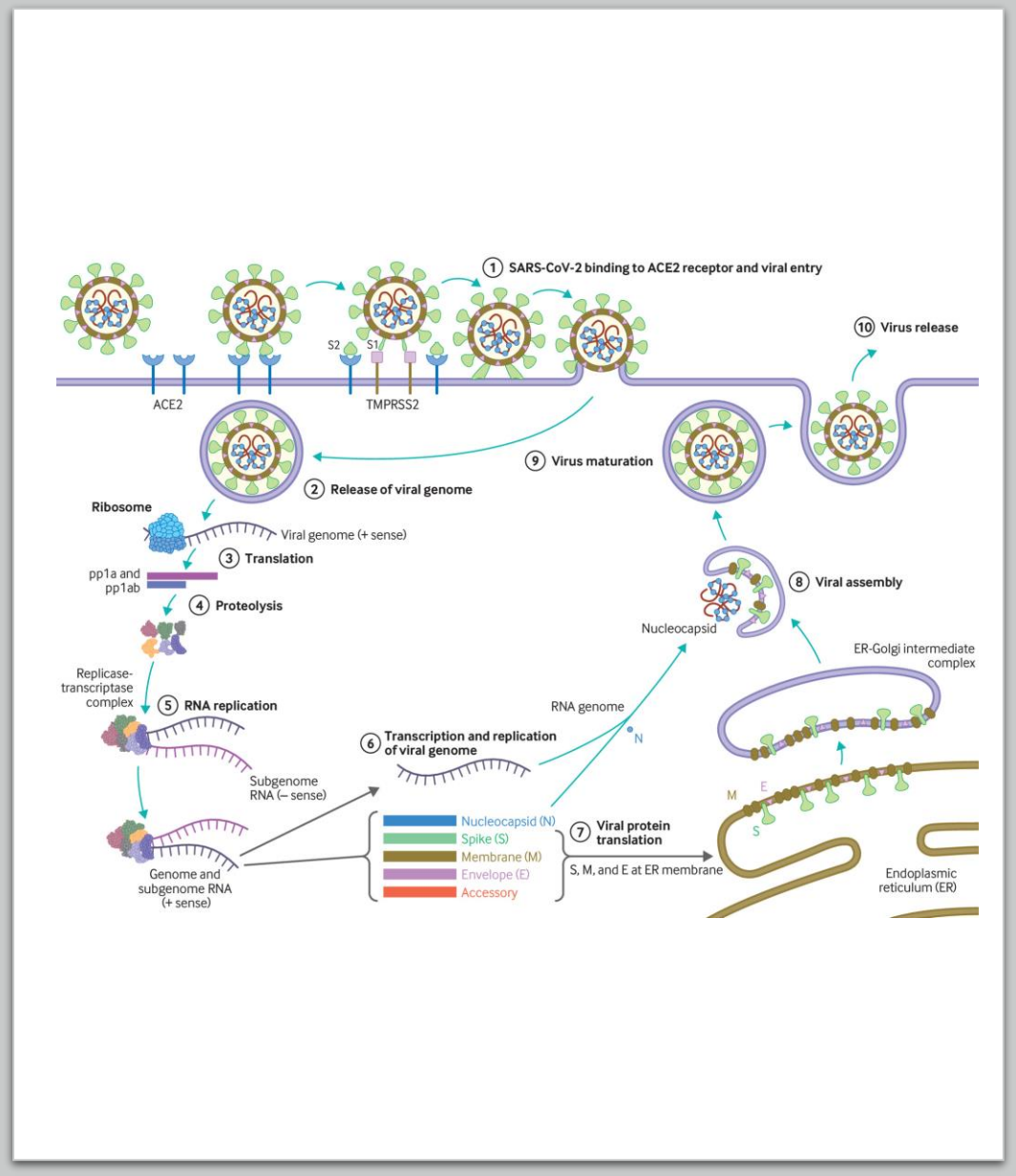
Paxlovid (Pfizer)

- PF-07321332: specifically designed SARS-CoV-2-3CL protease inhibitor with *in vitro* activity against all circulating SARS-CoV-2 VOCs and other known coronaviruses
  - Combined with low dose ritonavir
- In preclinical studies, no evidence of mutagenic DNA interactions but no details available



Mechanism of Action

- Paxlovid is extremely specific to inhibit coronavirus protease
- Ritonavir helps prevent its metabolism



Cevik M, et al. Virology, transmission, and pathogenesis of SARS-CoV-2
BMJ 2020; 371 :m3862 doi:10.1136/bmj.m3862

Ph 2/3 Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients (EPIC-HR)

Pfizer Press Release

Planned interim analysis of 1219 of 3,000 planned adult nonpregnant outpatients in 359 locations who had confirmed mild-mod COVID-19, within 3 days of onset, at risk for progression to severe disease

Significantly reduced the risk of hospitalization or death by ~89%. Through 28d post randomization:

- 0.8% of 389 in paxlovid group (3 hospitalized, 0 deaths)
- 7% of 385 in placebo (27 hospitalizations, 7 deaths)

85% reduction in hospitalization or death if used within 5 days of onset (1% vs 6.7%)

Incidence of AEs comparable in paxlovid and placebo groups

- Any AE 19% and 21% - most mild
- SAEs 1.7% and 6.6%
- AEs leading to discontinuation of therapy: 2.1% and 4.1%

Next Steps for Paxlovid

- Nov 16: requested FDA EUA
- Aug 2021: Phase 2/3 EPIC-SR (Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients – including subset with vaccination)
- Sept 2021: Phase 2/3 EPIC-PEP (Evaluation of Protease Inhibition for COVID-19 in Post-Exposure Prophylaxis [for household contacts])
- USG purchased 10M courses for $5B

Equitable Access for Molnupiravir and Paxlovid, Pending Regulatory Approvals

Merck/Ridgeback/Emory

- April 27: non-exclusive voluntary licensing agreements for molnupiravir with 5 Indian generic manufacturers to accelerate availability in 105 LMICs
- Oct: signed agreement with Medicines Patent Pool which will issue sublicenses to generic medicine producers for 105 countries
  - Companies will waive royalties as long as COVID-19 PHEIC

Pfizer

- Offer through tiered pricing approach based on income level of each country to promote equity
- Invest up to ~$1B to support manufacturing and distribution
- Nov 16: granted royalty-free license to Medicine Patent Pool to allow paxlovid to be made and sold inexpensively in 95 LMICs

Needed Research

- Human mitochondrial effects from molnupiravir
- DDI because of ritonavir with paxlovid
- Use in pregnancy, children
- Threshold for emergence drug resistance
- Pressure for mutuation
- To increase effectiveness and reduce likelihood of resistance to either drug, studies of combos of molnupiravir, paxlovid, remdesivir

Summary

	Molnupiravir	Paxlovid
Developer	Merck, Ridgeback, Emory	Pfizer
Mechanism of action	Lethal mutagenesis in transcription	Protease inhibitor
Dosing	4 pills Q12 5d	3 pills Q12 5d
Reduced the chance of hospitalization or death in COVID-19 adult patients at risk for severe illness	50% given within 5d of onset	- 89% given within 3d of illness onset - 85% within 5d of illness onset
Adverse effects	- 12% for treatment and 11% placebo - Drugs in same class linked to birth defects in animal studies	~20% both treatment and placebo
Supplies	High, with attention to equitable access	

CDC's Updated Recommendations for Use of COVID-19 Vaccines

Previous Recommendations on Additional COVID-19 Vaccine Doses

- Additional 3rd doses for people who are moderately or severely immunocompromised were only recommended for people 12 years of age or older (using the Pfizer-BioNTech vaccine) or 18 years of age or older (using the Moderna vaccine) after completing a primary 2-dose mRNA vaccine series (i.e., with the Pfizer-BioNTech or Moderna vaccines)
- Booster doses were only recommended for people 18 years of age or older who completed a primary series with either the Pfizer-BioNTech, Moderna, or Janssen vaccines (i.e., FDA authorized/approved vaccines)
- What about people vaccinated in another country with a different vaccine… could they get an additional primary series or booster dose?

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

CDC's Emergency Use Instructions (EUI)

- CDC issued (Nov 17th) Emergency Use Instructions (EUI) to provide additional recommendations for the Pfizer-BioNTech COVID-19 vaccine (the only FDA-approved, or fully licensed, vaccine)
- An EUI allows the CDC to recommend an FDA-approved vaccine (or other medical product) for emergency use in situations not included in the FDA-approval (i.e., not included in FDA's labeling and package insert)
- CDC's EUI provides guidance for administering the Pfizer-BioNTech COVID-19 vaccine as an additional primary series dose or as a booster to people who received a non-FDA authorized/approved COVID-19 vaccine (i.e., received a vaccine in another country, or as part of a clinical trial)

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

EUI Applies to the Following Non-FDA Approved/Authorized COVID-19 Vaccines

- COVID-19 vaccines that are World Health Organization (WHO) Emergency Use Listed (EUL):
  - AstraZeneca-Oxford
  - Sinopharm
  - Sinovac/CoronaVac
  - Bharat-Biotech
- COVID-19 vaccines that are not WHO-EUL but are part of a clinical trial for which "a U.S. data and safety monitoring board or equivalent has independently confirmed efficacy":
  - Novavax
  - Moderna (being studied in children <18 years of age)

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

EUI Recommendations (Applies to the Pfizer-BioNTech COVID-19 Vaccine Only)

- Under the CDC's EUI, the following persons who completed a primary series with one of the previously mentioned non-FDA authorized/approved vaccines can receive an additional primary series or booster dose of the Pfizer-BioNTech COVID-19 vaccine (*30 mcg dose from the purple cap vial*):
  - Persons 12 years of age or older who are moderate-severely immunocompromised can receive an additional primary series dose (i.e., additional 3rd dose for immunocompromised) of the Pfizer-BioNTech COVID-19 vaccine starting at least 28 days after completion of the primary series
  - Persons 18 years of age or older can receive a single booster dose of the Pfizer-BioNTech COVID-19 vaccine starting at least 6 months after completion of their primary vaccine series, per existing booster dose recommendations

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Review the Following Guidance and Resources

- CDC's Interim Clinical Considerations for Use of COVID-19 Vaccines, including the following sections:
  - Updated guidance on People who received COVID-19 vaccine outside the United States
  - Updated guidance on People who received COVID-19 vaccine as part of a clinical trial

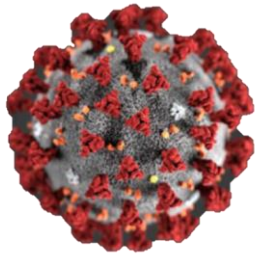
- CDC's EUI Healthcare Providers Fact Sheet

- CDC's EUI Fact Sheet for Recipients and Caregivers (which should be provided to vaccine recipients receiving the Pfizer-BioNTech COVID-19 vaccine under CDC's EUI)

Q&A

Healthcare Provider & Public Health Partner Calls

- **1st and 3rd Thursday** of each month from 12:00-1:00 pm (Next call will be December 2nd)
- Webinar/call information (stays the same):
  - Zoom link: https://nh-dhhs.zoom.us/s/94059287404
  - Webinar ID: 940 5928 7404
  - Passcode: 353809
  - Telephone: 646-558-8656



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