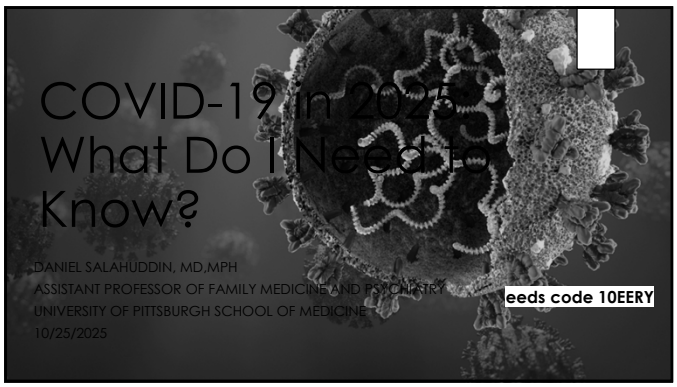
PENNSYLVANIA ACADEMY of FAMILY PHYSICIANS

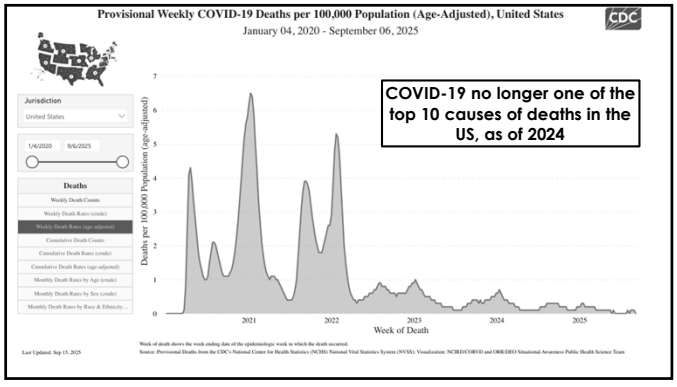


1

Learning Objectives

Explain	Define	Describe
Various treatment options available for COVID-19, taking patient risk profile into consideration	Long COVID and summarize associated risk factors and clinical approach	Various prevention strategies, including agents actively being investigated, for COVID-19

2



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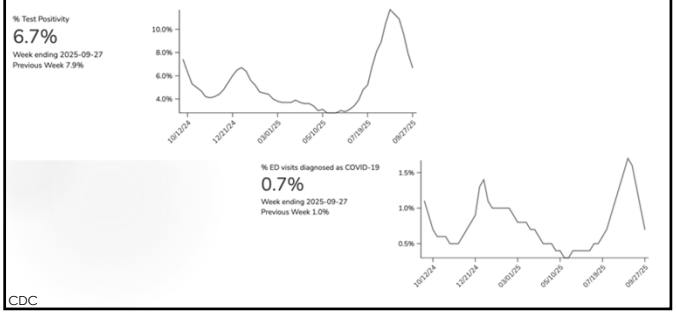
We've Come a Long Way



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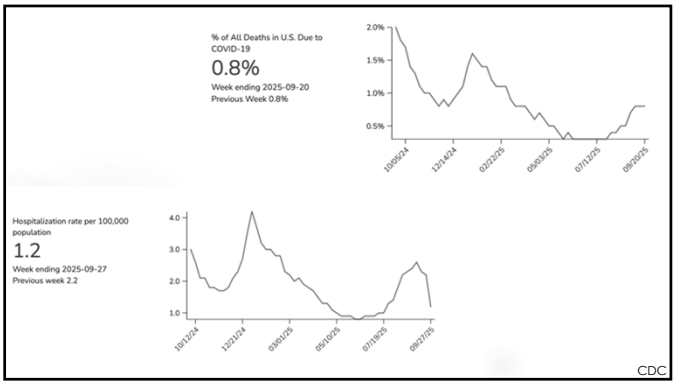

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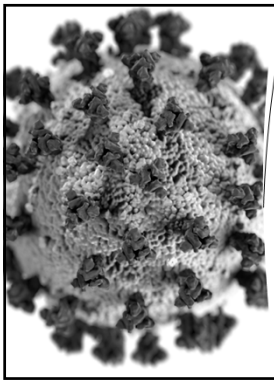

COVID-19 in 2025

- Annual bimodal peaks in late summer and winter
- Severe disease still prevalent, particularly in the West and South Central part of the US
  - Lower in the eastern US
- XFG variant, aka "Stratus," first detected in US in March 2025
  - Recombinant of two existing Omicron strains, LF.7 and LP.8.1.2 (WHO)
- Overtook NB.1.8.1 variant, aka "Nimbus," during summer months
- Highly contagious, although not as severe

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Surveillance Data

- Less reliable because of COVID-19 funding cuts
  - May 11, 2023: End of COVID-19 Public Health Emergency Declaration
  - May 1, 2024: Hospitals no longer being required to report their COVID data to CDC
    - Shift to COVID-NET, which uses hospitalization rates per 100,000 people instead of national counts
      - Only 13 states participating, covering ~10% of the US population (~34 million people), so questionable generalizability
  - March 24, 2025: Cancellation of $11.4 billion in grants awarded during height of pandemic since January 2025
    - Used by states to support COVID testing and vaccination, in addition to putting more trained community health workers in communities disproportionately impacted by COVID-19 to address disparities
    - National Institute of Allergy and Infectious Diseases also impacted
      - $577 million effort to develop new drugs to treat COVID-19
    - Office of Long COVID Research and Practice closed
- Wastewater data not as reliable as previous

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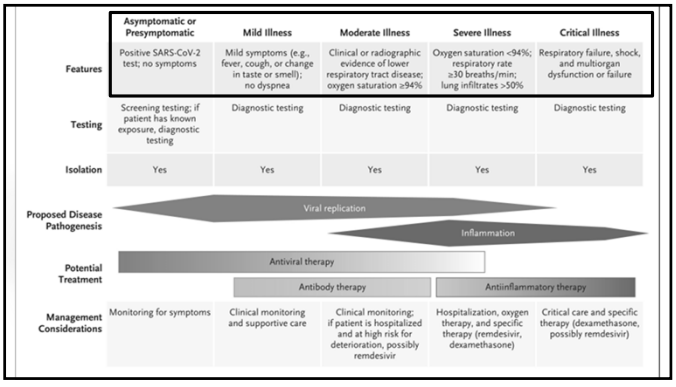
Outpatient Treatment Options

- Consider treatment in patients with mild-to-moderate symptoms who have one or more risk factors for severe COVID-19 **to reduce likelihood of progression to hospitalization and death**
  - Nirmatrelvir/ritonavir (Paxlovid)
  - Remdesevir (Veklury)
  - Molnupiravir (Lagrevio)
- Pre-exposure prophylaxis (PrEP) available for some people who are moderately or severely immunocompromised
- Age is most important risk factor for severe outcomes of COVID-19, with risk increasing substantially above 65 years
- Risk stratification
  - For patients with mild illness not at high risk, supportive care and home isolation remain the mainstay, with close monitoring for symptom progression
- Isolation guidelines

8



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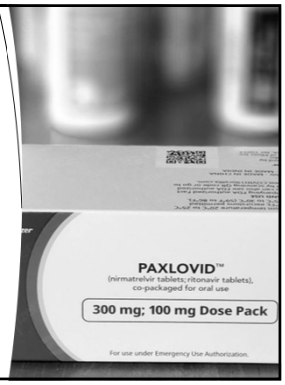
Nirmatrelvir/ritonavir (Paxlovid)

- Reduced risk of hospitalization and death by 86% in unvaccinated patients with COVID-19 at higher risk of severe disease
- Initiate within 5 days
- BID dosing x 5 days
- Approved for use in adults and pediatrics (12+, weighing at least 40kg)
- Some dosing adjustment may be needed
- Contraindicated in severe kidney (eGFR <30 mL/min) and liver disease (Child-Pugh Class C)
  - Renal dosing with eGFR between 30 to 60mL/min
- Presents a risk of rebound (mild symptoms 3-7 days following resolution of initial illness), however, benefits outweigh the risks for patients at higher risk for severe disease from COVID-19
  - Retreatment after rebound is safe and linked to a faster decline in viral RNA levels, however, no clear clinical benefit because rebound tends to be mild, short-lived, and does not lead to severe illness



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Nirmatrelvir/ritonavir (Paxlovid) Medication Interactions

- Due to ritonavir → potent inhibitor of cytochrome P450 3A4
  - Statins (hold for duration of treatment and for 5 days thereafeter)
  - Rivaroxaban (avoid due to increased bleeding risk)
  - Salmeterol (avoid due to cardiac effects)
  - Hormone contraceptives with ethinyl estradiol (nonhormonal contraception until one menstrual cycle after course)
  - Quetiapine (reduce dose to one-sixth of original dose during course)
  - Liverpool COVID-19 Interactions

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Absolute contraindications include co-administration with:

- Certain antiarrhythmics (amiodarone, dronedarone, flecainide, propafenone, quinidine)
- Ergot derivatives (dihydroergotamine, ergotamine, methylergonovine)
- Statins (lovastatin, simvastatin)
- Immunosuppressants (voclosporin)
- Antipsychotics (lurasidone, pimozide)
- Alpha-1 blockers (alfuzosin, silodosin)
- Cardiovascular agents (eplerenone, ivabradine)
- Migraine medications (eletriptan, ubrogepant)
- Opioid antagonists (naloxegol)
- Sedative/hypnotics (triazolam, oral midazolam)
- Flibanserin
- Vasopressin receptor antagonists (tolvaptan)
- St. John's Wort (a CYP3A inducer, which can reduce Paxlovid efficacy and promote resistance)

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Morbidity and Mortality Weekly Report

Racial and Ethnic Disparities in Outpatient Treatment of COVID-19 — United States, January–July 2022

Tegan K. Boehmer, PhD[1]; Emily H. Koumans, MD[1]; Elizabeth L. Skillen, PhD[1]; Michael D. Kappelman, MD[2]; Thomas W. Carton, PhD[3]; Aditiben Patel, MPH[1,4]; Euna M. August, PhD[5]; Ryan Bernstein[1,4]; Joshua L. Denson, MD[6]; Christine Draper[7]; Adi V. Gundlapalli, MD, PhD[1]; Anuradha Paranjape, MD[8]; Jon Puro, MHA[9]; Preetika Rao, MPH[1]; David A. Siegel, MD[1]; William E. Trick, MD[10]; Chastity L. Walker, DrPH[11]; Jason P. Block, MD[7]

- 700,000 patients who sought COVID-19 care at 30 sites participating in the National Patient-Centered Clinical Research Network
  - Dramatic increase in patients treated with nirmatrelvir/ritonavir during study period, from 0.6% to 34%, however, significant prescribing disparities
    - Black patients were 35.8% less likely to be prescribed nirmatrelvir/ritonavir than white patients
    - Hispanic patients were 29.9% less likely to be prescribed nirmatrelvir/ritonavir than non-Hispanic patients
    - 23.1% lower among American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander patients
    - 19.4% lower among Asian patients
  - Proportion of COVID-19 patients treated with monoclonal antibodies or the antivirals molnupiravir (Lagevrio) or remdesivir (Veklury) remained low throughout the study period

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Remdesevir (Veklury)

- Reduced risk of hospitalization and death by 87% in unvaccinated patients with COVID-19 at higher risk of severe disease
- Infusion over 30-120 min over 3 consecutive days within 7 days of symptom onset
- PT and liver function tests prior to initiation
- Approved for use in adults and pediatrics (>28 days, weighing >3kg)
- Some dosing adjustment may be needed
- Approved in mild to severe renal impairment

14

Molnupiravir (Lagrevio)

- To be used when nirmatrelvir/ritonavir or remdesivir are not accessible or clinically appropriate
- Net benefit in improving recovery and reducing time to recovery, however, no mortality benefit
- Little evidence of effectiveness, particularly among vaccinated individuals

15

Inpatient Treatment Options

- For moderate-to-severe COVID-19
  - Remdesevir (Veklury)
    - Reduces progression and mortality in hospitalized, non-ICU patients
  - Corticosteroids (i.e. dexamethasone)
    - Indicated for those requiring supplemental oxygen or ventilatory support
    - Reduces mortality and progression to critical illness
  - Immunomodulatory therapy (i.e. IL-6 receptor antagonists such as tocilizumab or sarilumab)
    - May improve outcomes when added to corticosteroids
  - Convalescent plasma
    - NOT recommended
    - Could consider in select high-risk outpatient cases when no alternatives exist

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Long COVID

- Also referred to as Post-COVID Conditions (PCC)
- Infection-associated chronic condition that is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state
  - Affects one or more organ systems
  - Associated with new or recurrent symptoms and conditions after symptoms of initial acute COVID-19 illness have resolved
  - Spectrum of physical, social, and psychological consequences
  - Functional limitations that affect patient wellness and quality of life, and may cause disability
  - Definition continues being refined
- Roughly 17 million Americans reported having long-COVID symptoms in March 2024
- Variability in long COVID prevalence across published definitions highlights the need for a standardized, validated definition to improve clinical recognition and research comparability, ultimately guiding more accurate diagnosis and treatment strategies

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Long COVID cont'd

- Difficult to distinguish from symptoms that occur for alternative reasons
  - Organ damage from acute phase infection
  - Complications from a dysregulated inflammatory state
  - Microvascular dysfunction
  - Ongoing viral activity associated with an intra-host viral reservoir
  - Autoimmunity
  - Inadequate antibody response
- More common in women, Latine individuals, infection from pre-Omicron variants, those experiencing more severe outcomes of COVID-19, people with underlying health conditions, and people who did not get the COVID-19 vaccine
- Best practices are to validate symptoms and to connect patients to additional care, services, and supports, as appropriate
- Should promote vaccination as a means of preventing Long COVID

18

Prevention

- COVID-19 Vaccines available in the US, 2025-26
  - Target the JN.1 lineage, preferentially using the LP.8.1 strain
    - Pfizer-BioNTech COVID-19 vaccine (Comirnaty), available for people age 6 months and older
    - Moderna COVID-19 vaccine (Spikevax), available for people age 6 months and older
    - Novavax COVID-19 vaccine (Nuvaxovid), available for people age 12 years and older
- Annual boosters work!
  - Last season's 2024–2025 mRNA COVID vaccines reduced people's risk of emergency department visits by 29 percent, their risk of hospitalizations by 39 percent and their risk of death by 64 percent
  - Across all age groups and "in persons with or without major chronic conditions"
- Call to action: Just 21% of the adult US Population got vaccinated against COVID last year

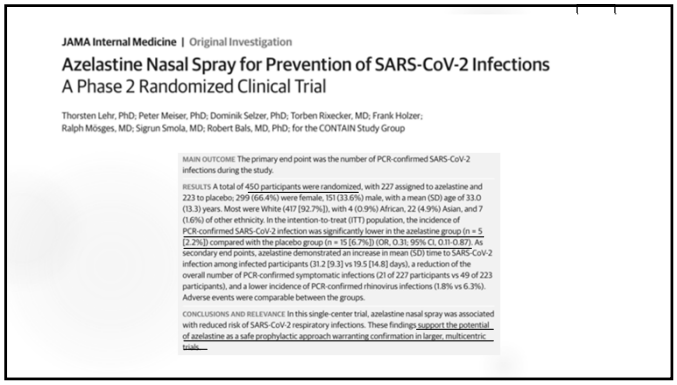
19

20

COVID-19 PrEP

- Available for individuals who are moderately or severely immunocompromised
- Pemivibart (Pemgarda)
  - IV-infusion mAb authorized for PrEP of COVID-19 for individuals 12+, weighing at least 40kg
  - Given at least 2 weeks following vaccination
  - Single infusion over 60 minutes q3 months
  - Still under active investigation, therefore limited safety and effectiveness data
  - Decreased potency among the latest Omicron sublingeages

21



JAMA Internal Medicine | Original Investigation

Azelastine Nasal Spray for Prevention of SARS-CoV-2 Infections
A Phase 2 Randomized Clinical Trial

Thorsten Lehr, PhD; Peter Meiser, PhD; Dominik Selzer, PhD; Torben Rixecker, MD; Frank Holzer; Ralph Mösges, MD; Sigrun Smola, MD; Robert Bals, MD, PhD; for the CONTAIN Study Group

MAIN OUTCOME The primary end point was the number of PCR-confirmed SARS-CoV-2 infections during the study.

RESULTS A total of 450 participants were randomized, with 227 assigned to azelastine and 223 to placebo; 299 (66.4%) were female, 151 (33.6%) male, with a mean (SD) age of 33.0 (13.3) years. Most were White (417 [92.7%]), with 4 (0.9%) African, 22 (4.9%) Asian, and 7 (1.6%) of other ethnicity. In the intention-to-treat (ITT) population, the incidence of PCR-confirmed SARS-CoV-2 infection was significantly lower in the azelastine group (n = 5 [2.2%]) compared with the placebo group (n = 15 [6.7%]) (OR, 0.31; 95% CI, 0.11-0.87). As secondary end points, azelastine demonstrated an increase in mean (SD) time to SARS-CoV-2 infection among infected participants (31.2 [9.3] vs 19.5 [14.8] days), a reduction of the overall number of PCR-confirmed symptomatic infections (21 of 227 participants vs 49 of 223 participants), and a lower incidence of PCR-confirmed rhinovirus infections (1.8% vs 6.3%). Adverse events were comparable between the groups.

CONCLUSIONS AND RELEVANCE In this single-center trial, azelastine nasal spray was associated with reduced risk of SARS-CoV-2 respiratory infections. These findings support the potential of azelastine as a safe prophylactic approach warranting confirmation in larger, multicentric trials.

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Post-Test Questions

23

True or False?

COVID-19 remained a top 10 cause of death in the US, based off data from 2024.

FALSE

24

True or False?

There are no other outpatient treatment options if a patient is not a candidate for nirmatrelvir/ritonavir (Paxlovid).

FALSE

25

True or False?

Vaccination remains the mainstay of prevention of severe disease from COVID-19 and Long COVID.

TRUE

26

Questions?

27

Please take a moment to complete the session evaluation. Your input is important!

28

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