Jackson Health Network COVID-19 Update

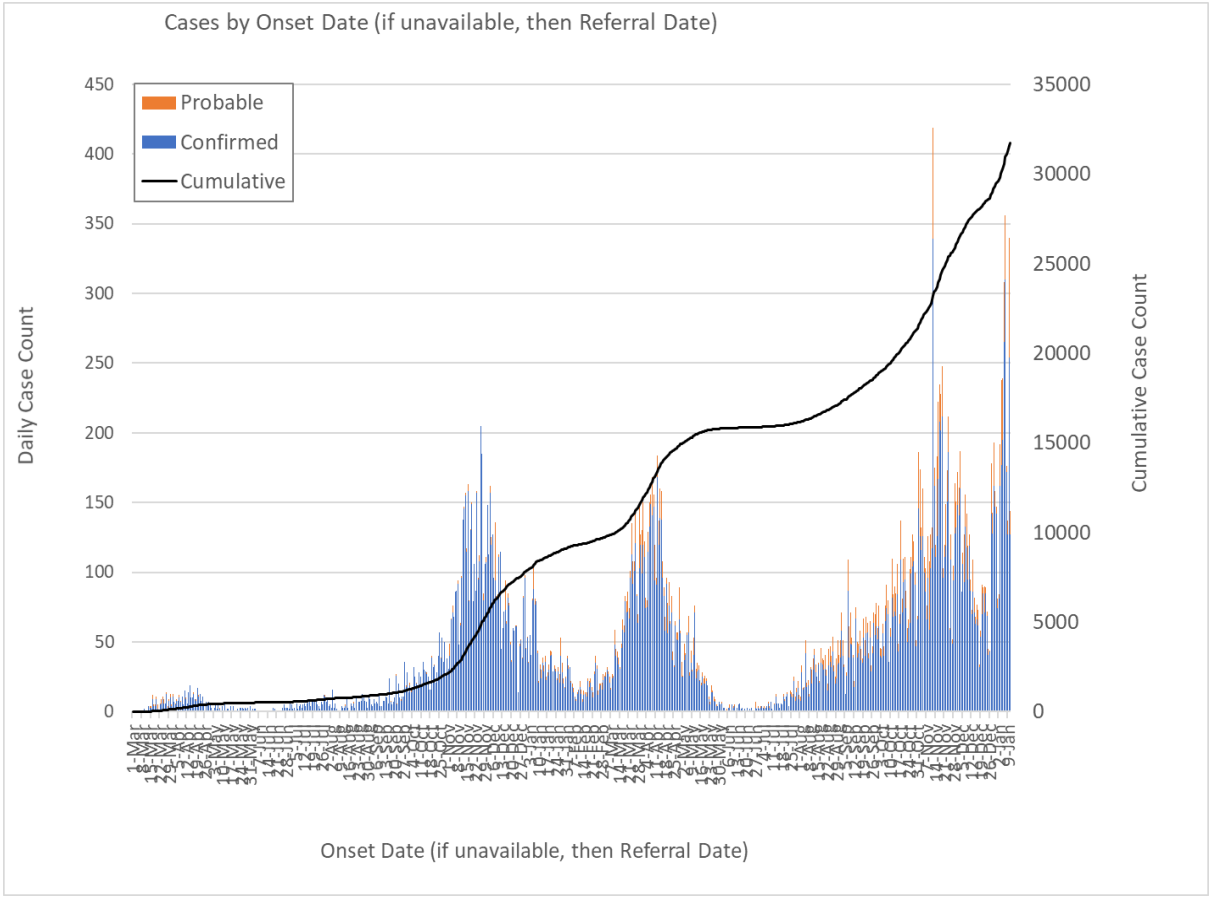
January 12, 2022

Agenda

- Local Jackson County Update
- CDC Isolation/Quarantine Guidelines
- CDC Vaccination Guidelines
- Monoclonal Antibody
- Emerging Treatment Options

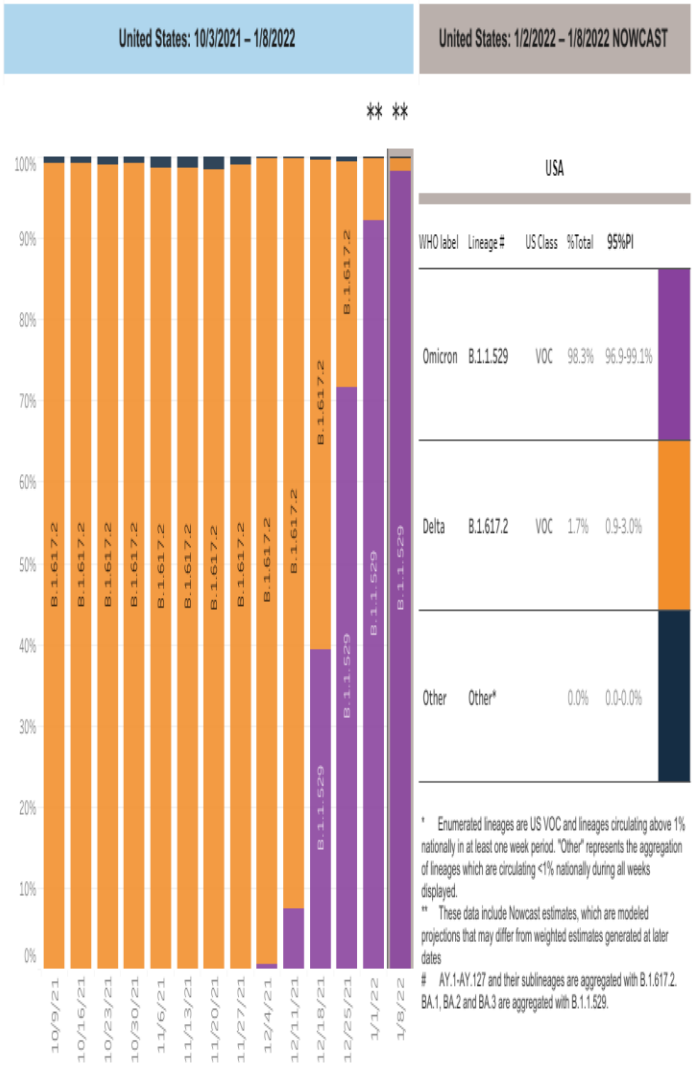
Jackson County

- 31,374 total cases since March 2020
- 3,838 active cases
  - 4,580 all time high on 12/8/21
- 2,150 new in last week
  - 20% in under 19
- 441 deaths
  - Average 2 per day since 11/1/21

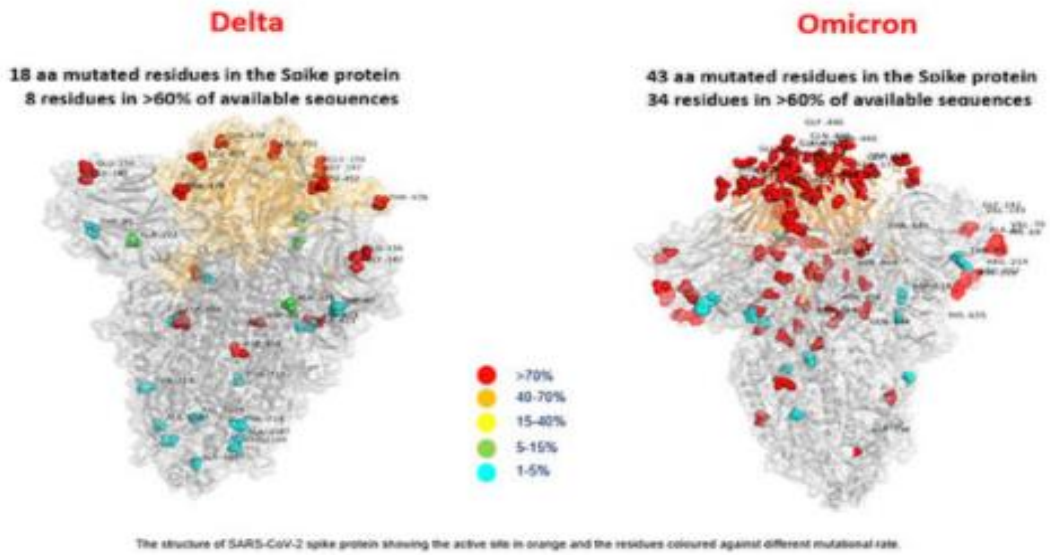


Omicron (B.1.1.529)

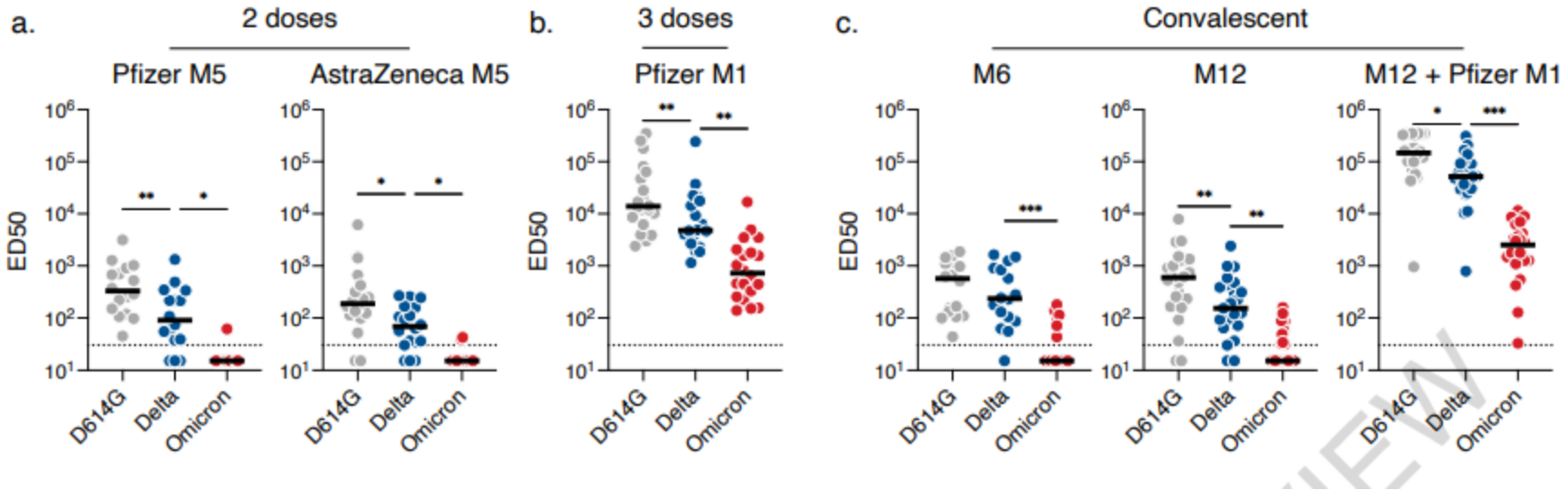
- Unprecedented increase in cases
- Expect 6 to 8 weeks of heavy numbers
- Omicron has two distinct viruses
  - 22K (PCR did not detect one of 3 primary PCR targets – S gene target failure)
  - 22L (stealth version: no SGTF, making it harder to detect)
- Challenging to know how much Omicron is in the state
  - Sequencing process takes 7 days at state lab
- CDC surveillance → virtually all Omicron



Omicron Escapes Immune Protection



Large number of mutations in the spike protein, especially the RBD where the spike protein binds to ACE2 receptors



Source: https://www.acrobiosystems.com/A1353-According-to-the-mutations%3A-Why-is-Omicron-causing-such-concern.html?gclid=EAIaIQobChMI7Lz13-Sb9QIVOWtvBB3ktwf7EAAYASAAEgLW_PD_BwE. Accessed January 11, 2021

Source: Schwartz et al. Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. Nature. December 23, 2021.

Quarantine: restricts movement of people exposed to a contagious disease.

Date of exposure is day 0, Day 1 is first full day after contact. Stay home and away from people for at least 5 days.			
IF YOU Were exposed to COVID-19 **AND** Not up-to-date with vaccination	**Quarantine at least 5 days**	**After Quarantine**	**Precautions through day 10**
	Stay home	Monitor for symptoms for full 10 days	Wear a mask
	Wear a mask around others at home	Isolate if symptoms develop	Avoid travel
	Get tested at least 5 days after exposure	Get tested if symptoms develop	Avoid other people at high risk

IF YOU Were exposed to COVID-19 **AND** Up-to-date with Vax **OR** COVID-19+ past 90 days	**No Quarantine**	**Monitor**	**Precautions through day 10**
		Monitor for symptoms for full 10 days	Wear a mask
		Isolate if symptoms develop	Avoid travel
	Get tested at least 5 days after exposure	Get tested if symptoms develop	Avoid other people at high risk

Source: https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html. Accessed January 11, 2022.

Isolation: separates sick people with a contagious disease from others.

Day 0 is your first day of symptoms or a positive viral test. Day 1 is the first full day after your symptoms developed or your test specimen was collected.

IF YOU	**Isolate at least 5 days**	**Ending Isolation**	**Precautions through day 10**
Tested positive for COVID-19 or have symptoms, regardless of vaccination status	Stay home	If Symptomatic: 5 days + fever free without medication for 24 hours and symptoms are improving.	Wear a mask
	Stay away from others in your home	If Asymptomatic: 5 days after positive test result.	Avoid travel
	Wear a mask if you must be around others in your home	If Severely Ill (hospitalized): At least 10 and up to 20 days.	Avoid other people at high risk

Source: https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html. Accessed January 11, 2022.

COVID-19 Vaccine

TABLE 1. COVID-19 vaccines: primary series and additional primary dose

Vaccine manufacturer	Age indication	Vial cap color denoting formulation	Dose	Injection volume	Number of doses in primary series (interval between doses)	Additional primary dose in immunocompromised people (interval since second dose)
Pfizer-BioNTech	5–11 years	Orange	10 µg	0.2 mL	2 (21 days)	1 (≥28 days)
Pfizer-BioNTech	≥12 years	Purple or gray	30 µg	0.3 mL	2 (21 days)	1 (≥28 days)
Moderna	≥18 years	Not applicable	100 µg	0.5 mL	2 (28 days)	1 (≥28 days)
Janssen	≥18 years	Not applicable	5×10^{10} viral particles	0.5 mL	1 (Not applicable)	Not applicable

TABLE 2. COVID-19 vaccines: booster dose by primary series

Vaccine completed for primary series	Authorized age for vaccine booster	Interval between last primary dose (including additional dose, when applicable) and booster dose	Number of doses	Injection volume and product that may be given as booster dose*†
Pfizer-BioNTech	≥12 years	≥5 months	1	0.3 mL Pfizer-BioNTech*, or 0.25 mL Moderna, or 0.5 mL Janssen†
Moderna	≥18 years	≥5 months	1	0.25 mL Moderna, or 0.3 mL Pfizer-BioNTech, or 0.5 mL Janssen†
Janssen	≥18 years	≥2 months	1	0.5 mL Janssen†, or 0.3 mL Pfizer-BioNTech, or 0.25 mL Moderna

*Only Pfizer BioNTech can be used as a booster dose in those ages 12–17 years.
†Use of an mRNA vaccine for a booster dose is preferred over Janssen vaccine.

Testing Resources

PCR Testing

- Henry Ford Allegiance Health
  - Drive-through, Walk-in, Clinic
  - Contact: 517-205-6100
  - Do Test: symptomatic, exposed, pre-procedure
  - Don't Test: no exposure, travel, return-to-work
  - Where: 2200 Springport Rd, Jackson, MI 49202
- Center for Family Health
  - Contact: 517-748-5363
  - Where: 505 N Jackson Street, Jackson, MI 49201
- IEP Urgent Care
  - Contact: 517-295-2473
  - Where: 729 E. Michigan Ave, Jackson, MI 49201
- Well Now Urgent Care*
  - Contact: 517-395-2246
  - Where: 1325 North West Avenue, Jackson, MI 49202

Antigen Testing

- Rite Aid*
- CVS*
- Walgreen's*
- Meijer*

*Not JHN member, which may impact out-of-pocket patient costs

Monoclonal Antibody Therapy

- Omicron is resistant to 2 of the 3 monoclonal antibody products available in the United States
  - Eli Lily (bamlanivimab + etesevimab) resistant
  - Regeneron (casirivimab + imdevimab) resistant
  - GSK (sotrovimab) susceptible
- HFHS moved to only administer sotrovimab as we had high suspicion that omicron dominated in Michigan
- Sotrovimab is in very limited supply → more strict criteria
  - Within 7 days onset of symptoms (vs 10)
  - Pregnancy
  - Immunocompromised (primary immunodeficiency, active chemo, transplant biologic immunomodulators, HIV with uncontrolled viral load, steroids 20 mg/day for at least two weeks)
  - Age 75 and older (vs 65)
  - Renal replacement therapy
  - Severe lung disease with supplemental O2 requirement
  - BMI $\geq$ 40 (vs 25)

Access to MAB

- For physicians on the HFHS instance of Epic (including Community Care Connect), order “Ambulatory Referral to Monoclonal Antibody Infusion (mAB)” in Epic. The order will trigger hub staff to contact the patient to arrange treatment.
- Physicians not on Epic should call the Referring Physician Office at 877-434-7470. The RPO will then connect with the hub, which arranges treatment.
- PIIC Center: 517-788-4781

OUTPATIENT MANAGEMENT

- Push vaccination
- Ensure everyone has gotten the booster
- Recommend masking
- As a clinician we can’t say if it’s the omicron variant despite some differences in presentation

MANAGEMENT

- Isolation
- Ensure that individuals especially elderly , patients with comorbidities, unvaccinated have a pulse oximeter at home and use it
- Do incentive spirometry
- Sleep prone

MANAGEMENT

- PROPHYLAXIS
- MONOCLONAL ANTIBODY
- ANTIVIRALS

OPTIONS

- Paxlovid (nirmatrelvir 300 mg plus ritonavir 100 mg) orally twice daily for 5 days
- Sotrovimab 500 mg administered as a single intravenous (IV) infusion
- Remdesivir 200 mg IV on Day 1 followed by remdesivir 100 mg IV on Days 2 and 3
- Molnupiravir 800 mg orally twice daily for 5 days

WHAT OPTIONS DON'T OUR OP PATIENT'S HAVE YET

- Remdesivir as OP; Suspect FDA will likely approve in the coming week
- Sotrovimab is in extremely short supply
- Antivirals are also in short supply

WHO IS ELIGIBLE : PAXLOVID

- Any age with moderate to severe immunocompromise (despite vaccine)
- >75 and not maximally vaccinated

GIVEN within first 5 days

LOTS OF DRUG-DRUG INTERACTIONS

SOTROVIMAB

- Any age with moderate to severe immunocompromise (despite vaccine)
- >75 and not maximally vaccinated
- 65-74: Not maximally vaccinated and comorbid conditions(obesity/ Chronic lung disease/ pregnancy/CVD/CKD/DM)
- >75 and maximally vaccinated
- 65-74: maximally vaccinated and comorbid conditions(obesity/ Chronic lung disease/ pregnancy/CVD/CKD/DM)

WITHIN first 10 days: though for system it is 7 days

MOLNUPIRAVIR

- Any age with moderate to severe immunocompromise (despite vaccine)
- >75 and not maximally vaccinated

ALTERNATIVE ONLY AND GIVEN FIRST 5 DAYS

HOW TO ORDER

- MAB: Through the Hub
- Antivirals;

  Only Meijer

  in Jackson: only the airport road Meijer:7830010

  Adrian : 2662110

  Ypsilanti: 7346777110
- Prescriber calls Meijer and sees if they have drug
- See if Eligible
- Discusses med and side effects and gives FDA sheet
- Fills the Electronic or Paper prescription and faxes it: can give to patient also but it delay filling
- NO TELEPHONE SCRIPTS

DATA SUMMARY

- Ritonavir-boosted nirmatrelvir (Paxlovid) reduced the risk of hospitalization or death by 88% compared to placebo in nonhospitalized adults with laboratory-confirmed SARS-CoV-2 infection
- Sotrovimab (i.e., 85% relative reduction)
- Remdesivir (i.e., 87% relative reduction)
- Molnupiravir (i.e., 30% relative reduction)

PREEXPOSURE PROPHYLAXIS (EVUSHELD)

- **Tixagevimab plus cilgavimab** as SARS-CoV-2 PrEP for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, **AND** who:
- Are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination ; *or*
- Are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe reactions to a COVID-19 vaccine or any of its component

PINETREE (REMDESIVIR)

- 3 consecutive days of IV remdesivir resulted in an 87% relative reduction in the risk of hospitalization or death compared to placebo.

- Remdesivir is currently approved by the FDA for use in hospitalized individuals, and outpatient treatment would be an off-label indication

- Needs Insurance coverage

WHAT ABOUT ORAL STEROIDS(RECOVERY)

- In hospitalized patients with severe COVID-19 who required supplemental oxygen, DEX reduced mortality at 28 days, with greatest benefit in those with MV at randomization

- No survival benefit of DEX in patients who did not require supplemental oxygen at base

- Would consider use in OP if any desaturation below 94

- Don’t go over 10 days: in OP would aim for 5-7 days

Unclear Benefits

- Inhaled Steroids
- Fluvoxamine

INHALED STEROIDS

•**Key Inclusion Criteria:** Aged ≥65 years or aged ≥50 years with comorbidities •PCR-confirmed or suspected COVID-19 •≤14 days of symptoms **Key Exclusion Criteria:** •Already taking inhaled or systemic corticosteroids •Unable to use an inhaler •Contraindication to inhaled budesonide **Interventions:** •Usual care plus budesonide 800 mcg inhaled twice daily for 14 days (n = 1,069) •Usual care (n = 787) **Primary Endpoints:** •COVID-19-related hospitalization or death up to 28 days from randomization •Time to reported recovery up to 28 days from randomization	**Participant Characteristics:** •Mean age 64.2 years; 52% women; 92% White •81% with comorbidities •Median time from symptom onset to randomization: 6 days **Primary Outcomes:** •Percentage of patients who were hospitalized or died due to COVID-19 within 28 days: 6.8% in budesonide arm vs. 8.8% in usual care arm (OR 0.75; 95% CrI, 0.55–1.03). •Median time to reported recovery: 11.8 days in budesonide arm vs. 14.7 days in usual care arm (HR 1.21; 95% CrI, 1.08–1.36).	•**Key Limitations:** Open-label trial •Primary endpoint of time to reported recovery based on participant self-report **Interpretation:** •Inhaled budesonide reduced time to reported recovery but not COVID-19-related hospitalization or death. •The clinical significance of self-reported time to recovery in an open-label study is unclear.

INHALED STEROIDS

•**Key Inclusion Criteria:** Aged ≥18 years •≤7 days of symptoms **Key Exclusion Criteria:** •Use of inhaled or systemic glucocorticoids in past 7 days •Known allergy or contraindication to budesonide **Interventions:** •Usual care plus budesonide 800 mcg inhaled twice daily until symptom resolution (n = 73) •Usual care (n = 73) **Primary Endpoint:** •COVID-19-related urgent care visit, including ED visit or hospitalization	**Participant Characteristics:** •Mean age 45 years; 58% women •9% with CVD, 5% with DM •95% with positive SARS-CoV-2 RT-PCR result •Median time from symptom onset to randomization: 3 days **Primary Outcomes:** •Median duration of budesonide use: 7 days. •Percentage of patients with COVID-19-related urgent care visit or hospitalization: 1% in budesonide arm vs.14% in usual care arm (relative risk reduction 91%).	•**Key Limitations:** Small, open-label trial •Early termination after statistical analysis determined that additional participants would not alter study outcome **Interpretation:** •In adult outpatients with mild COVID-19, inhaled budesonide may reduce the need for urgent care or ED assessment and/or hospitalization.

INHALED STEROIDS

•**Key Inclusion Criteria:** Aged ≥18 years •Positive SARS-CoV-2 molecular diagnostic test result •≥1 symptom of fever, cough, or shortness of breath •Symptom duration ≤6 days **Key Exclusion Criteria:** •Already taking an inhaled corticosteroid or taken PO or IM corticosteroids within 7 days of enrollment •Unable to use an inhaler •No respiratory symptoms •Use of oxygen at home •COVID-19 vaccinated **Interventions:** •Ciclesonide MDI 600 µg/actuation and intranasal ciclesonide 100 µg, both twice a day for 14 days (n = 105) •Saline placebo MDI and intranasal saline, both twice a day for 14 days (n = 98) **Primary Endpoint:** •Resolution of fever and all respiratory symptoms at Day 7 **Key Secondary Endpoints:** •Resolution of fever and all respiratory symptoms at Day 14 •Hospital admission by Day 14	**Participant Characteristics:** •Median age 35 years; 54% women; 61% White •20% with comorbid condition **Primary Outcome:** •Percentage of patients with resolution of fever and all respiratory symptoms at Day 7: 40% in ciclesonide arm vs. 35% in placebo arm (adjusted risk difference 5.5%; 95% CI, -7.8% to 18.8%). **Secondary Outcomes:** •Percentage of patients with resolution of fever and all respiratory symptoms at Day 14: 66% in ciclesonide arm vs. 58% in placebo arm (adjusted risk difference 7.5%; 95% CI, -5.9% to 20.8%). •Percentage of patients who were admitted to the hospital by Day 14: 6% in ciclesonide arm vs. 3% in placebo arm (adjusted risk difference 2.3%; 95% CI, -3.0% to 7.6%).	•**Key Limitation:** Small study with a relatively young, healthy population **Interpretation:** •The use of inhaled ciclesonide plus intranasal ciclesonide did not improve resolution of fever and respiratory symptoms in non-hospitalized patients with COVID-19.

FLUVOXAMINE (LUVOX)

•Fluvoxamine 50 mg PO for 1 dose, then fluvoxamine 100 mg twice daily, then fluvoxamine 100 mg 3 times daily through Day 15 (n = 80) •Placebo (n = 72) **Primary Endpoint:** •Clinical deterioration within 15 days of randomization. Clinical deterioration was defined as: • Having dyspnea or being hospitalized for dyspnea or pneumonia; *and* • Having SpO_2 <92% on room air or requiring supplemental oxygen to attain SpO_2 ≥92% **Key Secondary Endpoint:** •Hospitalization	**Participant Characteristics:** •Mean age 46 years; 72% women; 25% Black •56% with obesity; 20% with HTN; 17% with asthma •Median of 4 days from symptom onset to randomization **Primary Outcome:** •Clinical deterioration: 0% in fluvoxamine arm vs. 8.3% in placebo arm (absolute difference 8.7%; 95% CI, 1.8% to 16.4%) **Secondary Outcome:** •No patients in fluvoxamine arm and 4 patients in placebo arm were hospitalized.	•**Key Limitations:** Small sample size •Short follow-up period •Ascertaining clinical deterioration was challenging because all assessments were done remotely •24% of patients stopped responding to follow-up prior to Day 15 but were included in the final analysis **Interpretation:** •Fluvoxamine reduced the proportion of patients who experienced clinical deterioration. •Due to significant limitations, it is difficult to draw definitive conclusions about the efficacy of using fluvoxamine to treat COVID-19.

LUVOX

•**Key Inclusion Criteria:**Aged ≥50 years or aged ≥18 years with comorbidities •Laboratory-confirmed SARS-CoV-2 infection •≤7 days of symptoms **Key Exclusion Criteria:** •Use of an SSRI •Severe mental illness •Cirrhosis, recent seizures, severe ventricular cardia arrythmia **Interventions:** •Fluvoxamine 100 mg PO twice daily for 10 days (n = 741) •Placebo (route, dosing frequency, and duration for some patients may have differed from fluvoxamine) (n = 756) **Primary Endpoint:** •Composite endpoint of emergency setting observation for >6 hours or hospitalization due to progression of COVID-19 within 28 days after randomization **Key Secondary Endpoints:** •Occurrence of COVID-19-related hospitalizations •Time to symptom resolution •Proportion of patients who were adherent to study drugs, defined as receiving >80% of possible doses •Mortality in both the primary ITT population and a PP population that included patients who took >80% of the study medication doses	**Participant Characteristics:** •Median age 50 years; 58% women; 95% self-identified as mixed race •13% with uncontrolled HTN; 13% with type 2 DM; 50% with BMI ≥30 kg/m^2 •Mean of 3.8 days from symptom onset to randomization **Primary Outcome:** •Proportion of patients who met the primary composite endpoint: 11% in fluvoxamine arm vs. 16% in placebo arm (relative risk 0.68; 95% CrI, 0.52–0.88) **Secondary Outcomes:** •87% of clinical events were hospitalizations. •No difference between arms in COVID-19-related hospitalizations: 10% in fluvoxamine arm vs. 13% in placebo arm (OR 0.77; 95% CI, 0.55–1.05) •No difference between arms in time to symptom resolution. •Adherence: 74% in fluvoxamine arm vs. 82% in placebo arm (OR 0.62; 95% CI, 0.48–0.81). 11% in fluvoxamine arm vs. 8% in placebo arm stopped drug due to issues of tolerability. •Mortality (ITT): 2% in fluvoxamine arm vs. 3% in placebo arm (OR 0.68; 95% CI, 0.36–1.27) •Mortality (PP): <1% in fluvoxamine arm vs. 2% in placebo arm (OR 0.09; 95% CI, 0.01–0.47)	•**Key Limitations:** The >6-hour emergency setting observation endpoint has not been used in other studies of interventions for non-hospitalized patients who are at high risk for hospitalization and death •As this was an adaptive platform trial where multiple investigational treatments or placebos were being evaluated simultaneously, not all patients in the placebo arm received a placebo that was matched to fluvoxamine by route of administration, dosing frequency, or duration of therapy •PP analyses are not randomized comparisons, and they introduce bias when adherence is associated with factors that influence the outcome •Adherence was self-reported and not verified **Interpretation:** •Fluvoxamine reduced the proportion of patients who met the composite endpoint of COVID-19-related hospitalization or retention in an emergency setting for >6 hours. •The use of fluvoxamine did not impact the incidence of COVID-19-related hospitalizations. •It is difficult to define the clinical relevance of the >6-hour emergency setting observation endpoint and apply it to practice settings in different countries. •Fluvoxamine did not have a consistent impact on mortality. •Fluvoxamine did not impact time to symptom resolution.

No Benefits

- Ivermectin
- Colchicine

IVERMECTIN

- **Intervention** Patients were randomized to receive ivermectin, 300 µg/kg of body weight per day for 5 days (n = 200) or placebo (n = 200).
- **Main Outcomes and Measures** Primary outcome was time to resolution of symptoms within a 21-day follow-up period. Solicited adverse events and serious adverse events were also collected.
- **Results** Among 400 patients who were randomized in the primary analysis population (median age, 37 years [interquartile range {IQR}, 29-48]; 231 women [58%]), 398 (99.5%) completed the trial. The median time to resolution of symptoms was 10 days (IQR, 9-13) in the ivermectin group compared with 12 days (IQR, 9-13) in the placebo group (hazard ratio for resolution of symptoms, 1.07 [95% CI, 0.87 to 1.32]; *P* = .53 by log-rank test). By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. The most common solicited adverse event was headache, reported by 104 patients (52%) given ivermectin and 111 (56%) who received placebo. The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group).
- **Conclusion and Relevance** Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms.

IVERMECTIN

- Median time to symptom resolution: 10 days in IVM arm vs. 12 days in placebo arm (HR 1.07; *P* = 0.53)
- Symptoms resolved by Day 21: 82% in IVM arm vs. 79% in placebo arm

Secondary Outcomes:

- No difference between arms in proportion of patients who had clinical deterioration or who required escalation in care.

Safety Outcomes:

- Discontinued treatment due to an AE: 8% in IVM arm vs. 3% in placebo arm
- No SAEs were considered to be related to study interventions.

- **Key Limitations:** Primary endpoint changed from proportion of patients with clinical deterioration to time to symptom resolution during the trial due to low event rates
- Study enrolled younger, healthier patients; this population does not typically develop severe COVID-19

Interpretation:

- A 5-day course of IVM 300 µg/kg per day did not improve the time to resolution of symptoms in patients with mild COVID-19.

IVERMECTIN

•Mean age 42 years; 8% aged ≥65 years •47% were women •24% with HTN; 10% with DM; 58% with ≥1 comorbidity •Median time from symptom onset was 4 days **Primary Outcome:** •COVID-19-related hospitalizations: 5.6% in IVM arm vs. 8.3% in placebo arm (OR 0.65; 95% CI, 0.32–1.31; *P* = 0.23) **Secondary Outcomes:** •Need for MV: 2% in IVM arm vs. 1% in placebo arm (*P* = 0.7) •All-cause deaths: 2% in IVM arm vs. 1% in placebo arm (*P* = 0.7) •AEs: 18% in IVM arm vs. 21% in placebo arm (*P* = 0.6)	•**Key Limitation:** Study enrolled a fairly young population with few comorbidities that predict disease progression **Interpretation:** •In patients who had recently acquired SARS-CoV-2 infection, there was no evidence of a clinical benefit for IVM.

COLCHICINE

- PRINCIPLE trial, :the use of colchicine in non-hospitalized patients with COVID-19
- Results: NO benefit

Questions and Discussion