COVID-19: *Updates*

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December 1, 2021

ECHO CHICAGO

AT THE FOREFRONT
UChicago Medicine

Disclosures

- We have no relevant financial interests to disclose.

WORLD AIDS DAY

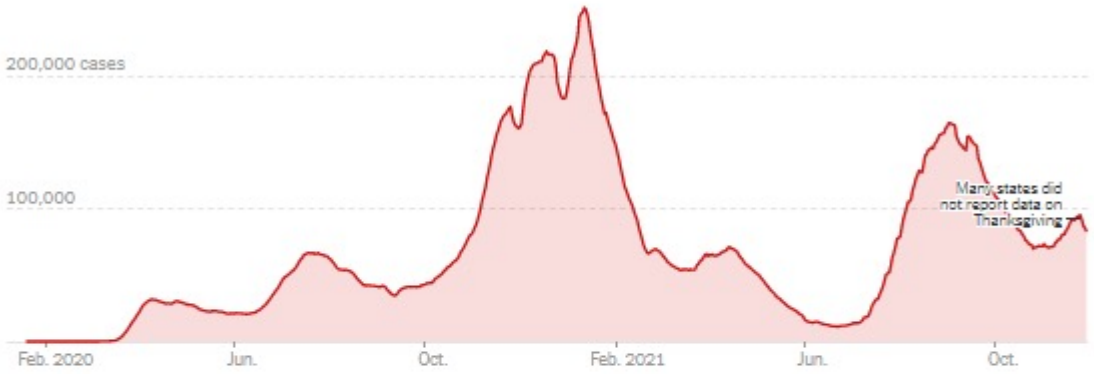
1 DECEMBER 2021

END INEQUALITIES.
END AIDS.
END PANDEMICS.

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

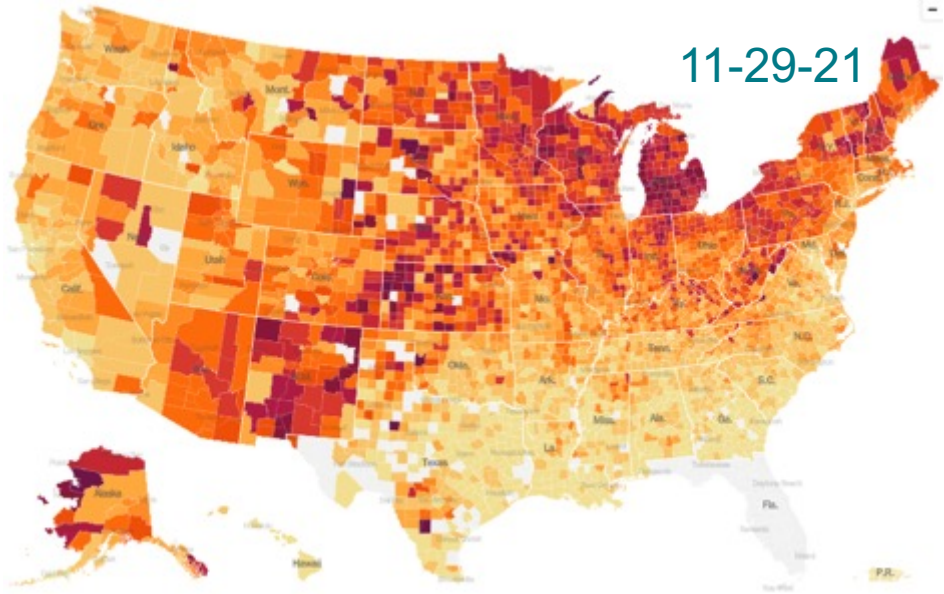
New reported cases

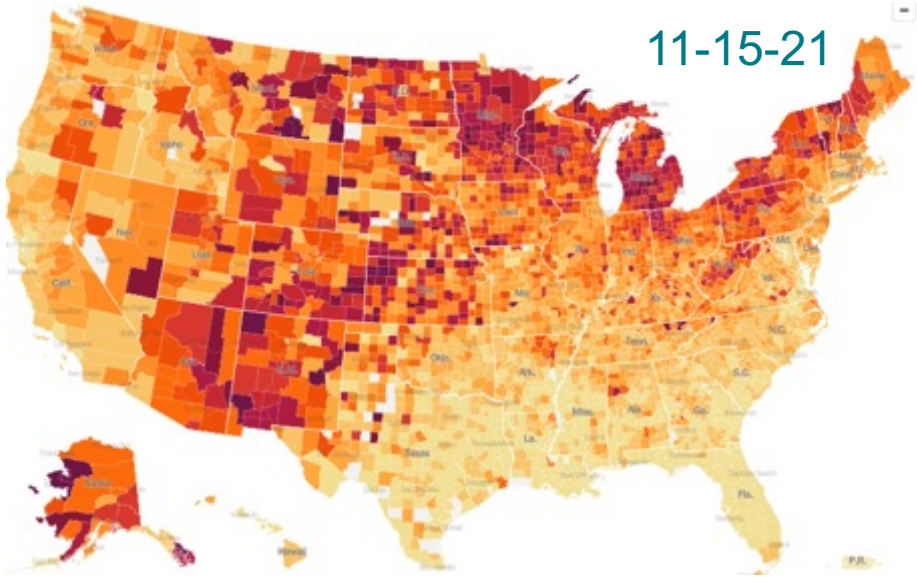
All time | Last 90 days



	DAILY AVG. ON NOV. 28	14-DAY CHANGE	TOTAL REPORTED
Cases	83,365	+3%	48,195,182
Tests	1,511,009	+18%	—
Hospitalized	52,416	+11%	—
Deaths	961	-10%	777,417

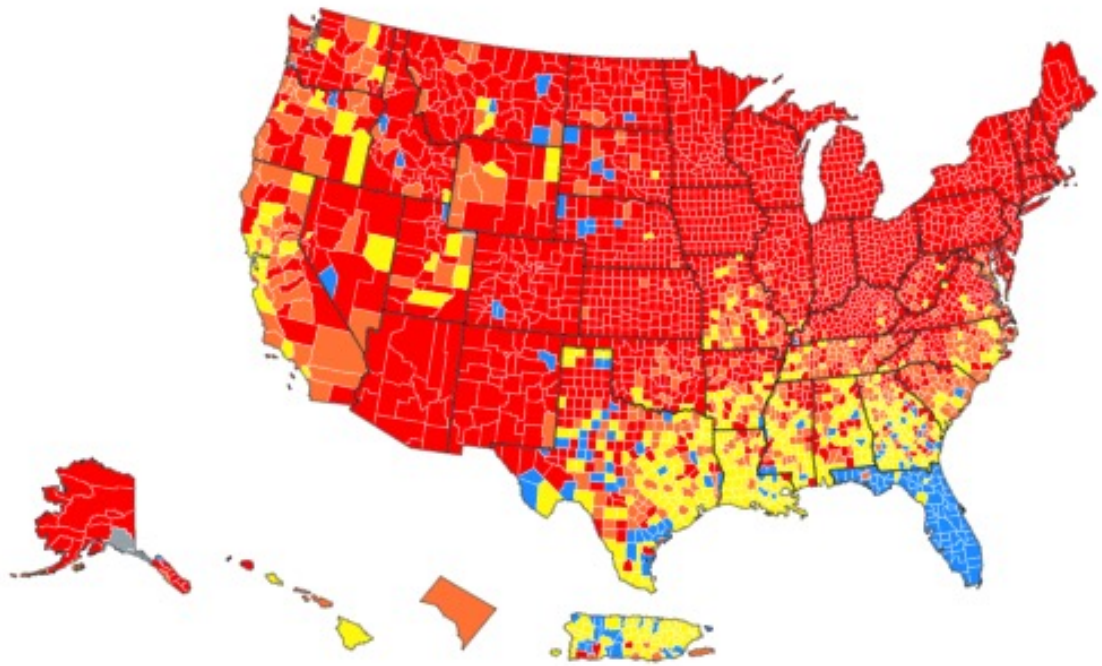
About this data





https://www.nytimes.com/interactive/2021/us/coronavirus-us-cases.html

Level of Community Transmission of All Counties in US



Community Transmission in US by County

	Total	Percent	% Change
High	2107	65.39%	-7.98%
Substantial	478	14.84%	1.55%
Moderate	457	14.18%	3.88%
Low	174	5.4%	2.55%

How is community transmission calculated?

High Substantial Moderate Low No Data

CHICAGO | COVID-19 Summary

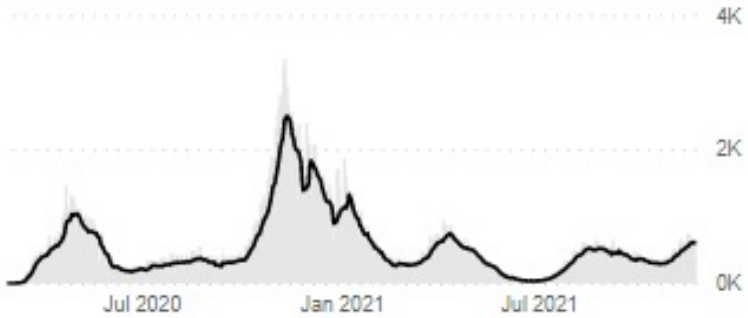
Data current as of Nov 26, 2021.
Data are updated M-F at 5:30 p.m., except for City holidays.
All data are provisional and subject to change.

SUMMARY | CASES | CASES BY ZIP | TESTS | VACCINES | VACCINES BY ZIP

Learn how to use this dashboard.

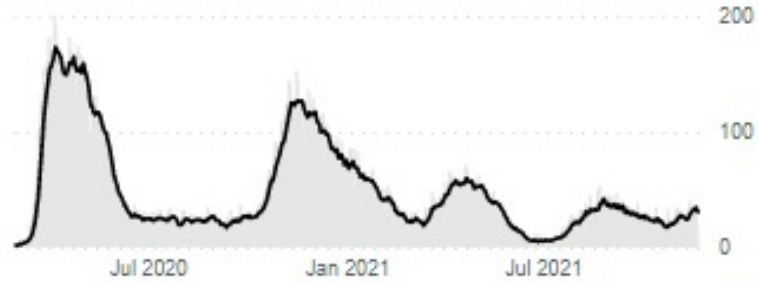
CASES

605 ▲	550 (+10%)	340,676	22.3
Current daily avg	Prior week	Cumulative	Daily rate per 100,000



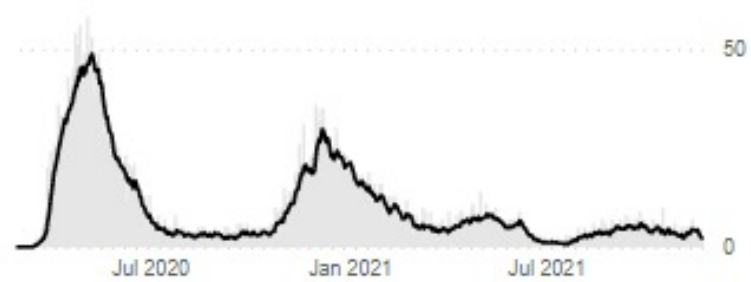
HOSPITALIZATIONS

31 ▲	30 (+4%)	31,390	1.1
Current daily avg	Prior week	Cumulative	Daily rate per 100,000



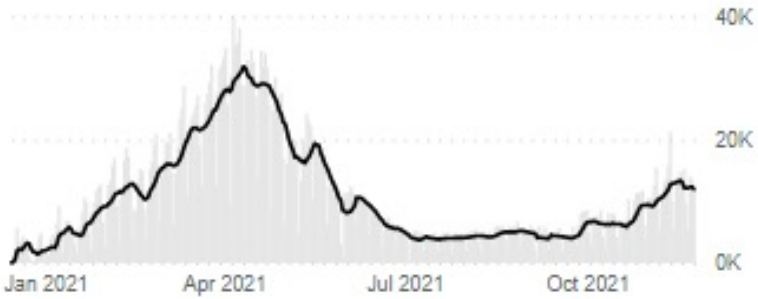
DEATHS

2.29 ▼	4.29 (-47%)	6,188	0.1
Current daily avg	Prior week	Cumulative	Daily rate per 100,000



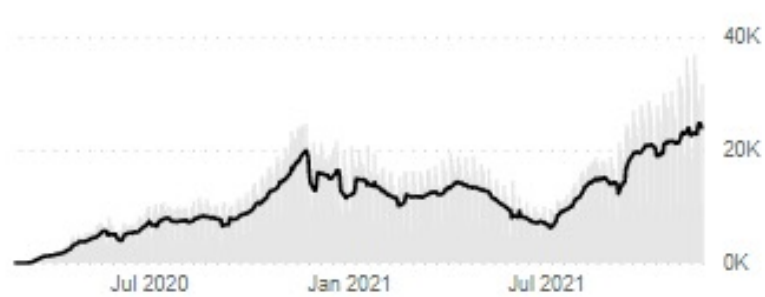
VACCINATIONS ADMINISTERED

11,967 ▼	3,695,191	60.9%	68.1%
Current daily avg	Cumulative	Completed series	At least one dose



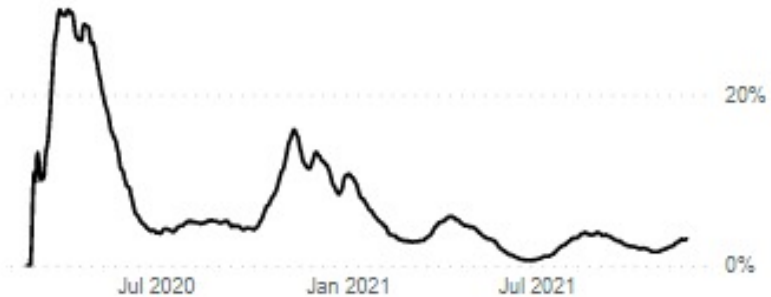
TESTS PERFORMED

23,937 ▲	23,033 (+4%)	6,984,125
Current daily avg	Prior week	Cumulative



POSITIVITY RATE

3.1% ▲	2.8%
Current daily avg	Prior week



built by slalom

New Admissions of Patients with Confirmed COVID-19, United States

Aug 01, 2020 - Nov 26, 2021

3,389,760
Total Admissions
Aug 01, 2020 - Nov 26, 2021

5,592
Current 7-Day Average
Nov 20, 2021 - Nov 26, 2021

5,789
Prior 7-Day Average
Nov 13, 2021 - Nov 19, 2021

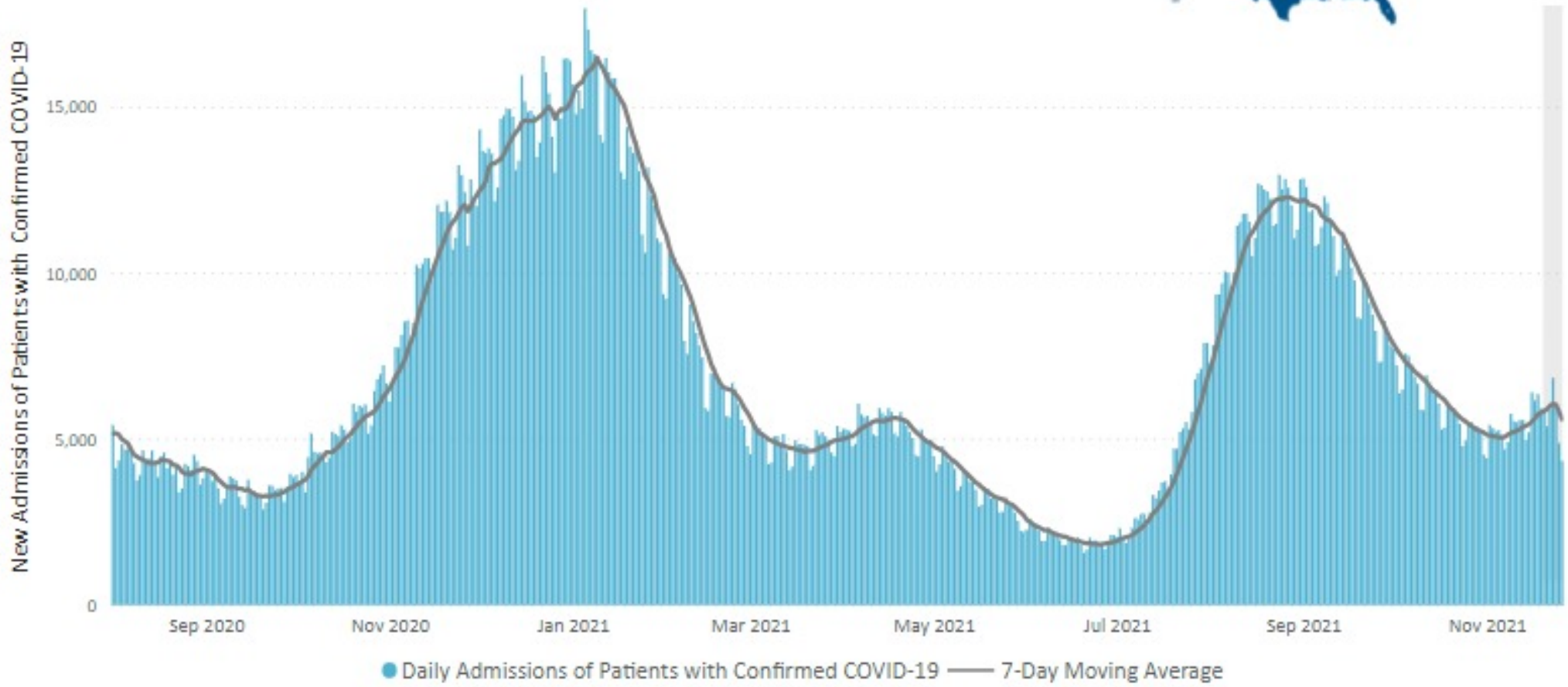
16,478
Peak 7-Day Average
Jan 03, 2021 - Jan 09, 2021

-3.4%
Percent change from prior 7-day avg. of Nov 13, 2021 - Nov 19, 2021

-66.1%
Percent change from peak 7-day avg. of Jan 03, 2021 - Jan 09, 2021

By Jurisdiction and Age Group | By Jurisdiction

Select a Jurisdiction: United States



Based on reporting from all hospitals (N=5,259). Due to potential reporting delays, data reported in the most recent 7 days (as represented by the shaded bar) should be interpreted with caution.

Small shifts in historic data may occur due to changes in the CMS Provider of Services file, which is used to identify the cohort of included hospitals. Data since December 1, 2020 have had error correction methodology applied. Data prior to this date may have anomalies that are still being resolved. Data prior to August 1, 2020 are unavailable.

Last Updated: Nov 28, 2021

Unified Hospital Dataset, White House COVID-19 Team, Data Strategy and Execution Workgroup

Total Vaccine Doses

Delivered	572,190,175
Administered	454,447,737

Learn more about the distribution of vaccines.

196.2M
People fully vaccinated

37.5M
People received a booster dose**

At Least One Dose	Fully Vaccinated	Booster Doses***

Vaccinated People	Count	Percent of US Population
Total	231,367,686	69.7%
Population ≥ 5 Years of Age	231,331,029	74.1%
Population ≥ 12 Years of Age	227,687,049	80.3%
Population ≥ 18 Years of Age	212,308,277	82.2%
Population ≥ 65 Years of Age	54,796,073	99.9%

***For surveillance purposes, COVID Data Tracker counts people as being "fully vaccinated" if they received two doses on different days (regardless of time interval) of the two-dose mRNA series or received one dose of a single-dose vaccine.**

****The count of people who received a booster dose includes anyone who is fully vaccinated and has received another dose of COVID-19 vaccine since August 13, 2021. This includes people who received booster doses and people who received additional doses.**

*****Some COVID-19 vaccine recipients are recommended to receive booster doses.**

About these data

CDC | Data as of: November 28, 2021 6:00am ET. Posted: Sunday, November 28, 2021 4:45 PM ET

CHICAGO | COVID-19 Vaccines

Data current as of Nov 26, 2021.
Data are updated M-F at 5:30 p.m., except for City holidays.
All data are provisional and subject to change.

DAILY TRENDS TOTALS BY PHASE

Cumulative totals are since 12/15/2020. Daily averages are a 7-day average as of 11/24/2021 to account for reporting lags.

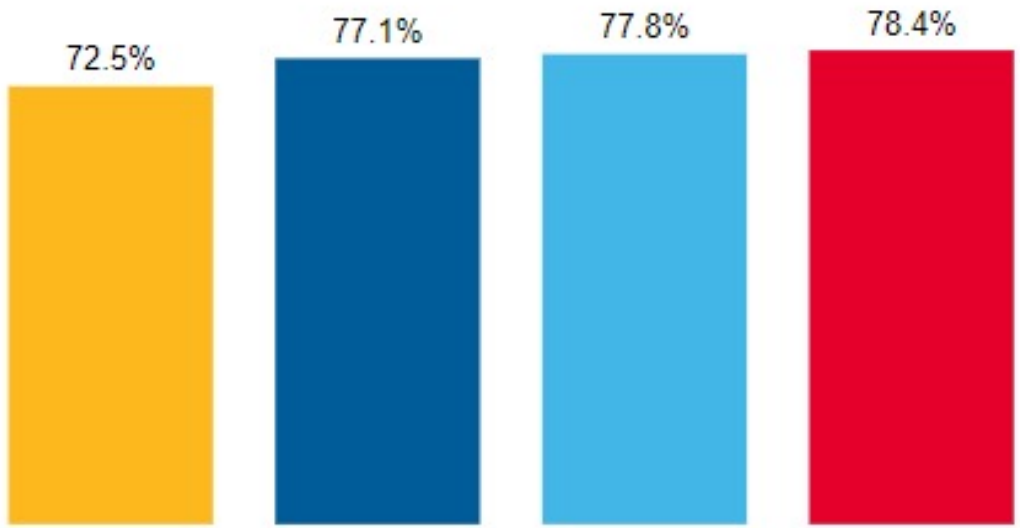
Citywide | Age | Gender | Race-Ethnicity

Select subgroup(s)

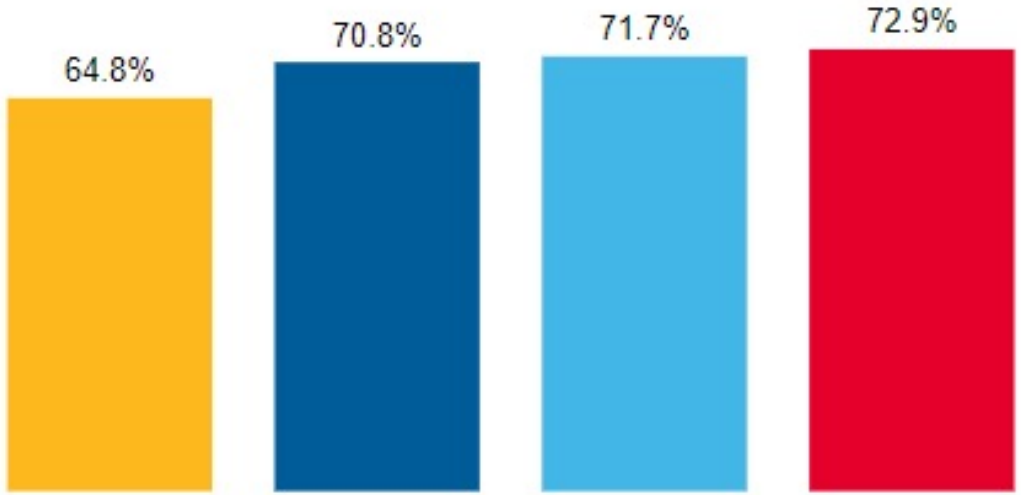
All

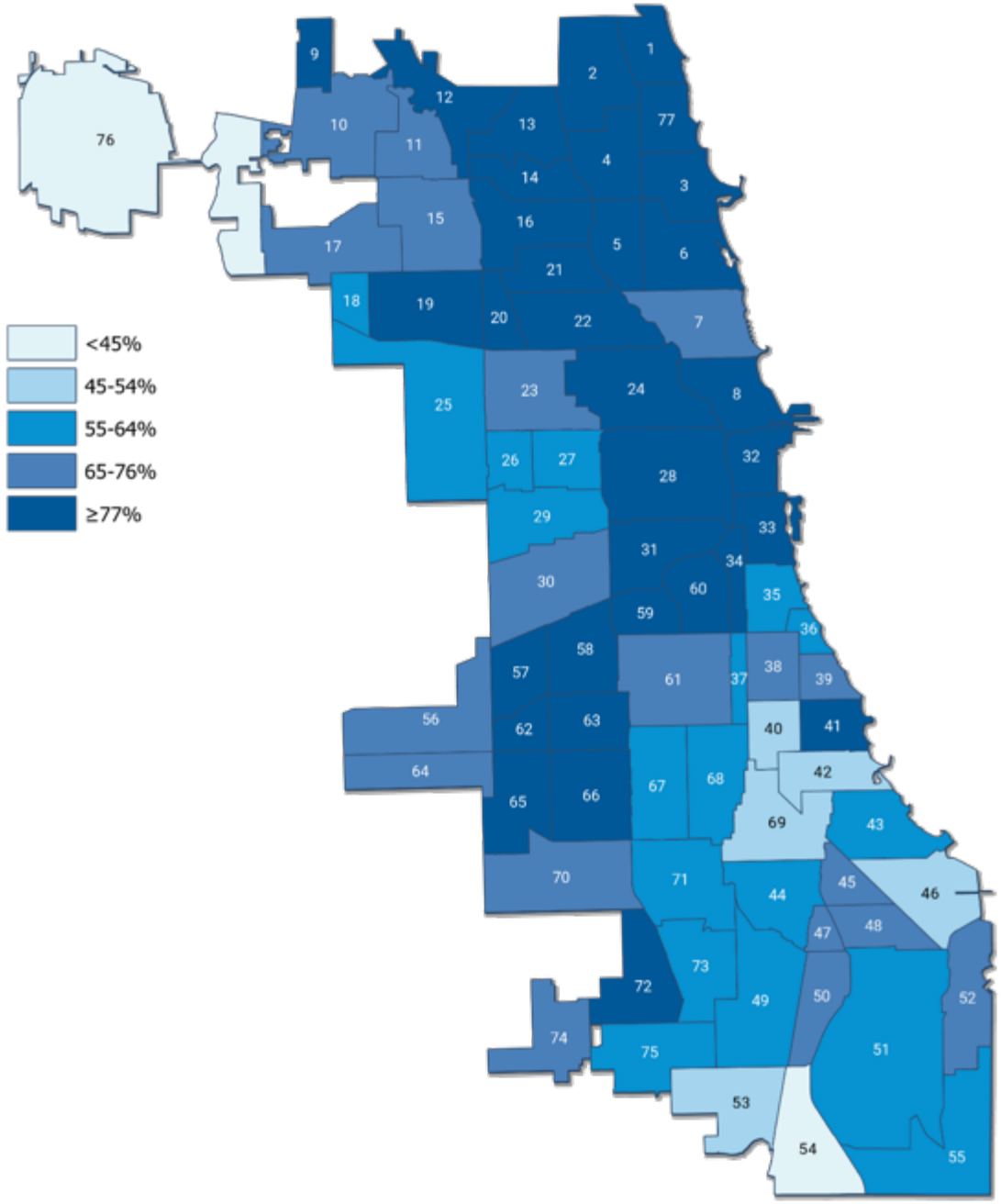
PERCENT VACCINATED % VACCINATED OVER TIME DAILY AVERAGE DOSES

At least one dose (% vaccinated as of 11/25/2021)



Completed vaccine series (% vaccinated as of 11/25/2021)





PERCENT OF CHICAGOANS 12+ WITH AT LEAST ONE DOSE OF COVID-19 VACCINE

CITYWIDE: 76.7%

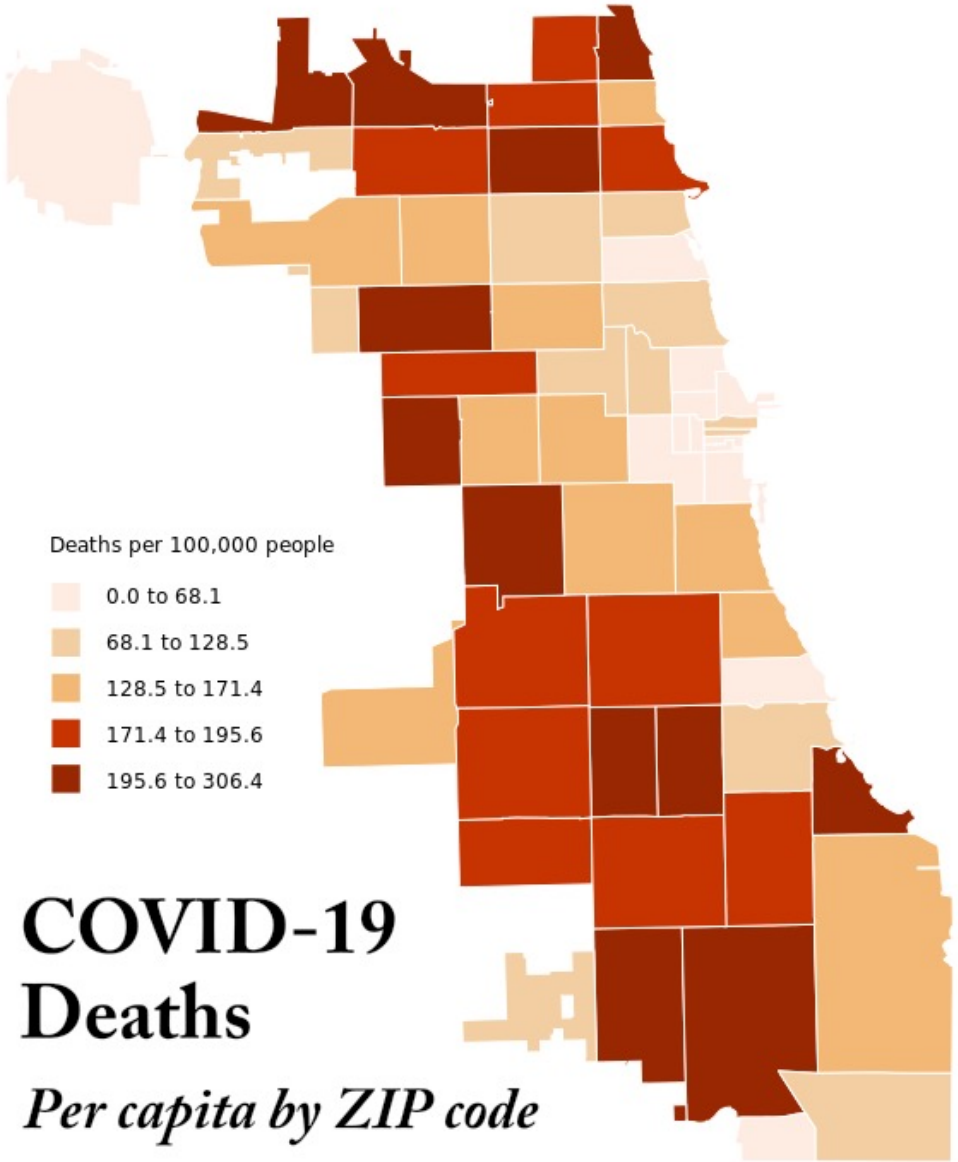
(DATA THROUGH 11/20/2021)

Chicago Department of Public Health - CDPH
@ChiPublicHealth

Chicago COVID-19 Vaccine 1st dose coverage (12+) shoutouts:

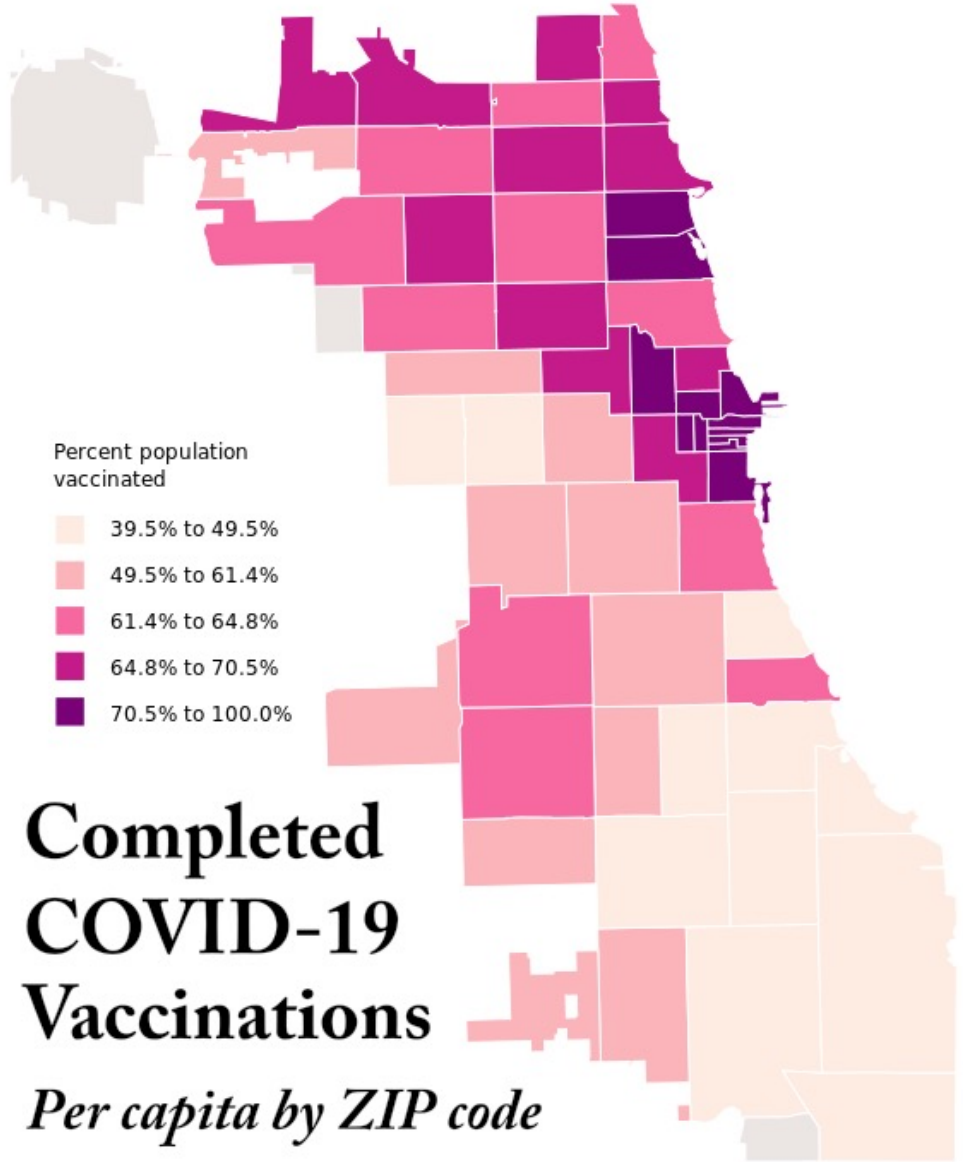
✅ Chicago Lawn reached 77%
✅ Near West Side reached 80%
✅ West Lawn reached 90%
✅ Roseland reached 60%

Learn more at Chi.gov/77pledge. #WeCanChicago #ProtectChicago



COVID-19 Deaths

Per capita by ZIP code

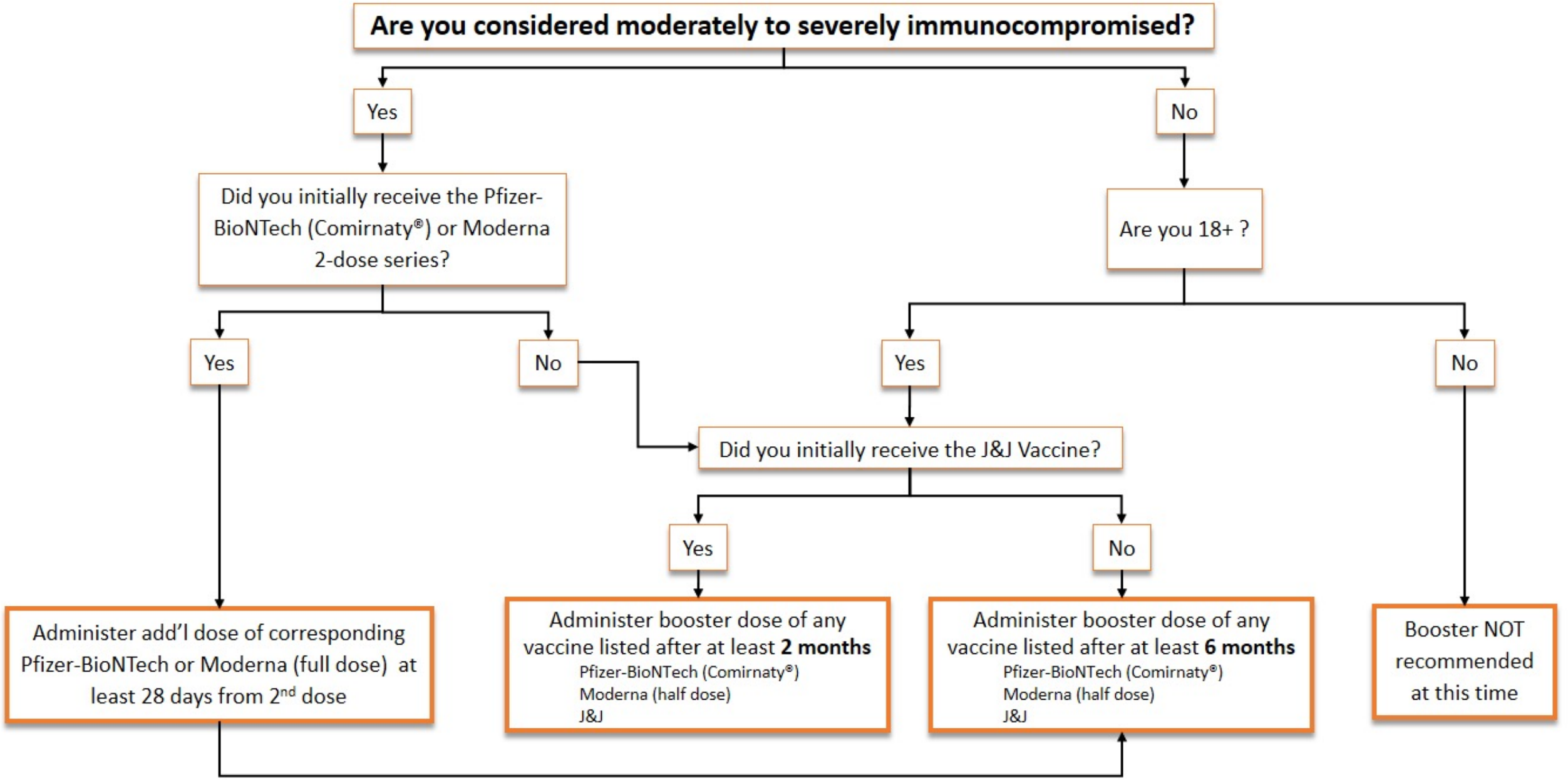


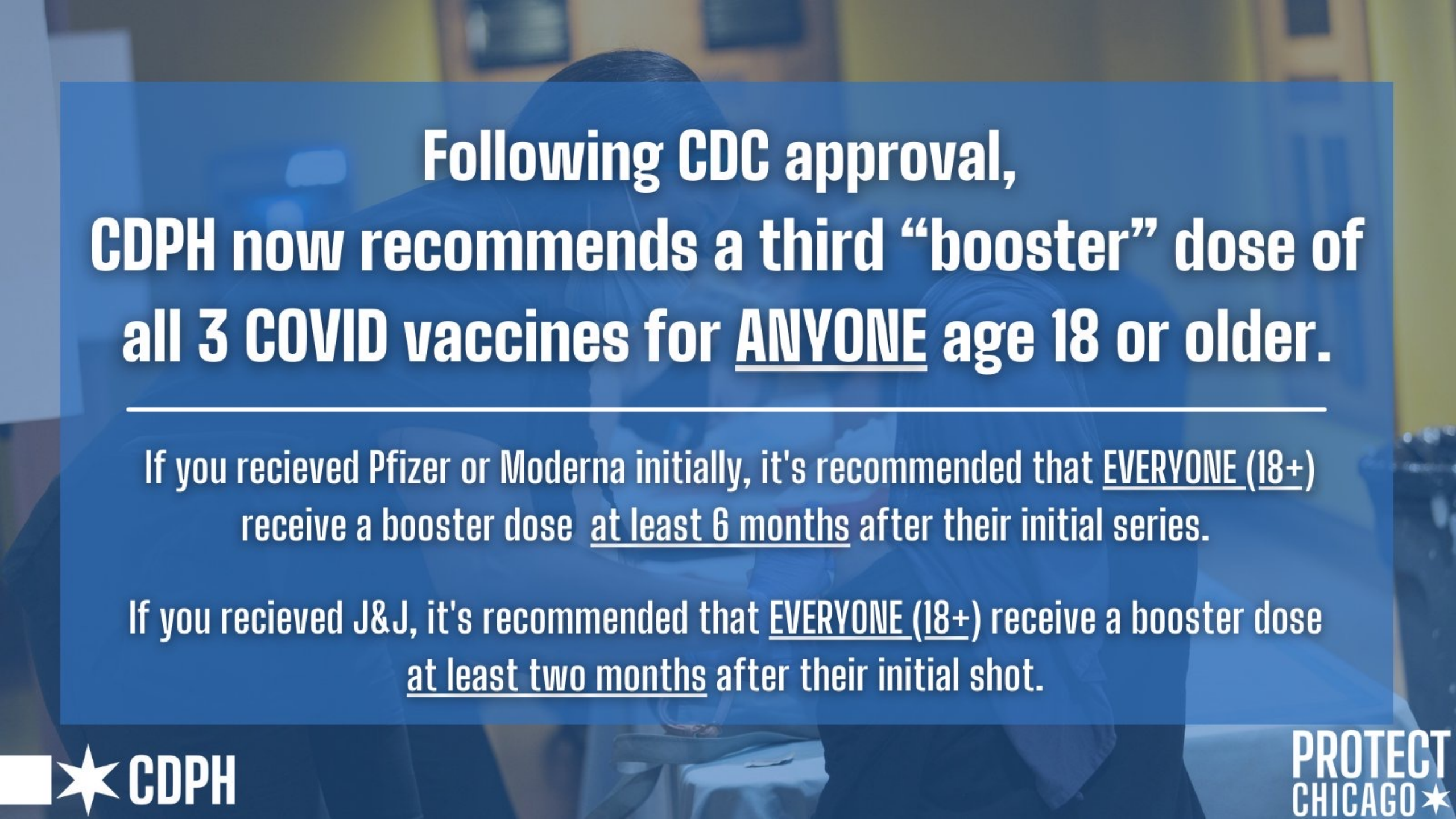
Completed COVID-19 Vaccinations

Per capita by ZIP code

@ChiVaxBot

COVID-19 Vaccine Third Dose/Booster Dose Workflow





Following CDC approval, CDPH now recommends a third "booster" dose of all 3 COVID vaccines for ANYONE age 18 or older.

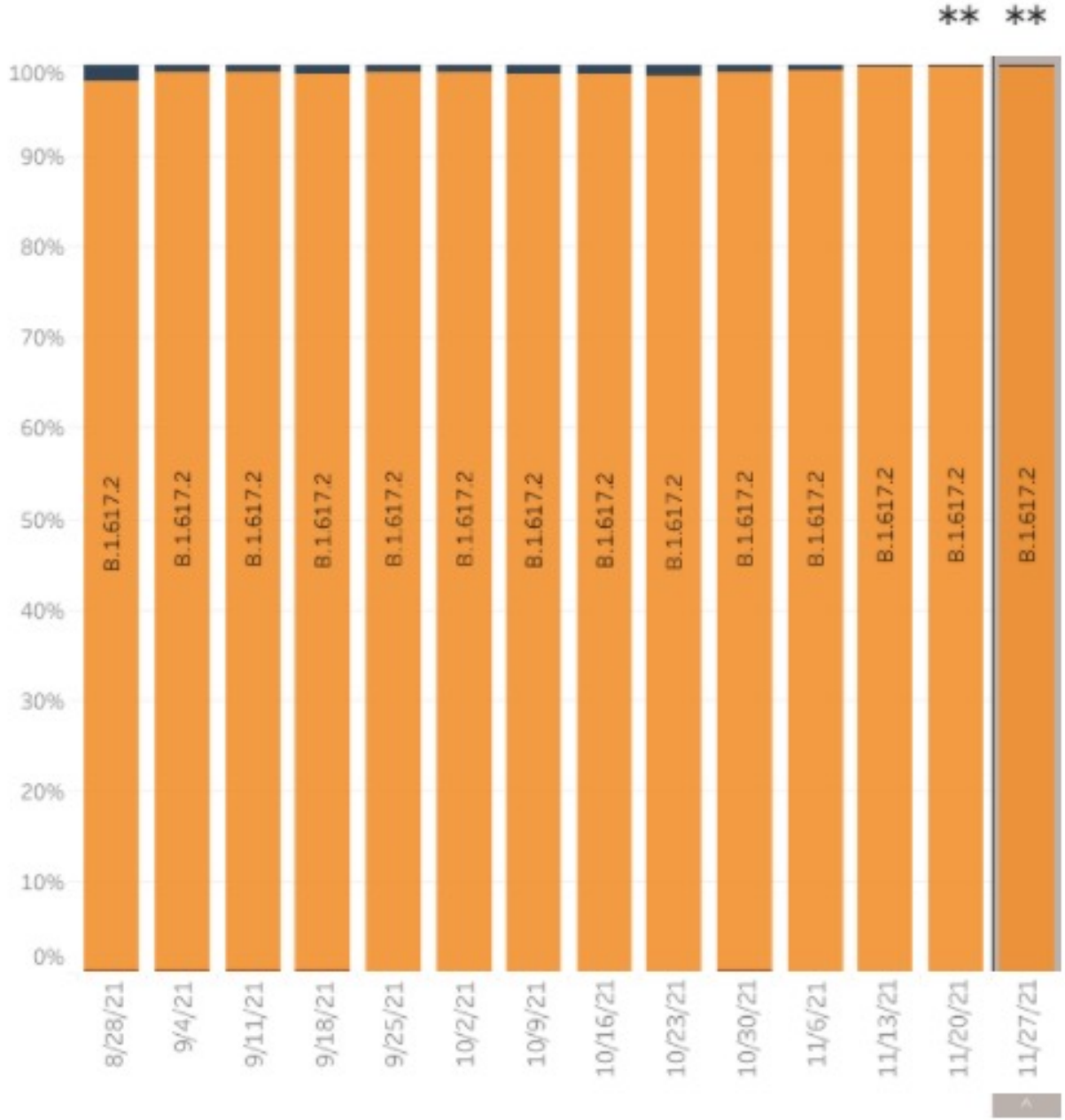
If you recieved Pfizer or Moderna initially, it's recommended that EVERYONE (18+) receive a booster dose at least 6 months after their initial series.

If you recieved J&J, it's recommended that EVERYONE (18+) receive a booster dose at least two months after their initial shot.

CDPH

PROTECT CHICAGO

United States: 8/22/2021 – 11/27/2021



United States: 11/21/2021 – 11/27/2021 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Delta	B.1.617.2	VOC	99.9%	99.9-99.9%
	AY.1	VOC	0.1%	0.0-0.1%
	AY.2	VOC	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.1%

* Enumerated lineages are US VOC and lineages circulating above 1..

Omicron Variant (B.1.1.529)

- S. Africa and Botswana first reported new variant to WHO Nov 24th
- >30 mutations to SARS-CoV2 spike protein
- Appears to be outcompeting Delta Variant in S. Africa
- Designated VOC by WHO on Nov 26th
- Since been identified in 20 other countries
- Most cases have no contact to Africa, indicating community-level transmission
- US has joined others in imposing travel bans to S. Africa, Bostwana, Zimbabwe, Namibia, Lesotho, Eswatini, Mozambique, and Malawi, effective Nov 29th

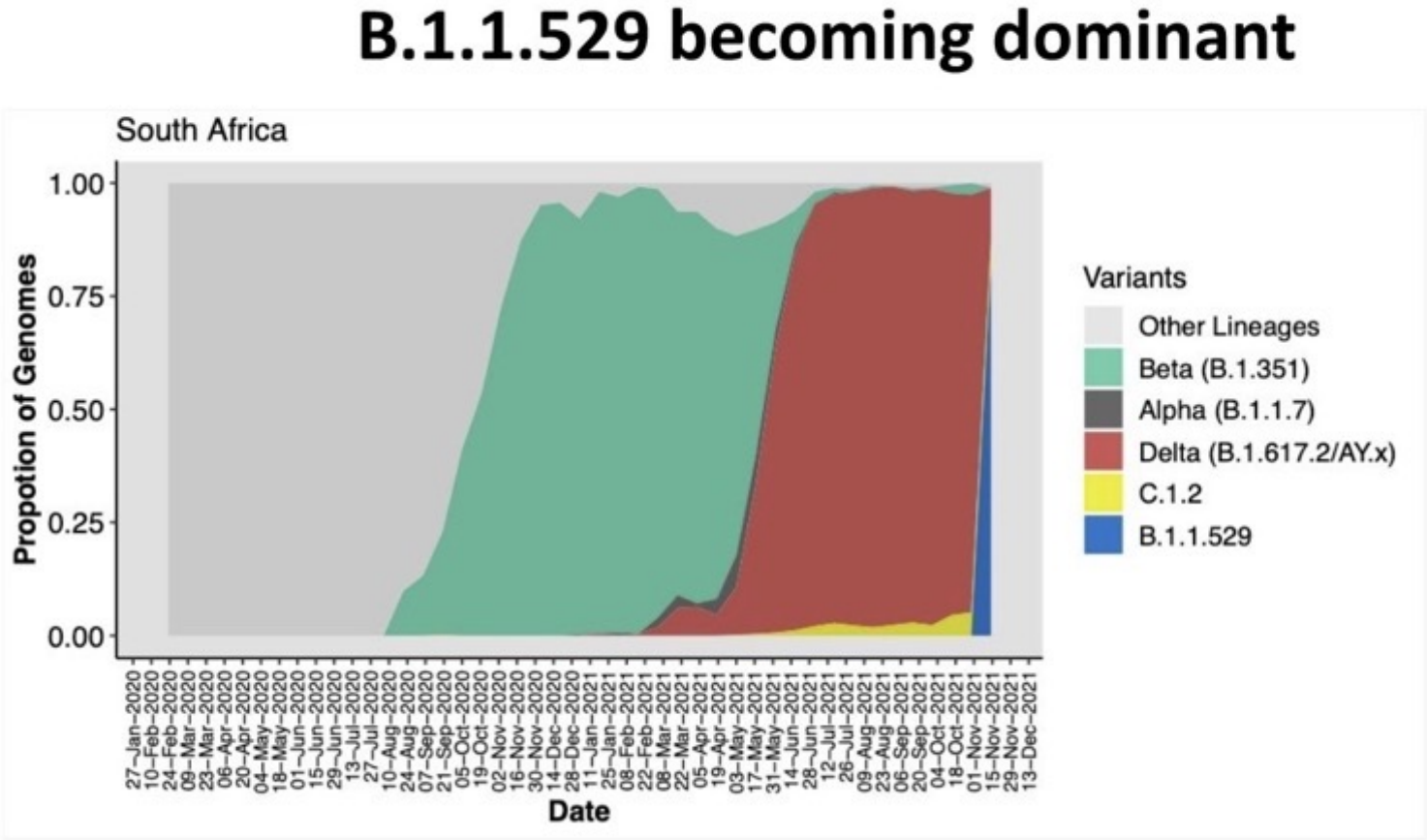
Omicron Variant (B.1.1.529)

Three questions left to be answered:

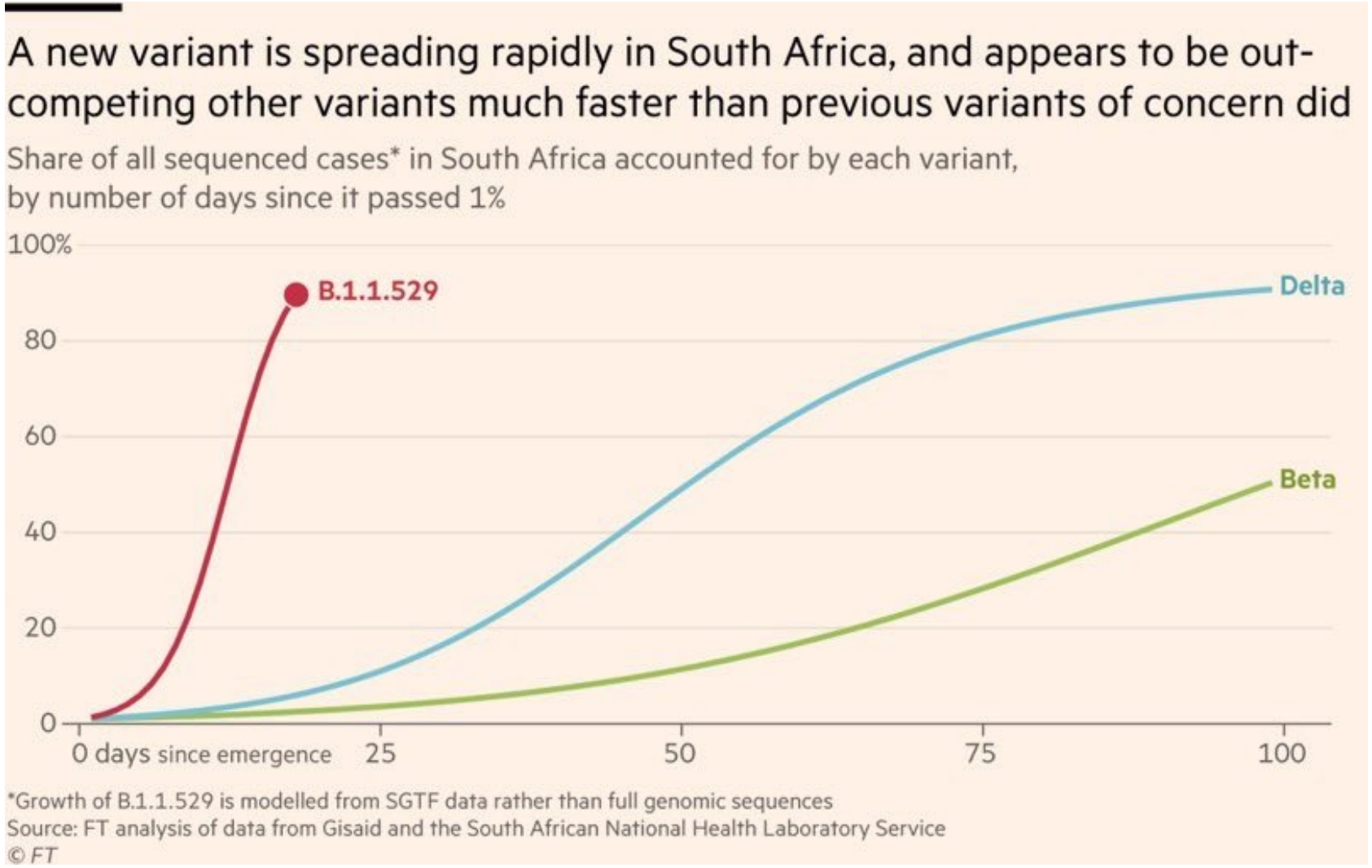
- Is Omicron variant is more transmissible than the current Delta variant?
- Does the Omicron variant cause more severe disease?
- Does the Omicron variant escape our immune response (via prior infection or vaccination)?

Omicron Variant (B.1.1.529) Transmissibility

- Omicron has become the predominant variant in Gauteng Province in less than 3 weeks
- Early studies show that it has a $R_0$2
- 2,828 new confirmed cases recorded Friday Nov 26th
  - 65% not vaccinated
  - ~25% partially vaccinated



Omicron Variant (B.1.1.529) Transmissibility



Omicron Variant (B.1.1.529) and Severity of Disease

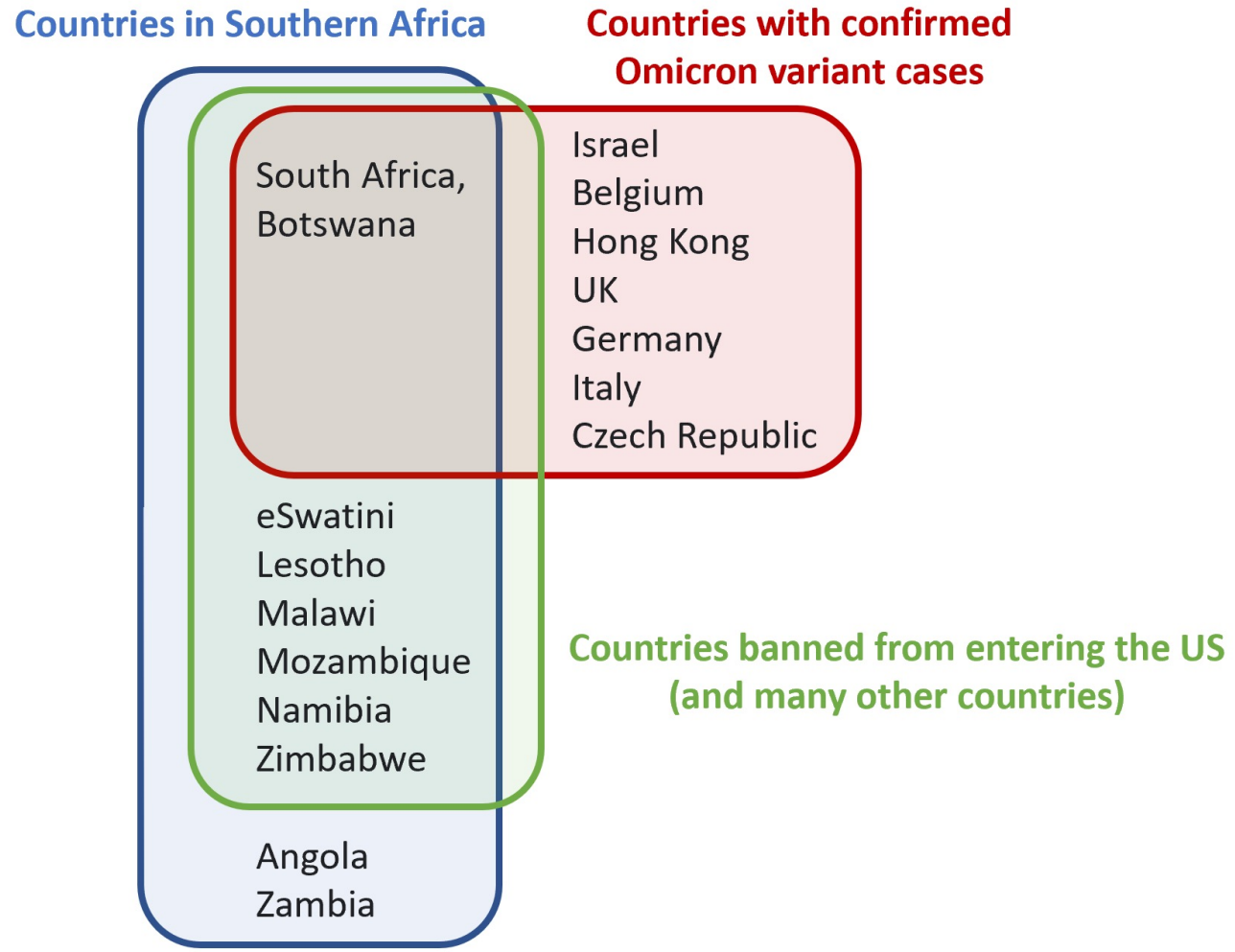
- Many of the Omicron cases in S Africa have been in younger people (<40)
- Many of the other cases have been identified in travelers (meaning feel well enough to travel)
- Rising hospitalization count in S Africa matches the proportion in past waves
- Majority of hospital admissions continue to be among people who were not vaccinated
- Bottom line – we just do not know yet, needs to tracked closely

Omicron Variant (B.1.1.529) and Immune Evasion

- >30 mutations of spike protein, some mirroring Beta (which exhibited immune escape)
- Still unclear if Ab produce can neutralize Omicron variant
- Still need more information on T-cell response/immune effect on variant

Utility of Travel Bans?

- While Omicron not identified yet in the US, likely only a matter of time
- Travel Bans at this point with limited utility
- Newer data shows presence of Omicron in Europe prior to Africa



Outpatient toolkit vs. COVID-19

Currently available

- **VACCINES + boosters**
- Behavioral mitigation strategies
  - Social distancing
  - Mask wearing
  - Hand hygiene
- Rapid testing/surveillance testing
- Monoclonal antibodies

Coming soon?

- Oral antivirals
  - Molnupiravir
  - Paxlovid
  - Fluvoxamine?

Molnupiravir

- **MOA**: Oral prodrug -> metabolized to cytidine nucleoside analogue, N4-hydroxycytidine (NHC). Acts via viral lethal mutagenesis through incorporation in the RNA by the viral dependent RNA-dependent RNA polymerase promoting accumulation of viral mutations and leading to inhibition of replication
- **MOVe-OUT Study population**: Unvaccinated patients with high risk for progression to severe illness (age >60y, diabetes, obesity and heart disease) with COVID-19 and symptoms **within 5 days** of starting the therapy
- **Course**: Four pills of the drug twice a day for five days
- **Primary outcome studied**: Risk of hospitalization or death through Day 29
- 10-1-21 Initial efficacy data on interim analysis (n=775 participants)
  - Molnupiravir **reduced the risk of hospitalization or death by approximately 50%; 7.3% of patients who received molnupiravir were either hospitalized or died through Day 29 following randomization (28/385), compared with 14.1% of placebo-treated patients (53/377); p=0.0012.**
  - Through Day 29, no deaths were reported in patients who received molnupiravir, as compared to 8 deaths in patients who received placebo.
  - Recruitment was stopped based on these results, although 90% of the intended sample size had been enrolled
  - Based on the participants with available viral sequencing data (approximately 40% of participants), molnupiravir demonstrated consistent efficacy across viral variants Gamma, Delta, and Mu.

https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-results-from-move-out-study-of-molnupiravir-an-investigational-oral-antiviral-medicine-in-at-risk-adults-with-mild-to-moderate-covid-19/

Molnupiravir

- 11-4-21 The UK's Medicines and Healthcare Products Regulatory Agency approved Merck & Co. and Ridgeback Biotherapeutics' molnupiravir for the treatment of COVID-19 -> first to authorize the use of the oral medication
- 11-26-21 Update on results from interim analysis (n=1433 participants)
  - In this study population, molnupiravir **reduced the risk of hospitalization or death from 9.7% in the placebo group (68/699) to 6.8% (48/709) in the molnupiravir group, for an absolute risk reduction of 3.0% (95% confidence interval [CI]: 0.1, 5.9; nominal p-value=0.0218) and a relative risk reduction of 30%** (relative risk 0.70; 95% CI: 0.49, 0.99).
  - Nine deaths were reported in the placebo group, and one in the molnupiravir group.
  - The adverse event profile for molnupiravir remained consistent with the profile reported at the planned interim analysis.
- 11-30-21 FDA Antimicrobial Drugs Advisory Committee voted 13 to 10 vote to recommend emergency authorization of molnupiravir
- Awaiting final authorization from FDA and CDC

Molnupiravir Safety/AE

- Safety/adverse events:
  - Incidence of any adverse event was comparable in the molnupiravir and placebo groups (35% v 40%)
  - incidence of drug-related adverse events was also comparable (12% v 11%)
  - Fewer subjects discontinued study therapy due to an adverse event in the molnupiravir group (1.3%) compared to the placebo group (3.4%)

- Prelim concerns reported from FDA discussion
  - Expected not to be recommended for use in pregnant women and require a pregnancy test prior to Rx to women of child bearing age
    - Found to be lethal to embryos in pregnant rats, causing birth defects and reducing fetal body weight; interfered with bone and cartilage growth in young pups
  - ?Efficacy data
  - ?Likelihood of escape mutants

Monoclonal antibody therapy vs. SARS-CoV2

Bamlanivimab 700mg plus etesevimab 1400mg IV x 1
OR Casirivimab 600mg plus indevimab 600mg IV or as SC x 1
OR Sotrovimab 500mg IV x 1

- Treatment should be started ASAP and within 10 days of symptom onset
- High risk outpatients with conditions that were represented in patients in clinical trials and other medical conditions and factors that had limited representation in patients in clinical trials
- High risk inpatients with mild to moderate COVID-19 admitted for a reason other than COVID-19
- Available for patients admitted with severe COVID-19 who have not developed an antibody response (or are not expected to mount a response) through expanded access protocols
- As post-exposure prophylaxis (C/I) in high risk persons with significant exposures who are not fully vaccinated or not expected to mount a full immune response to vaccination

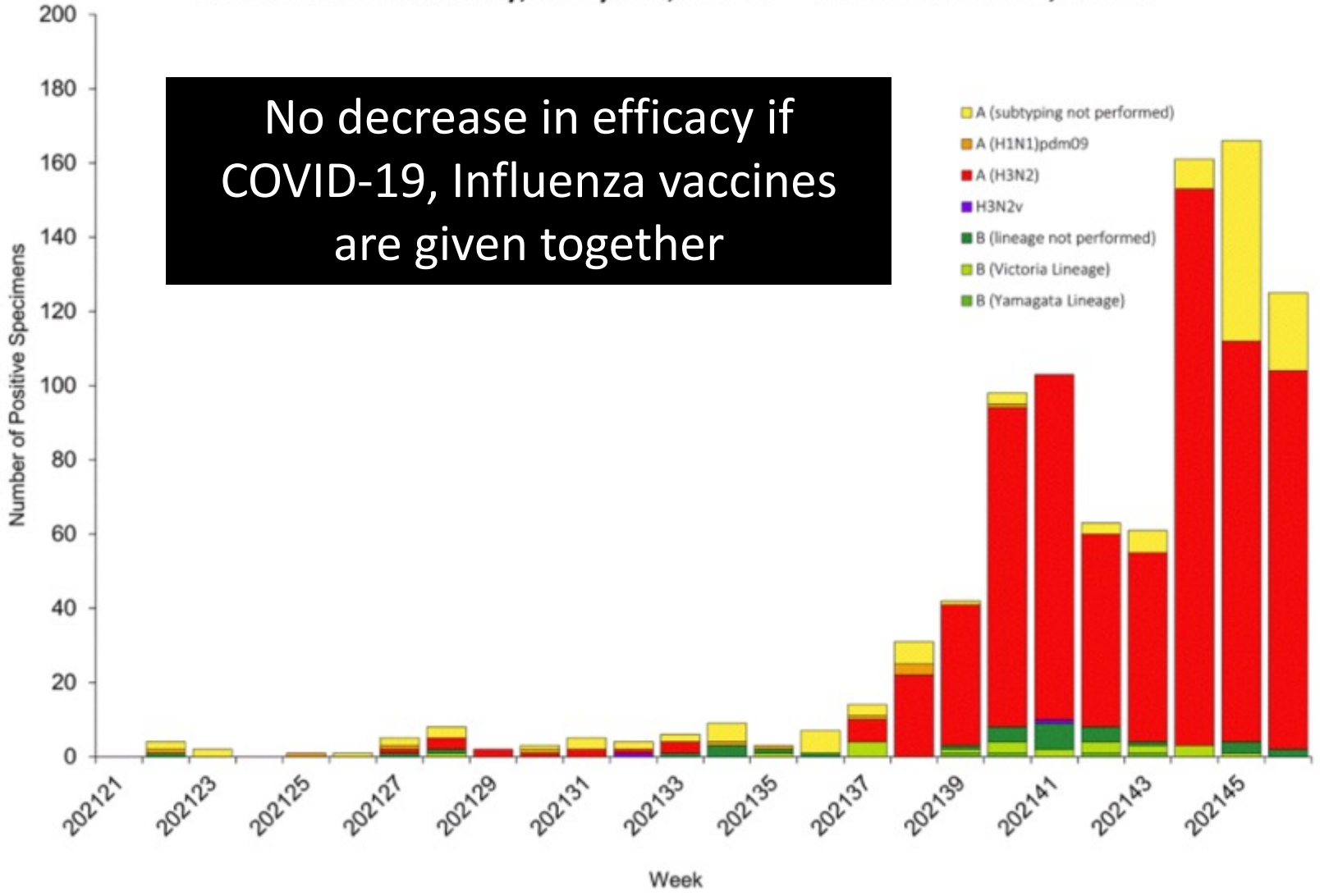
Monoclonal antibodies	MOA	Study Data	Notes
Bamlanivimab/etesivimab (Treatment/PEP) IV Mean duration of symptoms 4 days Tx/PEP	Binds to overlapping epitopes in the spike protein RBD of SARS-CoV-2	BLAZE-1: DB, phase3 RCT or BAM + ETE vs. placebo COVID-19 related hospitalization or all cause death by day 29 **4 (0.8%) (BAM+ETE) vs. 15 (6%) in placebo arm; relative risk difference: 87%; P<0.0001.** All cause death 0 in BAM+ ETE arm vs. 4 (1.6%) in placebo arm P=0.01.	Interpretation: **4.8% absolute risk reduction** **70% relative risk reduction** Decreased efficacy vs. P.1(Gamma) and B.1.351 (Beta)
Casirivimab/indevimab (Treatment/PEP) IV or SQ Median duration of symptoms prior to enrollment 3 days	Bind to non-overlapping epitopes of the spike protein RBD of SARS-CoV2	DB phase 3 RCT of CSV/IMD vs. placebo COVID-19 related hospitalization or all-cause death by day 29 **7(1.0%) CSV/IMD vs. 24(3.2%) in placebo arm (P=0.002)** All cause death 1(0.1%) CSV/IMD vs. 1 (o.1%) in placebo arm	Interpretation: **2.2% absolute reduction** **70% relative risk reduction**
Sotrovimab (Treatment) IV Symptom onset <5 days prior to enrollment	Binds to epitope in RBD of the spike protein conserved between SARS-CoV and SARS-CoV-2	COMET-ICE: DB Phase 3 RCT of Sotrovimab vs. placebo All cause hospitalizations or deaths by Day 29: **3 (1%) in SOT arm vs. 21 (7% in placebo arm (P=0.002)**	Interpretation: **6% absolute reduction** **85% relative risk reduction**

Adapted from:
https://www.covid19treatmentguidelines.nih.gov/tables/table-3a/

Oral antivirals	MOA	Study Data	Notes
Molnupiravir PO Mean duration of symptoms 5 days https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-results-from-move-out-study-of-molnupiravir-an-investigational-oral-antiviral-medicine-in-at-risk-adults-with-mild-to-moderate-covid-19/	Oral prodrug -> incorporated into RNA promoting accumulation of viral mutations and leading to inhibition of replication	**MOVe-OUT**: Phase 3 DB RCT of molnupiravir vs. placebo, n=1433 high risk adults **6.8% (48/709) patients receiving molnupiravir were hospitalized or died through day 29 vs. 9.7% (68/699) of patients receiving placebo (p=0.0218)** Nine deaths were reported in the placebo group, and one in the molnupiravir group.	Interpretation: **3.0% absolute risk reduction** **30% relative risk reduction**
Paxlovid (PF-07321332 + ritonavir) PO Median duration of symptoms prior to enrollment **3** days https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate	3CL protease inhibitor	**EPIC-HR**: Phase 2/3 RCT, DB of PF-07321332 + ritonavir vs. placebo; n=1219 high risk adults **1% of patients who received Paxlovid were hospitalized through Day 28 following randomization (6/607 hospitalized, with no deaths) vs 6.7% of patients who received a placebo (41/612 hospitalized with 10 subsequent deaths (p<0.0001).** Zero deaths were reported in patients who received Paxlovid vs 10 (1.6%) deaths in patients who received placebo.	Interpretation: **6.2% absolute reduction** **89% relative risk reduction** Co-administration with ritonavir
Fluvoxamine PO Symptom onset ? days prior to enrollment Reis et al, The Lancet, 10/2021	SSRI and s1 Receptor agonist Potential MOA vs. SARS-CoV-2 • Anti-inflammatory • Anti-viral • Anti-platelet?	**TOGETHER**: Placebo-controlled, randomized, adaptive platform trial in high-risk symptomatic Brazilian adults, n=1497 **79 (11%) participants receiving fluvoxamine had a were hospitalized or retained in a COVID-19 ED through Day 28 vs. 119 (16%) in the placebo group.** Most events (87%) were hospitalizations. There were 17 deaths in the fluvoxamine group and 25 deaths in the placebo group in the primary intention-to-treat analysis	Interpretation: **5% absolute reduction** **33% relative risk reduction**

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, May 23, 2021 – November 20, 2021

No decrease in efficacy if COVID-19, Influenza vaccines are given together



Influenza activity is low nationally, but the numbers of influenza viruses detected by labs has increased in recent weeks
Majority are A (H3N2)
>90% children and young adults ages 5-24

https://www.cdc.gov/flu/weekly/