Disclosures

• We have no relevant financial interests to disclose.
Coronavirus in the U.S.: Latest Map and Case Count

New reported cases

<table>
<thead>
<tr>
<th></th>
<th>All time</th>
<th>Last 90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>93,365</td>
<td>-3%</td>
</tr>
<tr>
<td>Tests</td>
<td>1,511,099</td>
<td>-18%</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>52,416</td>
<td>-11%</td>
</tr>
<tr>
<td>Deaths</td>
<td>961</td>
<td>-10%</td>
</tr>
</tbody>
</table>

CHICAGO COVID-19 Summary

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

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

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

**VACCINATIONS ADMINISTERED**
- Current daily avg: 11,967
- Cumulative: 3,695,191
- Completed series: 60.9%
- At least one dose: 68.1%

**TESTS PERFORMED**
- Current daily avg: 23,937
- Prior week: 23,033 (+4%)
- Cumulative: 6,984,125

**POSITIVITY RATE**
- Current daily avg: 3.1%
- Prior week: 2.8%
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

Daily Admissions of Patients with Confirmed COVID-19 — 7-Day Moving Average

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.
<table>
<thead>
<tr>
<th>Vaccinated People</th>
<th>Count</th>
<th>Percent of US Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>231,367,686</td>
<td>69.7%</td>
</tr>
<tr>
<td>Population ≥ 5 Years of Age</td>
<td>231,331,029</td>
<td>74.1%</td>
</tr>
<tr>
<td>Population ≥ 12 Years of Age</td>
<td>227,687,049</td>
<td>80.3%</td>
</tr>
<tr>
<td>Population ≥ 18 Years of Age</td>
<td>212,308,277</td>
<td>82.2%</td>
</tr>
<tr>
<td>Population ≥ 65 Years of Age</td>
<td>54,796,073</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

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

At least one dose (% vaccinated as of 11/25/2021)
- Citywide: 72.5%
- Age: 77.1%
- Gender: 77.8%
- Race-Ethnicity: 78.4%

Completed vaccine series (% vaccinated as of 11/25/2021)
- Citywide: 64.8%
- Age: 70.8%
- Gender: 71.7%
- Race-Ethnicity: 72.9%
PERCENT OF CHICAGOANS 12+ WITH AT LEAST ONE DOSE OF COVID-19 VACCINE
CITYWIDE: 76.7%
(DATA THROUGH 11/20/2021)

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 Vaccine Third Dose/Booster Dose Workflow

Are you considered moderately to severely immunocompromised?

Yes

Did you initially receive the Pfizer-BioNTech (Comirnaty®) or Moderna 2-dose series?

Yes

Administer add’l dose of corresponding Pfizer-BioNTech or Moderna (full dose) at least 28 days from 2nd dose

No

Administer booster dose of any vaccine listed after at least 2 months
- Pfizer-BioNTech (Comirnaty®)
- Moderna (half dose)
- J&J

No

Are you 18+?

Yes

Did you initially receive the J&J Vaccine?

Yes

Administer booster dose of any vaccine listed after at least 6 months
- Pfizer-BioNTech (Comirnaty®)
- Moderna (half dose)
- J&J

No

Booster NOT recommended at this time
Following CDC approval, CDPH now recommends a third “booster” dose of all 3 COVID vaccines for **ANYONE** age 18 or older.

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

If you received J&J, it’s recommended that **EVERYONE (18+)** receive a booster dose at least two months after their initial shot.
United States: 8/22/2021 – 11/27/2021

** USA **

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Lineage #</th>
<th>US Class</th>
<th>%Total</th>
<th>95% PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>B.1.617.2</td>
<td>VOC</td>
<td>99.9%</td>
<td>99.9-99.9%</td>
</tr>
<tr>
<td>AY.1</td>
<td>VOC</td>
<td>0.1%</td>
<td>0.0-0.1%</td>
<td></td>
</tr>
<tr>
<td>AY.2</td>
<td>VOC</td>
<td>0.0%</td>
<td>0.0-0.0%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Other*</td>
<td>0.0%</td>
<td>0.0-0.1%</td>
<td></td>
</tr>
</tbody>
</table>

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

Collection date, week ending
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
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 $R_0$ of 2
- 2,828 new confirmed cases recorded Friday Nov 26th
  - 65% not vaccinated
  - ~25% partially vaccinated
Omicron Variant (B.1.1.529) Transmissibility

A new variant is spreading rapidly in South Africa, and appears to be out-competing other variants much faster than previous variants of concern did.

Share of all sequenced cases* in South Africa accounted for by each variant, by number of days since it passed 1%

*Growth of B.1.1.529 is modelled from SGTG data rather than full genomic sequences
Source: FT analysis of data from Gisaid and the South African National Health Laboratory Service
© FT
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.

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

- 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

<table>
<thead>
<tr>
<th>Bamlanivimab 700mg plus etesevimab 1400mg IV x 1</th>
<th>OR Casirivimab 600mg plus indevimab 600mg IV or as SC x 1</th>
<th>OR Sotrovimab 500mg IV x 1</th>
</tr>
</thead>
</table>

- OR 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
<table>
<thead>
<tr>
<th>Monoclonal antibodies</th>
<th>MOA</th>
<th>Study Data</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bamlanivimab/etesevimab</strong> (Treatment/PEP)</td>
<td>Binds to overlapping epitopes in the spike protein RBD of SARS-CoV-2</td>
<td><strong>BLAZE-1</strong>: DB, phase 3 RCT or BAM + ETE vs. placebo</td>
<td><strong>Interpretation:</strong> 4.8% absolute risk reduction 70% relative risk reduction</td>
</tr>
<tr>
<td>IV</td>
<td>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&lt;0.0001. All cause death 0 in BAM+ ETE arm vs. 4 (1.6%) in placebo arm P=0.01.</td>
<td><strong>Decreased efficacy vs. P.1 (Gamma) and B.1.351 (Beta)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean duration of symptoms 4 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx/PEP</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Casirivimab/indevimab** (Treatment/PEP) | Bind to non-overlapping epitopes of the spike protein RBD of SARS-CoV2 | **DB phase 3 RCT of CSV/IMD vs. placebo** | **Interpretation:** 2.2% absolute reduction 70% relative risk reduction |
| IV or SQ | 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) | | |
| Median duration of symptoms prior to enrollment 3 days | All cause death 1(0.1%) CSV/IMD vs. 1 (0.1%) in placebo arm | | |

<p>| <strong>Sotrovimab</strong> (Treatment) | Binds to epitope in RBD of the spike protein conserved between SARS-CoV and SARS-CoV-2 | <strong>COMET-ICE</strong>: DB Phase 3 RCT of Sotrovimab vs. placebo | <strong>Interpretation:</strong> 6% absolute reduction 85% relative risk reduction |
| IV | All cause hospitalizations or deaths by Day 29: 3 (1%) in SOT arm vs. 21 (7%) in placebo arm (P=0.002) | | |
| Symptom onset &lt;5 days prior to enrollment | | | Adapted from: <a href="https://www.covid19treatmentguidelines.nih.gov/tables/table-3a/">https://www.covid19treatmentguidelines.nih.gov/tables/table-3a/</a> |</p>
<table>
<thead>
<tr>
<th>Oral antivirals</th>
<th>MOA</th>
<th>Study Data</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molnupiravir</strong></td>
<td>Oral prodrug -&gt; incorporated into RNA promoting accumulation of viral mutations and leading to inhibition of replication</td>
<td>MOVE-OUT: Phase 3 DB RCT of molnupiravir vs. placebo, n=1433 high risk adults</td>
<td>Interpretation: 3.0% absolute risk reduction 30% relative risk reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nine deaths were reported in the placebo group, and one in the molnupiravir group.</td>
<td></td>
</tr>
<tr>
<td><strong>Paxlovid (PF-07321332 + ritonavir)</strong></td>
<td>3CL protease inhibitor</td>
<td>EPIC-HR: Phase 2/3 RCT, DB of PF-07321332 + ritonavir vs. placebo; n=1219 high risk adults</td>
<td>Interpretation: 6.2% absolute reduction 89% relative risk reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>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&lt;0.0001).</td>
<td>Co-administration with ritonavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zero deaths were reported in patients who received Paxlovid vs 10 (1.6%) deaths in patients who received placebo.</td>
<td></td>
</tr>
<tr>
<td><strong>Fluvoxamine</strong></td>
<td>SSRI and s1 Receptor agonist Potential MOA vs. SARS-CoV-2</td>
<td>TOGETHER: Placebo-controlled, randomized, adaptive platform trial in high-risk symptomatic Brazilian adults, n=1497</td>
<td>Interpretation: 5% absolute reduction 33% relative risk reduction</td>
</tr>
<tr>
<td></td>
<td>• Anti-inflammatory</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Anti-viral</td>
<td>There were 17 deaths in the fluvoxamine group and 25 deaths in the placebo group in the primary intention-to-treat analysis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Anti-platelet?</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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.

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

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