COVID Update
January 2022

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Healthy Driven™

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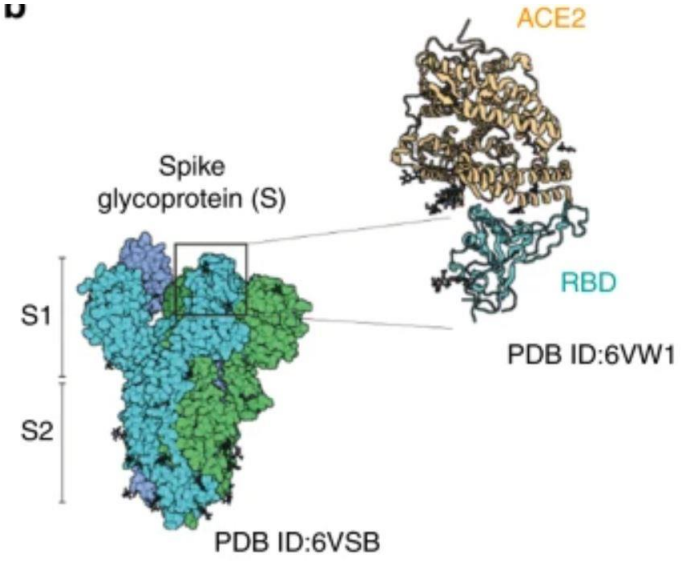
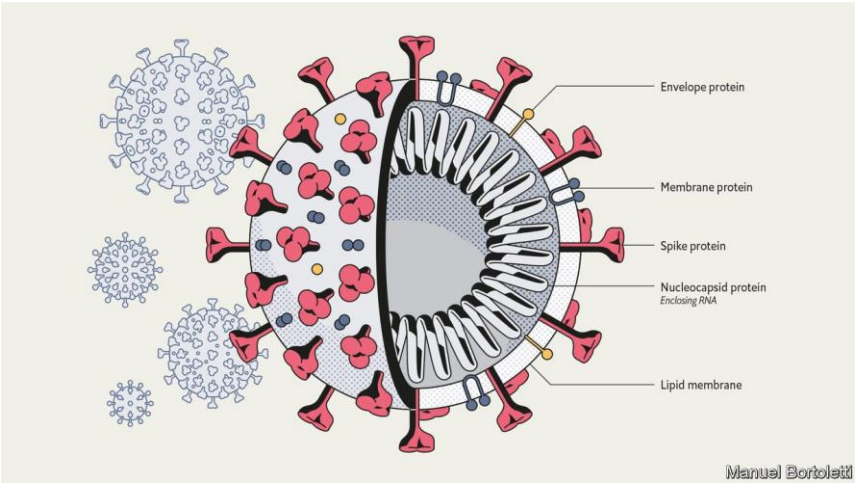
SARS-COV-2 SPIKE PROTEIN -Attaches to ACE-2 RECEPTOR

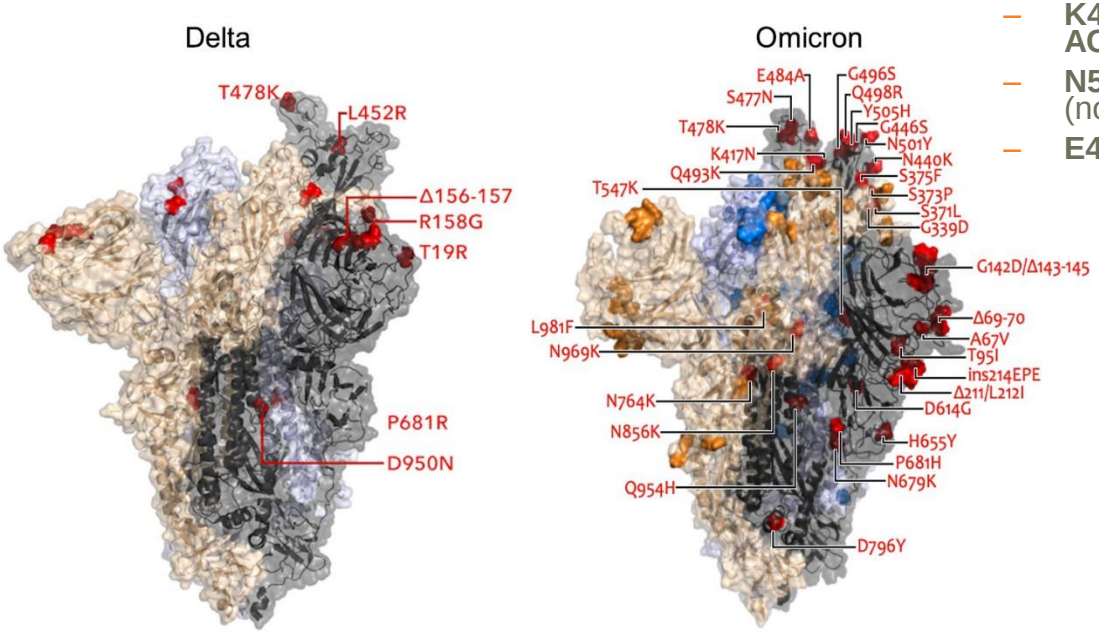




Variants of SARS-CoV-2

- Mutations that result in increased transmission out compete previous variants
- Alpha variant emerged in US in January 2021, became predominant variant Spring 2021
- Delta variant responsible for the spring surge in India, emerged US predominant variant summer
- Omicron emerged US in December 2021, and has rapidly become predominant variant in a few weeks

Mutations on Delta compared to Omicron



- **H655Y, N679K, and P681 cluster** (adjacent to S1/S2
- **D614G preserved**
- **K417N: helps virus bind more tightly to ACE2**
- **N501Y: helps virus latch on more tightly** (not seen with Delta)
- **E484K: additional spike protein mutation**
  - Significant: Alters binding of current neutralizing antibodies to spike protein
    - **Plasma from previously infected individuals did not neutralize**
    - **Partially and fully resistant to monoclonal antiboidies: Casirivimab and Bamlanivimab, respectively**
  - The virus remains infective in the face of previously effective neutralizing antibodies

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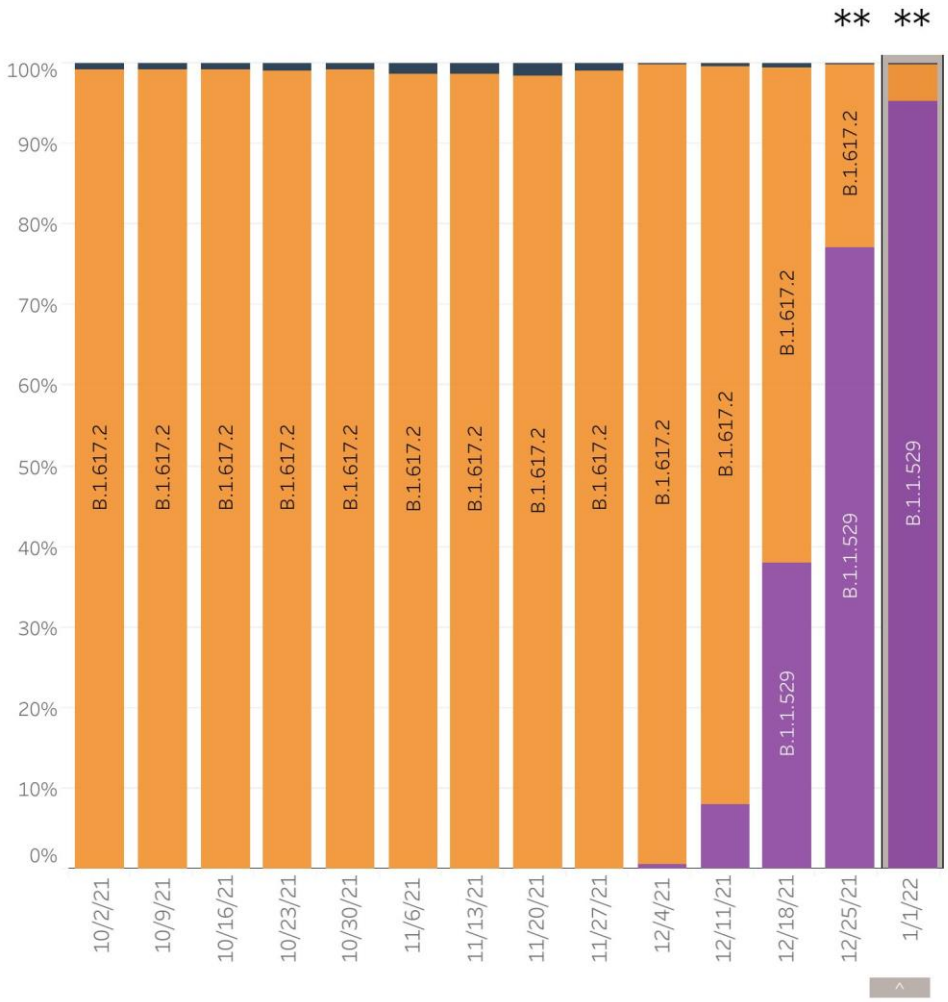
Omicron variant in the United States



USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	95.4%	92.9-97.0%
Delta	B.1.617.2	VOC	4.6%	2.9-7.0%
Other	Other*		0.0%	0.0-0.1%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

\# AY.1-AY.127 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

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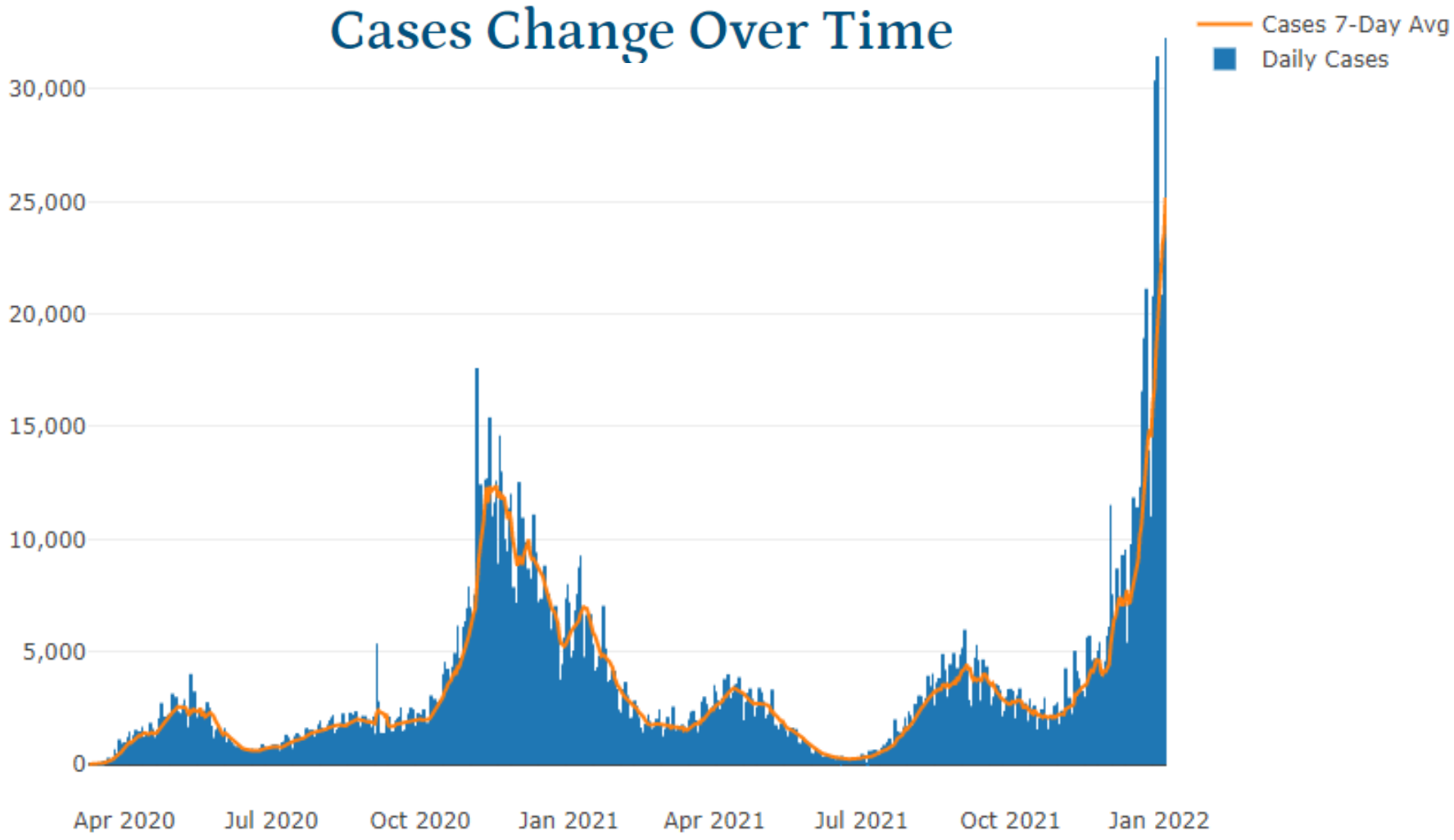
Statewide Metrics



https://dph.illinois.gov/covid19.html

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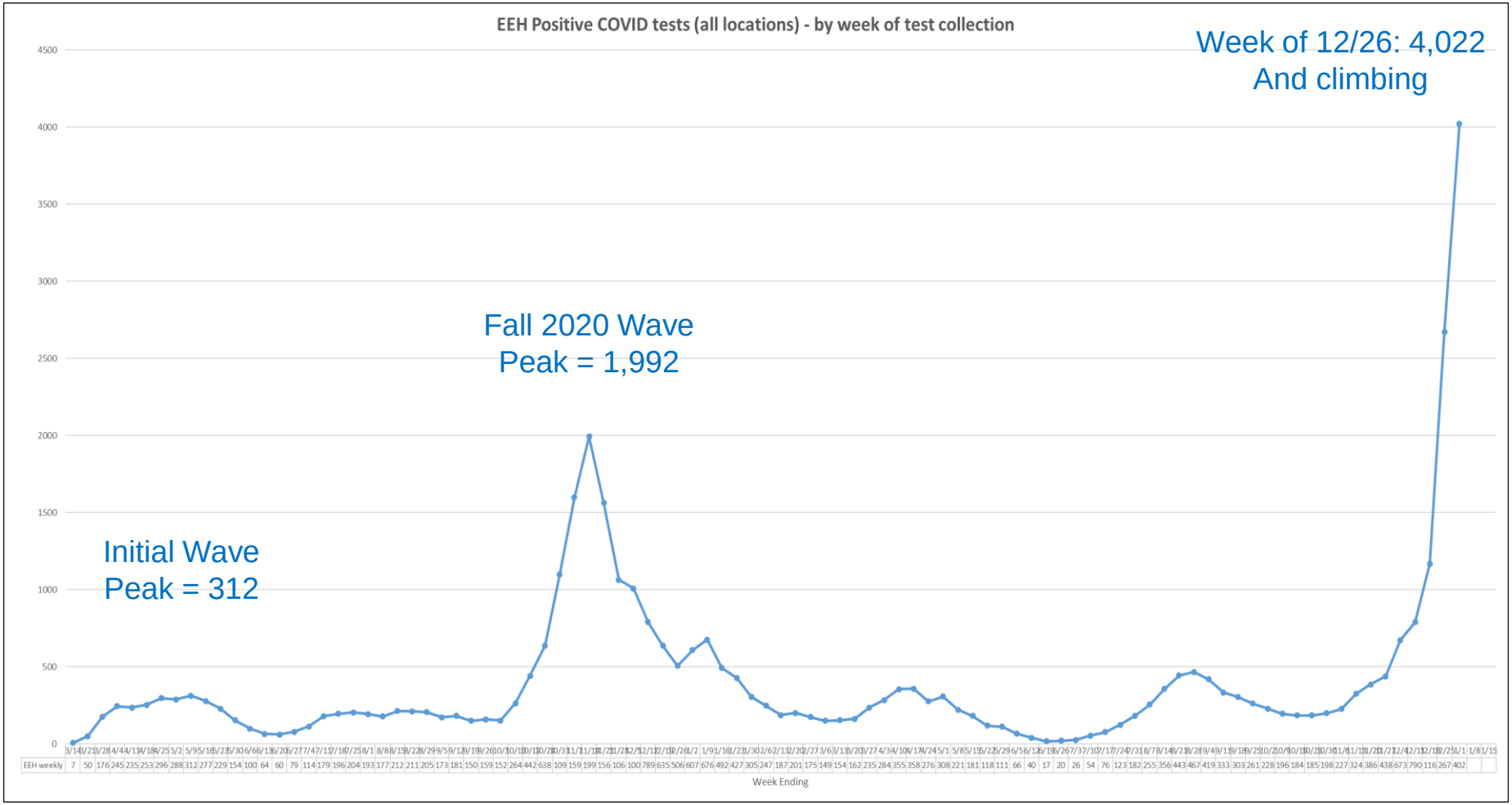
Edward-Elmhurst Health COVID Data
(System-wide, all locations)



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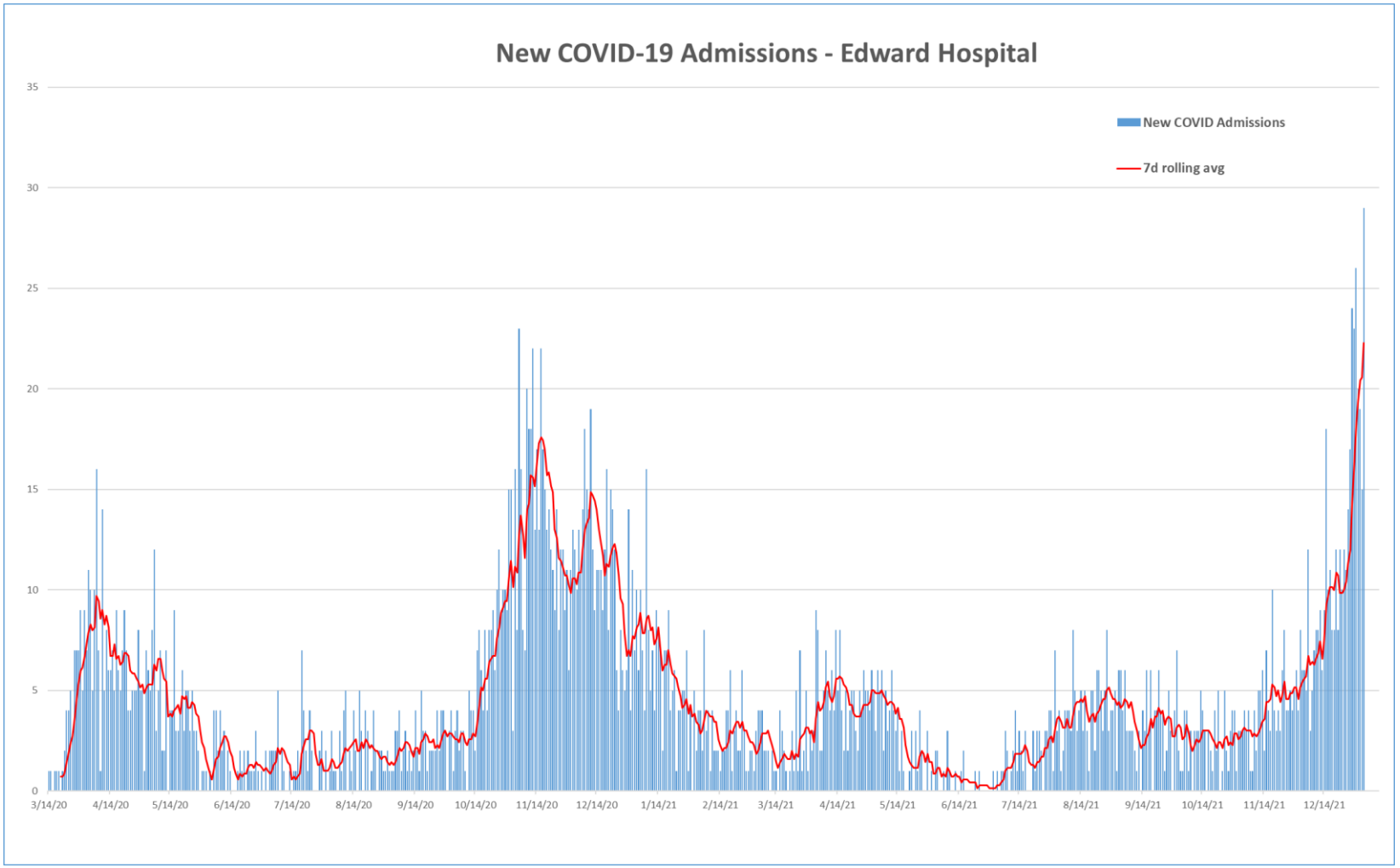
Edward Hospital COVID Admissions Data



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How m-RNA vaccines works

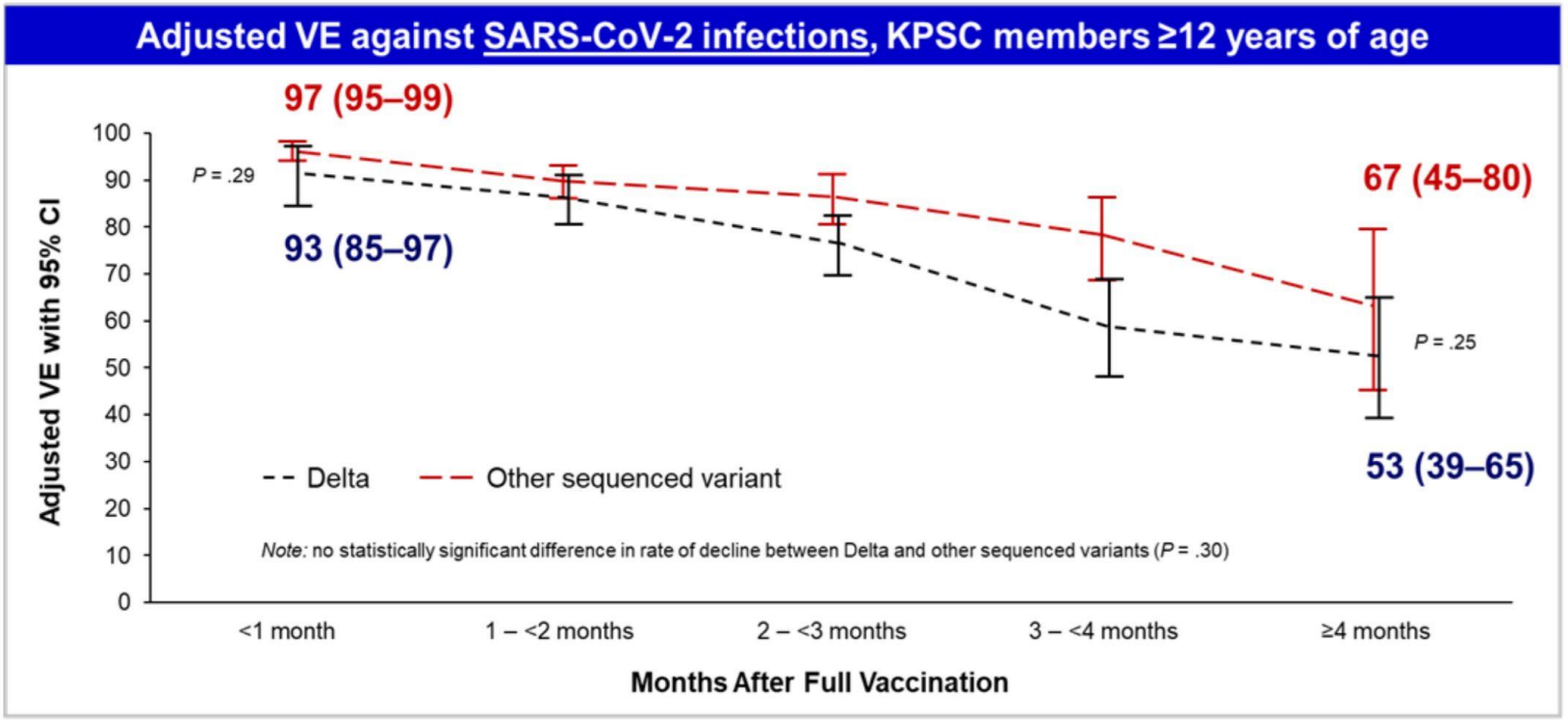
- Pfizer and Moderna vaccines contain m-RNA for the whole spike protein (1,273 pieces), encased in a protective lipid nanoparticle
- In the cytoplasm of the muscle cells and dendritic cells, m-RNA encodes spike protein, m-RNA quickly degraded, and IS NOT incorporated into DNA
- SPIKE protein elicits immune response, leading to production of memory B cells (that produce antibodies) and T cells (that can recognize spike protein and eradicate cells infected with virus)
- Memory B cells mature with time
- Booster doses elicit mature B cells to produce more antibodies, increase in breadth of antibodies, along with increased T cells

Impact of time from vaccination on vaccine effectiveness

- Prior to delta, Pfizer released efficacy through 6 months, through March 2021
- 0-2 months 95%
- 2-4 months 91%
- 4-6 months 84%

Impact of Delta variant on vaccine effectiveness over time

Figure 1. Adjusted VE Against SARS-CoV-2 Infections: KPSC Members ≥12 Years of Age



*Whole genome sequencing was performed on all PCR+ samples collected Mar 4, 2021 – Jul 21, 2021.

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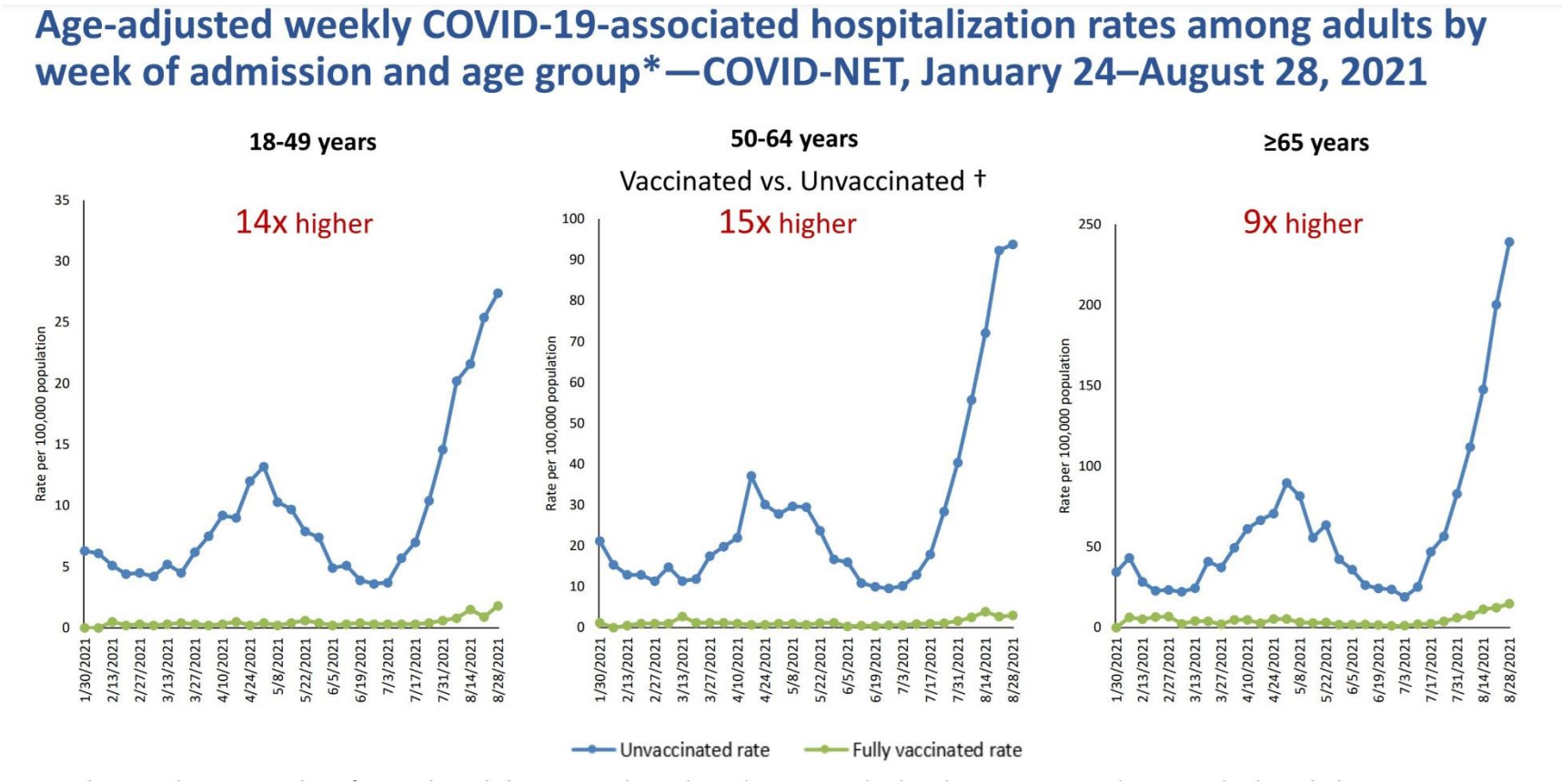
Vaccine effectiveness agains hospitalization



Effect of boosters on delta variant

Pfizer

- Neutralizing antibody levels 3.1 x higher (4 weeks after booster than 4 weeks after 2nd dose)
- Neutralizing antibodies against delta 6-8x higher
- 95% better protection with a booster than with 2-doses

Moderna

- Neutralizing antibodies 1.9 x higher after booster, and several fold higher against delta variant

J&J

- Vaccine efficacy 71% with 1-dose, and 94% with 2-doses (in the United States) compared to no vacciation

Impact of OMICRON on vaccine effectiveness

- Serum from previously infected or vaccinated but not boosted poorly neutralized Omicron
- Serum from those vaccinated and boosted did neutralize Omicron variant, but not as well as delta
- Vaccine effectiveness against infection 30-35% with 2-dose primary series m-RNA vaccine, down from 80% for delta
- Vaccine effectiveness against infection 70-75% with a booster
- Early estimates of vaccine effectiveness against hospitalization is 70% (for the primary series), compared to 93% for Delta
- Boosters likely providing significantly higher protection against severe infection with Omicron

Omicron severity compared with Delta

Omicron's signature is its ability to re-infect and cause vaccine breakthrough infections

Vaccine breaktrhough infections and re-infections are more often mild compared to infections in unvaccinated

Animal studies show Omicron may be more efficient at infecting the upper airway than the lungs compared to delta

Omicron causes a GREATER NUMBER of severe infections than delta by infecting more people, many who develop pneumonia, and need hospitalization

Hospitalizations and ICU admissions are rising due to Omicron variant, predominantly among unvaccinated

Hosptialization during Omicron -local experience

- Hospitalizations are at the highest since the beginning of the pandemic (147 admissions week ending 1/1/21 compared to peak of 118 admissions week of 11/14/2020)
- During summer, fall 70% of patients admitted and testing positive for COVID-19 were unvaccinated
- In January 2022, over 40% of patients admitted for COVID-19 are vaccinated
- Vaccinated patients admitted for COVID-19 tend to be older(median age 71), and less often severe (33% requiring oxygen)
- Vaccinated patients with severe infection requiring oxygen are much older, median age of 80, are immune compromised or not had boosters
- Unvaccinated patients admitted with COVID-19 are younger, median age 57, and more often severe (71% requiring oxygen)

TESTING

- Viral tests (for the presence of virus)

PCR(or NAAT): detects RNA

-traditional PCR or rapid PCR (ID NOW)

Antigen tests (rapid tests): detects viral proteins

Both PCR and antigen tests are based on viral nuclear proteins, rather than spike protein and generally sensitivity not effected by variants

-FDA issued notice that some antigen tests have lower sensitivity for OMICRON

- Antibody tests (for evidence of previous infection)

-does not measure level of immune protection and should not be used to make decisions on vaccination or boosters

ISOLATION for COVID-19

- Infectious virus is not detected after 10 days in those with mild/moderate symptoms
- Virus can be cultured up to 20 days in critically ill hospitalized
- Transmission peaks beginning 1 day prior to day of symptoms, and decreases over the next 3-4 days, transmission rare after 5th day
- PCR can stay positive for weeks to months and not indicative of infectious virus
- Antigen detects viral proteins and better correlates with infectiousness than PCR

Isolation(when you test positive)

- 10 days after the onset of symptoms or positive test(if asymptomatic)
- 20 days for severe infection requiring hospitalization
- Updated CDC guidance 12/2021
- Day 0-5: stay home and isolate from others
- Day 6-10: can leave home for essential activities and wear a well fitted mask around others (if asymptomatic or mild resolving symptoms)
- Test option: antigen test after day 5 (if negative can leave home and mask around other until day 10)

Quarantine (when you are exposed)

- If you are exposed:
- If symptoms get tested
- If no symptoms, test on day 5 after first exposure
- If vaccinated and up to date with booster wear a mask when around others for 10 days
- If not vaccinated or not up to date with booster:

-stay at home until day 5 and wear a mask around others for the next 5 days

-if you are unable to stay at home, mask when around others for 10 days

Layered approach to prevention

- Get vaccinated and a booster if eligible
- Make sure everyone in your household who is eligible get vaccinated and boosted
- Wear a mask when with others who are not in your household
- Avoid gatherings where others are not masked or cannot safely distance, consider testing if available
- Assess the level of transmission in the community
- During high levels of transmission enhance mitigation measures

COVID-19 vaccines

- PFIZER (m-RNA)

Ages 5-11 years (pediatric dose 10ug)

-2 doses 3weeks apart

Ages 12 years and older (30ug dose)

-2 doses 3 weeks apart, booster 5 months after 2nd dose

- MODERNA(m-RNA)

Ages 18 years and older

-2 doses (100ug), 4 weeks apart

-booster (50ug), 5 months after 2nd dose

- J&J

Ages 18 and older

-1 dose with booster after 2 months

MONOCLONAL ANTIBODIES

- Antibodies that target epitopes on the spike protein
- Omicron variant is poorly neutralized by Bamlamivimab/Esetevimab and not neutralized by Casirivimab/imdvimab
- SOTROVIMAB targets a conserved epitope at the base of the spike protein and maintains activity against OMICRON
- When given within 5 days of symptoms onset to high-risk patients, reduced hospitalization or by 85%

Monoclonal antibodies as prevention

- For patients who are immune compromised
- Vaccination is beneficial for immune compromised, but they remain at higher risk than non immune compromised
- AstraZeneca's *Evusheld* (tixagevimab co-packaged with cilgavimab), a long-acting antibody (LAAB) combination
- FDA EUA for pre-exposure prophylaxis for patients immune compromised or who have medical contra-indications to vaccination
- Not a replacement for vaccination

REMDESIVIR

- Intravenous, FDA authorized for hospitalized patients with COVID-19 pneumonia, given for upt to 5 days
- Improves time to resolution of symptoms, shortens hospitalization (15 days in placebo compared to 10 days with Remdesivir)
- Decreased mortality in those requiring oxygen but not intubated (4% with Remdesivir, compared to 12% with Placebo)
- 87% reduction in need for hospitalization if given for 3 days, for outpatients symptoms < 7days, not yet FDA authorized for this use

PAXLOVID

- Oral protease inhibitor
- FDA authorized under Emergency Use Authroization for high risk patients
- Nirmatrelivir inhibits protease enzyme, stopping viral replication
- Ritonivir boosts levels of Nirmatrelivir
- *reduced risk of hospitalization or death by 89% (within three days of symptom onset) and 88% (within five days of symptom onset)*

Molnuperivir

- Oral medication
- Nucleoside analog, introduced into viral RNA creating mistakes, stopping replication
- When given within 5 days of symptoms onset, 30% reduction in need for hospitalization
- FDA authorized under emergency use authorization, for high risk patients, when other treatments are not available

Who qualifies for COVID-19 treatments

Emergency use authorization (EUA)
-age >=65 or high risk medical conditons

-Immune compromised (e.g, organ transplant, on chemotherapy, on biologics for autoimmune conditions)

-Obesity, chronic kidney disease, diabetes mellitus, chronic lung disease, sickle cell, pregnancy, neurodevelopmental disorder, chronic lung disease

Monoclonal antibodies EUA symptoms up to 10 days, but effectiveness diminishes each day, best given as early as possible

Antivirals should be given as early as possible and were found to be effective when given within 5 days of symptom onset

COVID-19 treatment risk tiers

Treatments allocated first to the patients at highest risk of hospitalization and death

Expand to lower tiers as supply increases

Tier 1: IMMUNE COMPROMISED OR unvaccinated and age >=75 or Un vaccinated and age 65-74 with high-risk medical condition

Tier 2: unvaccinated and age >=65 or unvaccinated and age < 65 with high risk medical condtion

Tier 3: Vaccinated age >=75 or Vaccinated age 65-74 with high -risk medical condition

Tier 4: Vaccinated age <65 with high risk medical condtion