COVID-19 UPDATE: FOCUS ON XBB SUBLINEAGES

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Disclosures: Consultancy; Pfizer, Merck, Sanofi, PDI, BD, Germitec, Wellair
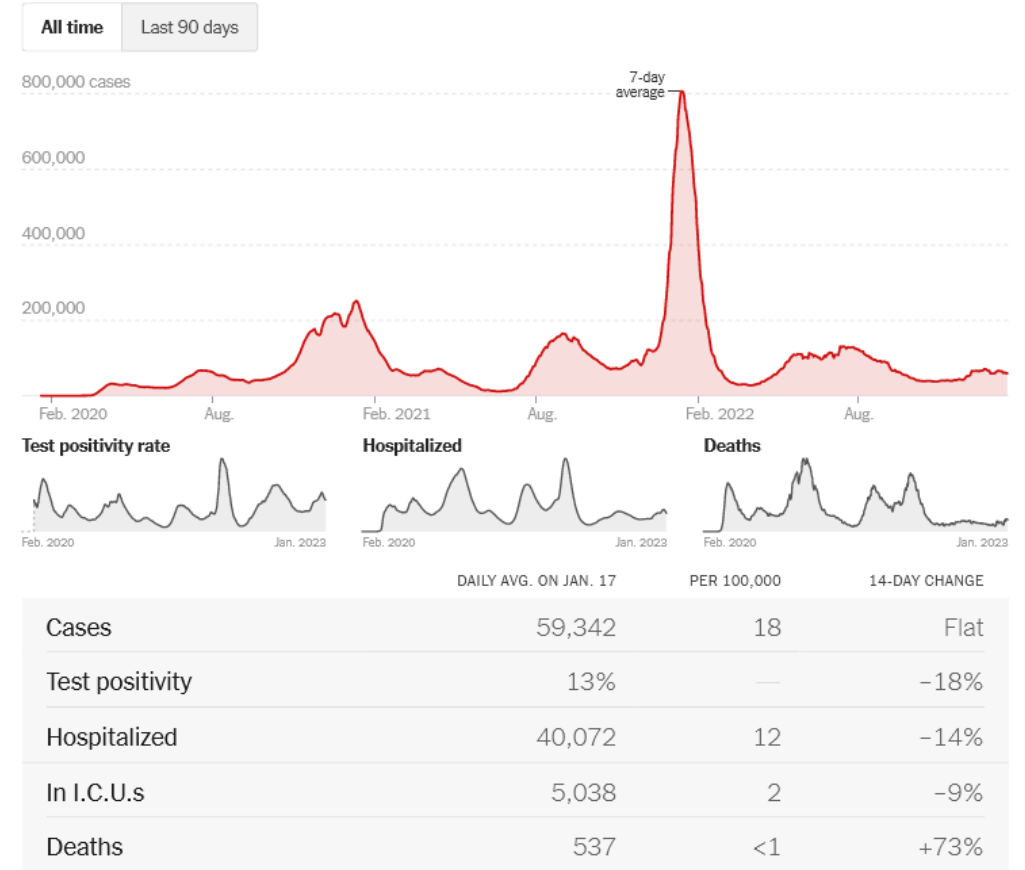All drugs/vaccines issues discussed consistent with FDA approvals or authorizations

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COVID-19: UPDATE, 1/18

- Regional differences are increasingly driving the current state of the virus in the United States.

- On the East Coast, cases and hospitalizations are rising notably — and, due to the area's large population, these increases are enough to drive up national figures. The Carolinas are especially hard hit, with new cases nearly twice as high as they were a month ago.

- In the West, however, many metrics are flat or falling. Several states, including South Dakota and Wyoming, are currently near their all-time lows for reported cases and hospitalizations.

- Deaths are rising, but data anomalies in recent reporting may have inflated these counts.

- Orange County community level = Moderate

New reported cases

All time | Last 90 days

800,000 cases

600,000

400,000

200,000

7-day average

Feb. 2020 | Aug. | Feb. 2021 | Aug. | Feb. 2022 | Aug.

Test positivity rate

Feb. 2020 — Jan. 2023

Hospitalized

Feb. 2020 — Jan. 2023

Deaths

Feb. 2020 — Jan. 2023

	DAILY AVG. ON JAN. 17	PER 100,000	14-DAY CHANGE
Cases	59,342	18	Flat
Test positivity	13%	—	−18%
Hospitalized	40,072	12	−14%
In I.C.U.s	5,038	2	−9%
Deaths	537	<1	+73%

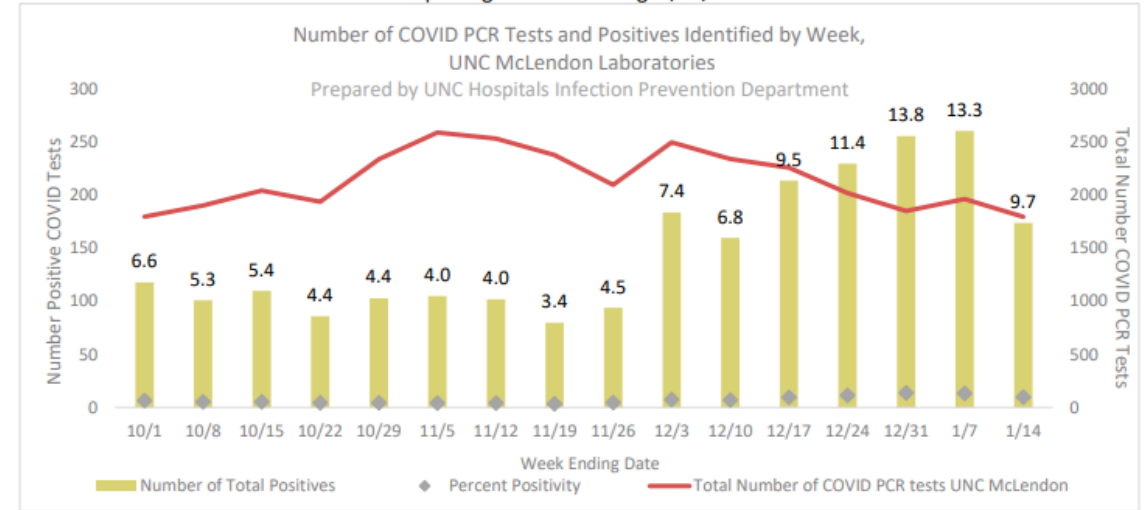https://www.nytimes.com/interactive/2021/us/covid-cases.html

COVID-19 IMPACT ON UNC-MC

- Occupational Hlealth: 50-60 COVID-19 related absences

- COVID-19 hospitalizations: ~50-60

- Viral respiratory report (week ending)
  - Overall percent positivity of COVID tests was 9.7%
  - Percent positivity for symptomatic patients being tested was 12.7% (COVID-19)
  - Percent positivity for asymptomatic patients being tested was 4.9% (COVID-19)
  - 43 Flu positive (8 deaths this season) – sustained decline
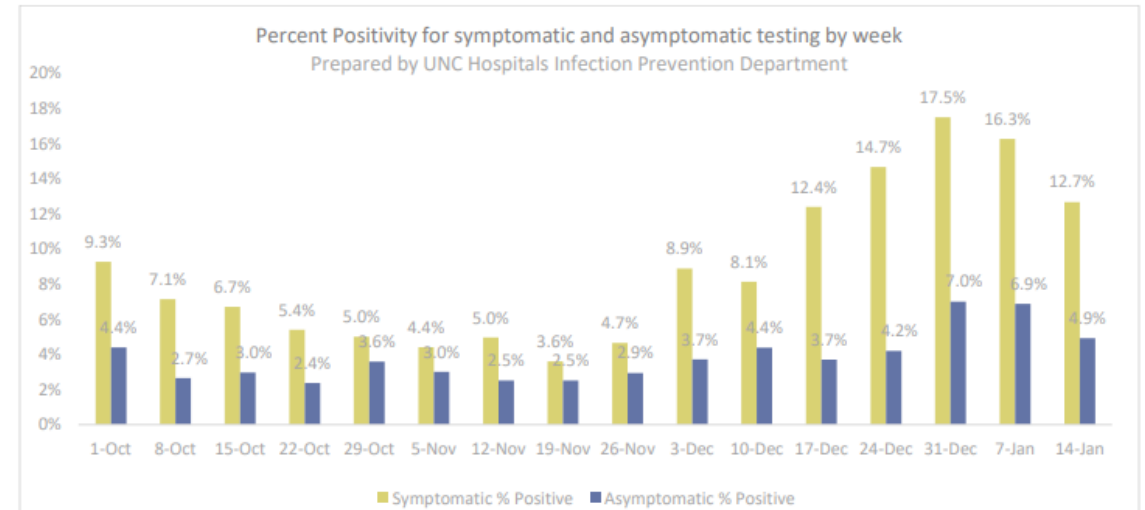 - 22 – 50% reduction compared to last week

UNCH Infection Prevention COVID-19 and Respiratory Virus Weekly Data Report
Reporting for week ending: 1/14/2023

Number of COVID PCR Tests and Positives Identified by Week, UNC McLendon Laboratories
Prepared by UNC Hospitals Infection Prevention Department

Data represents COVID-19 tests performed by UNC McLendon labs for UNC Hospitals' facilities and includes re-tests. COVID testing done as part of the RPP with COVID order and the RSV/influenza with COVID order is included.
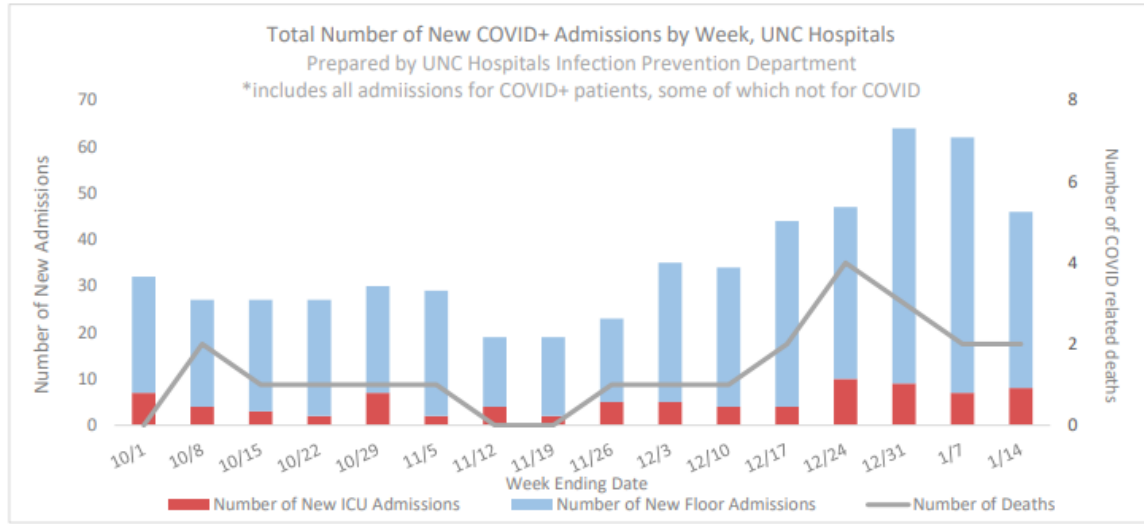
Note: Testing of asymptomatic persons in certain populations was expanded beginning 5/3. Number of tests and positive results included on the graph are not reflective of all COVID testing done by UNC McLendon Laboratories.

Percent Positivity for symptomatic and asymptomatic testing by week
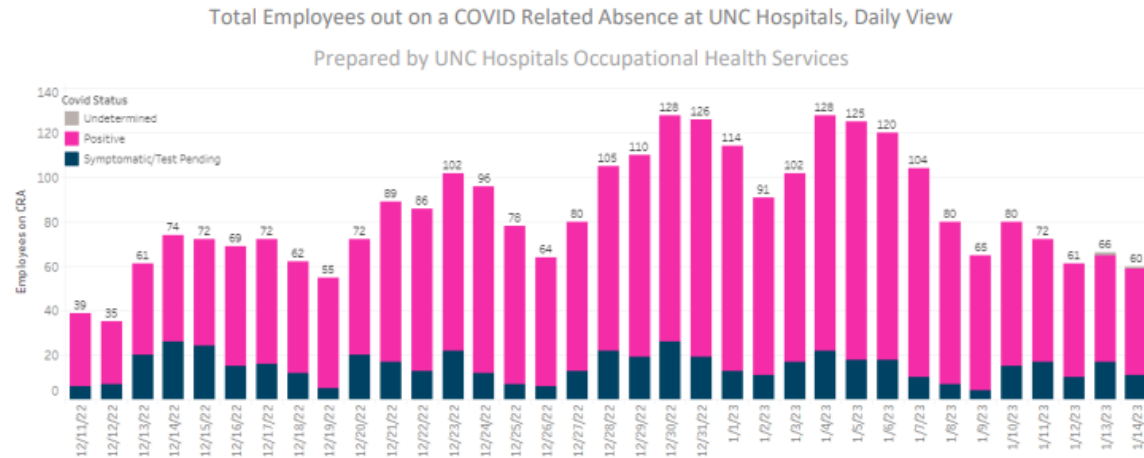Prepared by UNC Hospitals Infection Prevention Department

Percent positivity for COVID-19 tests performed by UNC McLendon labs for UNC Hospitals' facilities and includes re-tests. Symptomatic and asymptomatic testing categories determined by answer to question in COVID-19 test order.

UNCH Infection Prevention COVID-19 and Respiratory Virus Weekly Data Report
Reporting for week ending: 1/14/2023

Total Number of New COVID+ Admissions by Week, UNC Hospitals
Prepared by UNC Hospitals Infection Prevention Department
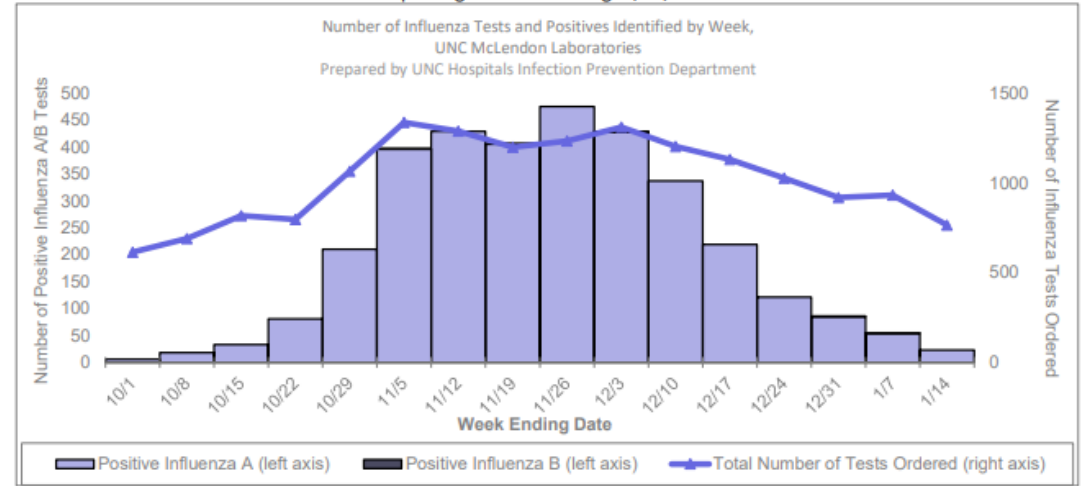*includes all admiissions for COVID+ patients, some of which not for COVID

Admissions to UNC Hospitals for patients with COVID-19 broken down by intensive care and floor units. Data includes transfers of patients between intensive care and floor units. Graph also displays number of weekly COVID related deaths.

Total Employees out on a COVID Related Absence at UNC Hospitals, Daily View
Prepared by UNC Hospitals Occupational Health Services

Count of UNC Hospitals' employees out of work on a COVID related Absence (CRA) by day. Data from OHS e-COVID database. Does not include UNC Medical School employees.
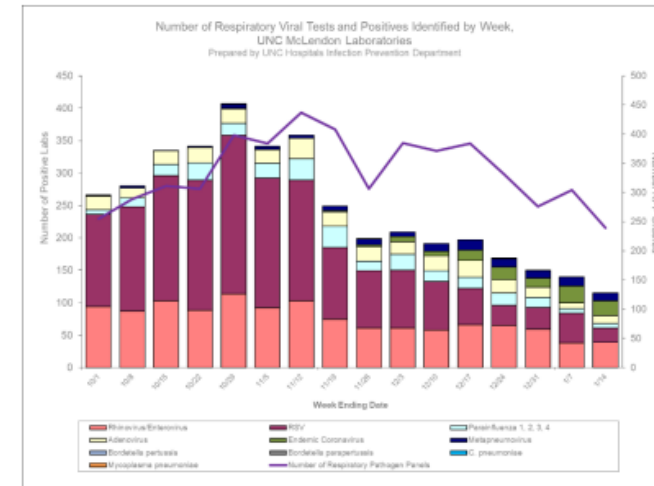
UNCH Infection Prevention COVID-19 and Respiratory Virus Weekly Data Report
Reporting for week ending: 1/14/2023

Number of Influenza Tests and Positives Identified by Week,
UNC McLendon Laboratories
Prepared by UNC Hospitals Infection Prevention Department

Data represents influenza PCR tests performed by UNC McLendon labs for UNC Hospitals' facilities.
<u>Note</u>: Number of tests and positive results included on the graph are not reflective of *all* influenza testing done by UNC McLendon Laboratories.

Number of Respiratory Viral Tests and Positives Identified by Week,
UNC McLendon Laboratories
Prepared by UNC Hospitals Infection Prevention Department

Data represents respiratory pathogen panel tests performed by UNC McLendon labs for UNC Hospitals' facilities.
<u>Note</u>: Number of tests and positive results included on the graph are not reflective of *all* RPP testing done by UNC McLendon Laboratories. COVID19 positives from RPP with COVID orders are included in the first graph of this report.
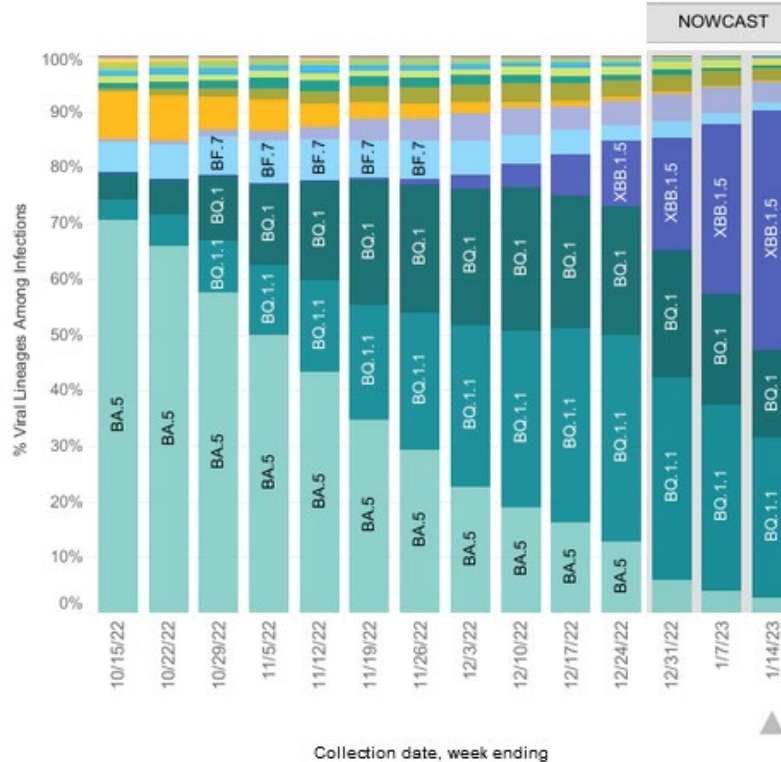
SARS-CoV-2 Variants: Current Summary

- XBB.1 first reported from India in August 2022; XBB.1.5 first reported from US (NY, CT) in late October 2022

- Epidemiology, US
  - The sublineages BQ.1, BQ.1.1, XBB and XBB.1.5 carry an additional spike mutation in a key antigenic site (i.e. R346T); these sublineages show a significant growth advantage over other circulating Omicron sublineages in many settings
  - Rapid increase of XBB.1 and XBB.1.5 – subvariant with greatest escape from vaccines and natural immunity (also not impacted by Evusheld or Bebtelovimab); similar severity of disease
  - XBB.1.5 = effective Ro, 1.6; 40% higher than any other sublineage (https://www.cnn.com/2023/01/03/health/covid-variant-xbb-explainer/index.html)

- XBB.1: Recombinant of BA.2.10.1 and BA.2.75 sublineages; evidence pointing at a higher reinfection risk, as compared to other circulating Omicron sublineages

- Best evidence suggests that antivirals (e.g., Remdesivir, Paxlovid, Molnupivir) retain activity against all variants
  - Paxlovid effectiveness ~50% prevent hospitalizations & 75% to prevent death; also effective in reducing risk of long COVID-19

- Bivalent COVID-19 vaccine elicits lower neutralizing antibodies to XBB than other SARS-CoV-2 variants and Omicron sublineages but is superior to monovalent vaccines including persons who have had 2 boosters (i.e., 4 doses)
  - Vaccination also reduces risk post-COVID-19 of vascular events (heart attacks, strokes; 30-90 days) and long COVID-19

- Only ~18% of Americans 5+ have received bivalent booster; ~35% of persons 65 years and older

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COVID-19 VARIANTS, US

United States: 1/8/2023 – 1/14/2023 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI	
Omicron	XBB.1.5	VOC	43.0%	26.4-61.1%	
	BQ.1.1	VOC	28.8%	20.5-38.7%	
	BQ.1	VOC	15.9%	11.0-22.2%	
	XBB	VOC	3.9%	3.0-5.1%	
	BA.5	VOC	2.6%	1.8-3.7%	
	BN.1	VOC	2.1%	1.5-3.1%	
	BF.7	VOC	1.4%	0.9-2.1%	
	BA.2.75	VOC	1.3%	0.8-1.9%	
	BA.5.2.6	VOC	0.5%	0.3-0.8%	
	BA.2	VOC	0.2%	0.1-0.4%	
	BF.11	VOC	0.2%	0.1-0.3%	
	BA.4.6	VOC	0.1%	0.1-0.2%	
	BA.2.75.2	VOC	0.1%	0.0-0.1%	
	BA.1.1	VOC	0.0%	0.0-0.0%	
	BA.4	VOC	0.0%	0.0-0.0%	
	B.1.1.529	VOC	0.0%	0.0-0.0%	
	BA.2.12.1	VOC	0.0%	0.0-0.0%	
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%	
Other	Other*		0.0%	0.0-0.0%	

* 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
\# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1,XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except XBB.1.5, sublineages of XBB are aggregated to XBB. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB.1.5 was aggregated to XBB. Lineages BA.2.75.2, XBB, XBB.1.5, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

Multiple sublineages escape from monoclonal antibody prophylaxis (i.e., Evusheld) and treatment (i.e., bebtelovimab) including BQ.1., BQ.1.1, XBB.1, XBB.1.5

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Effectiveness of the Bivalent mRNA Vaccine in Preventing Severe Covid-19 Outcomes: an observational cohort study

- Methods: This retrospective cohort study included all members of Clalit Health Services, aged ≥65, eligible for a bivalent booster. Hospitalizations and death due to Covid-19 among participants who received the bivalent vaccine were compared with those who did not. A Cox proportional-hazards regression model with time-dependent covariates was used to estimate the association between the bivalent vaccine and Covid-19 outcomes while adjusting for demographic factors and coexisting illnesses. Study enrollment, 9/24/22-12/12/23 (data extraction, 12/14/23)

- Findings: A total of 622,701 participants met the eligibility criteria. Of those, 85,314 (14%) received a bivalent-booster during the 70-day study period. Hospitalization due to Covid-19 occurred in 6 bivalent recipients and 297 participants who did not, adjusted hazard ratio (HR): 0.19 (95% CI, 0.08-0.43). Death due to Covid-19 occurred in 1 bivalent recipient and 73 participants who did not, adjusted HR 0.14: (95% CI, 0.02-1.04).
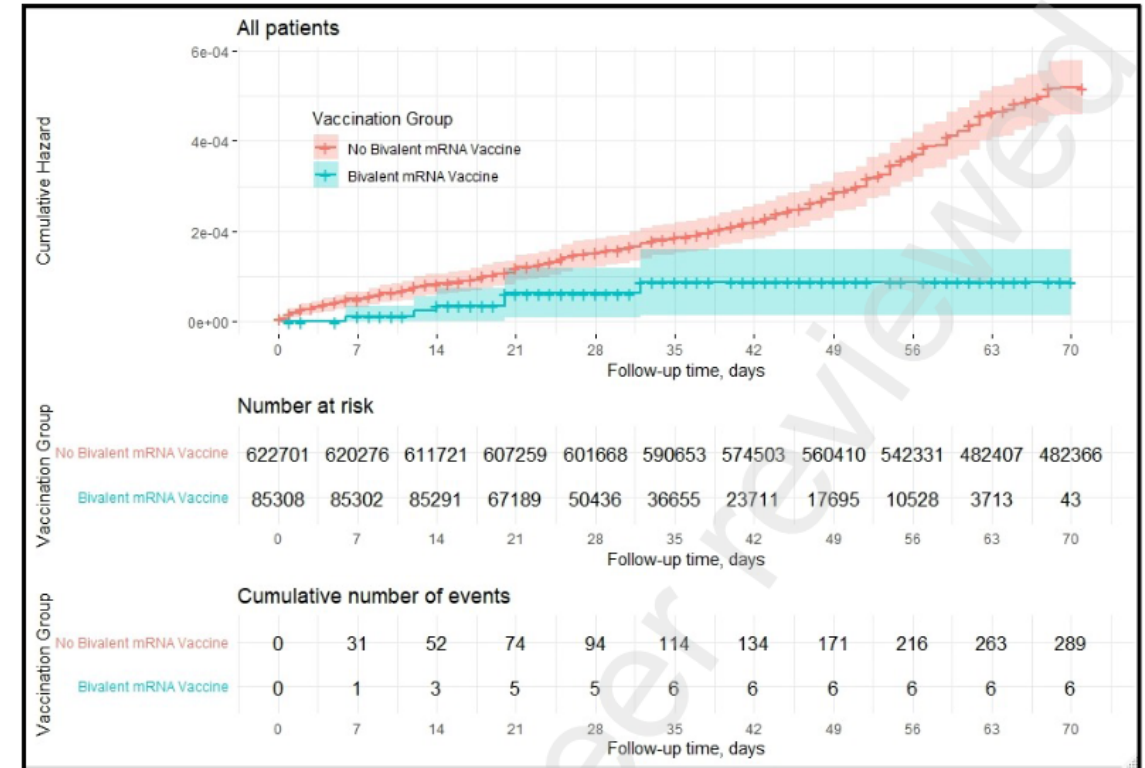

Figure 1: Cumulative hazard for Covid-19 hospitalization

Arbel R, et al. Lancet 2023;3 January

Rates of laboratory-confirmed COVID-19 hospitalizations by vaccination status, CDC

In November 2022, compared to adults ages 18 years and older who received an updated COVID-19 bivalent booster dose, monthly rates of COVID-19-associated hospitalizations were **16.0x Higher in Unvaccinated** and **2.7x Higher in Vaccinated Adults without an updated booster.***

29.9x Higher
in Unvaccinated Adults Ages 18-49 Years

13.6x Higher
in Unvaccinated Adults Ages 50-64 Years

13.5x Higher
in Unvaccinated Adults Ages 65 Years and Older

3.2x Higher
in Adults Ages 18-49 Years Vaccinated but Without an Updated booster

2.9x Higher
in Adults Ages 50-64 Years Vaccinated but Without an Updated booster

2.5x Higher
in Adults Ages 65 Years and Older Vaccinated but Without an Updated booster

https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

Monthly Age-Adjusted Rates of COVID-19-Associated Hospitalization by Vaccination Status in Patients Ages ≥18 Years January 2021 - November 2022