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COVID-19 Update

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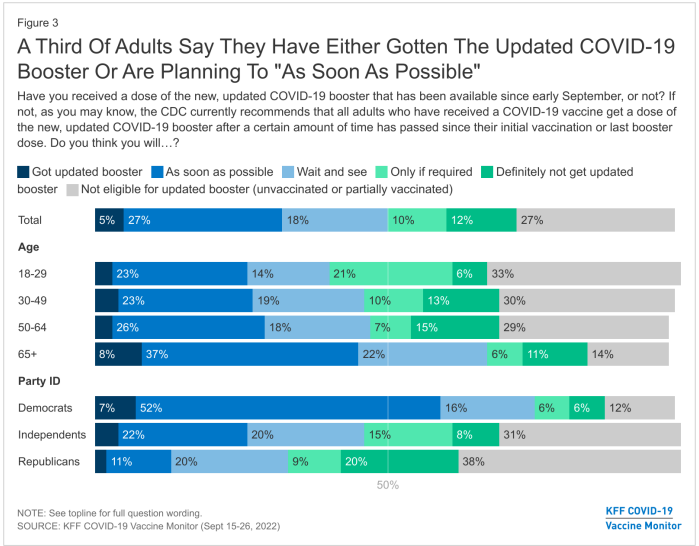
Monday, November 21st, 2022

HP2030 HEALTHY PEOPLE 2030 CHAMPION

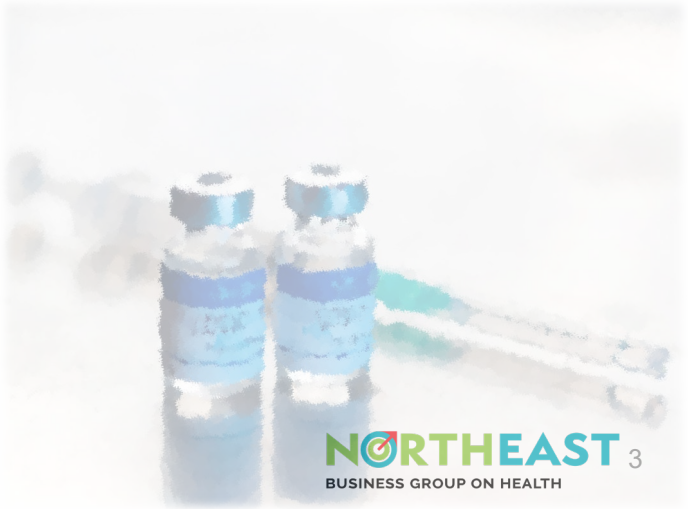
Up-Dated Booster Vaccines

- In September, a KFF survey found A Third Of Adults Say They Have Either Gotten The Updated COVID-19 Booster Or Are Planning To "As Soon As Possible"
- However, to date uptake has been slow and to date only have had the updated booster:
  - 11.3% of the population ≥ 5 Years of Age
  - 12.3% of the population ≥ 12 Years of Age
  - 13.1% of the population ≥ 18 Years of Age
  - 29.6% of the population ≥ 65 Years of Age

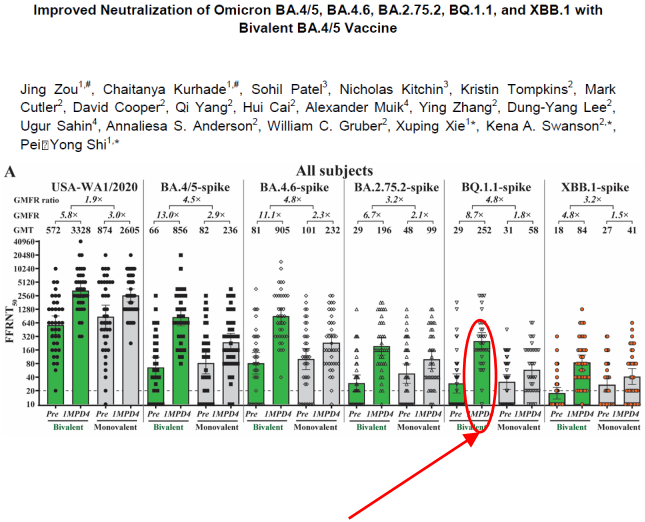


The Reasons Why People are not Getting the Updated Booster

- Confusion:
  - 40% not sure if they are eligible
- Rejections:
  - 22% would not get the vaccine unless they had to and 27% unlikely to as not eligible because they haven't had the primary course
- Concern over side-effects
  - Minor side-effects post injection but may make some people feel unwell for a day or two
  - Rare but more serious side-effects e.g., myocarditis
- Beliefs:
  - "COVID is now mild a disease"
  - "I have been vaccinated and had COVID, so I am immune"
  - "The pandemic is over"
- Mixed Messaging:
  - Divergence of 'expert' views
  - Breakthrough infections vs. protection
  - Confusing studies that show range of benefits – from little to great



What we Know and Don't Know About the Updated Boosters



Good antibody response against BQ.1.1 (BQ.1 and BQ.1.1 make up 50-75% of cases in the US)

https://www.biorxiv.org/content/10.1101/2022.11.17.516898v1

What we know:

- Effective against BQ.1 and BA.1.1
- Also work against BA.4 and BA.5 – but study indicates similar to effectiveness of previous boosters
- Breakthrough infections are occurring, but people protected from serious illness
- Side-effect profile similar to existing boosters (good safety profile)

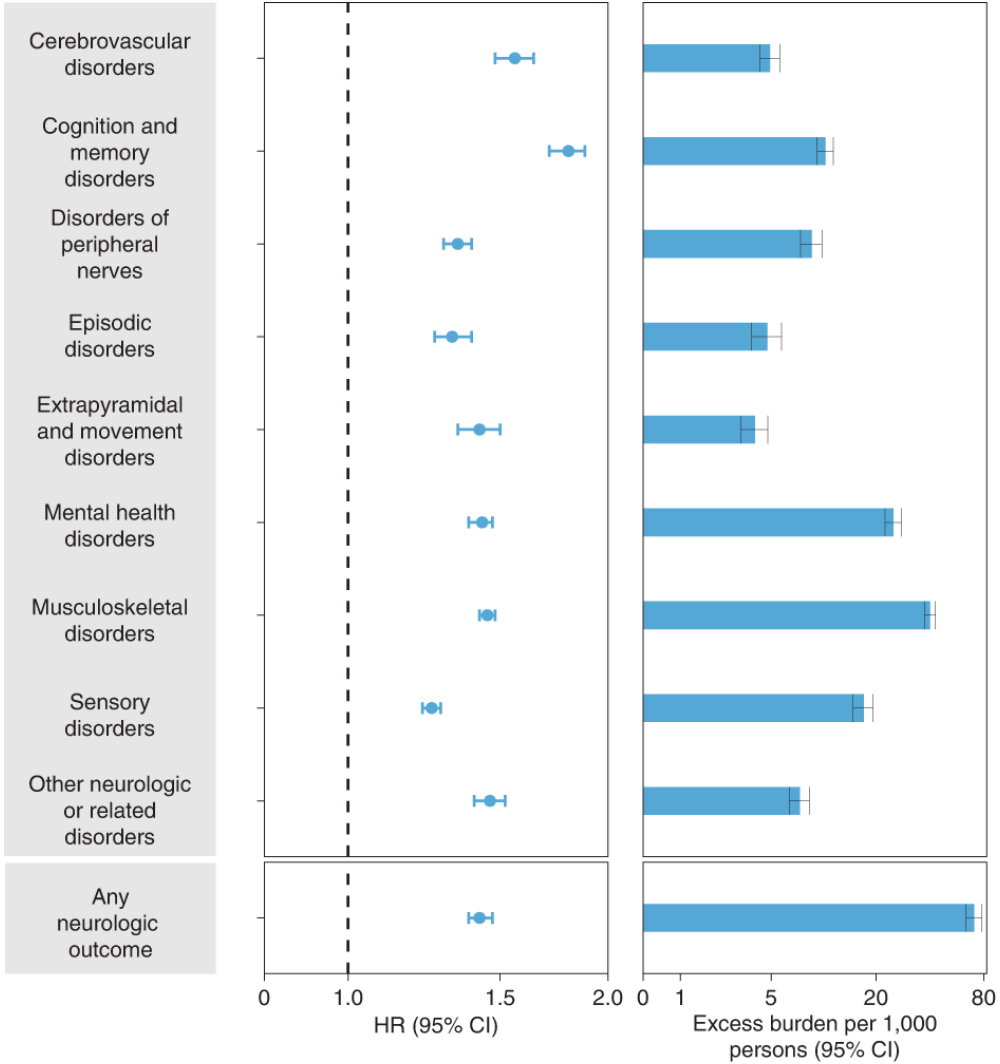
What we don't know:

- Updated boosters may broaden immune response but not yet proven
- Duration of protection
- Impact on Long-COVID

Mixed Messaging for Experts

- Experts generally agree that new updated boosters recommended for 65+ and those at higher risk
- Some differing views on need for boosters for healthy younger adults – depends on how they look at risk vs. benefit.
  - One view – risk of serious illness is low in healthy young adults vs. risks from side-effects (mostly local/short lived, rare more serious side-effects) suggest only vaccinated those at risk\
  - Other view –
    - boosters add additional protection(self and community), may offer some protection against long-COVID, some decrease in transmission risk – helping those around a person vs very safe vaccines
    - All other controls dropped by society
    - So best to be vaccinated and boosted

Overall, study estimate that patients with COVID-19 have a 42% increased risk of developing a neurological sequela in the year after infection, translating to a burden of 7% of infected people



https://www.nature.com/articles/s41591-022-02018-4

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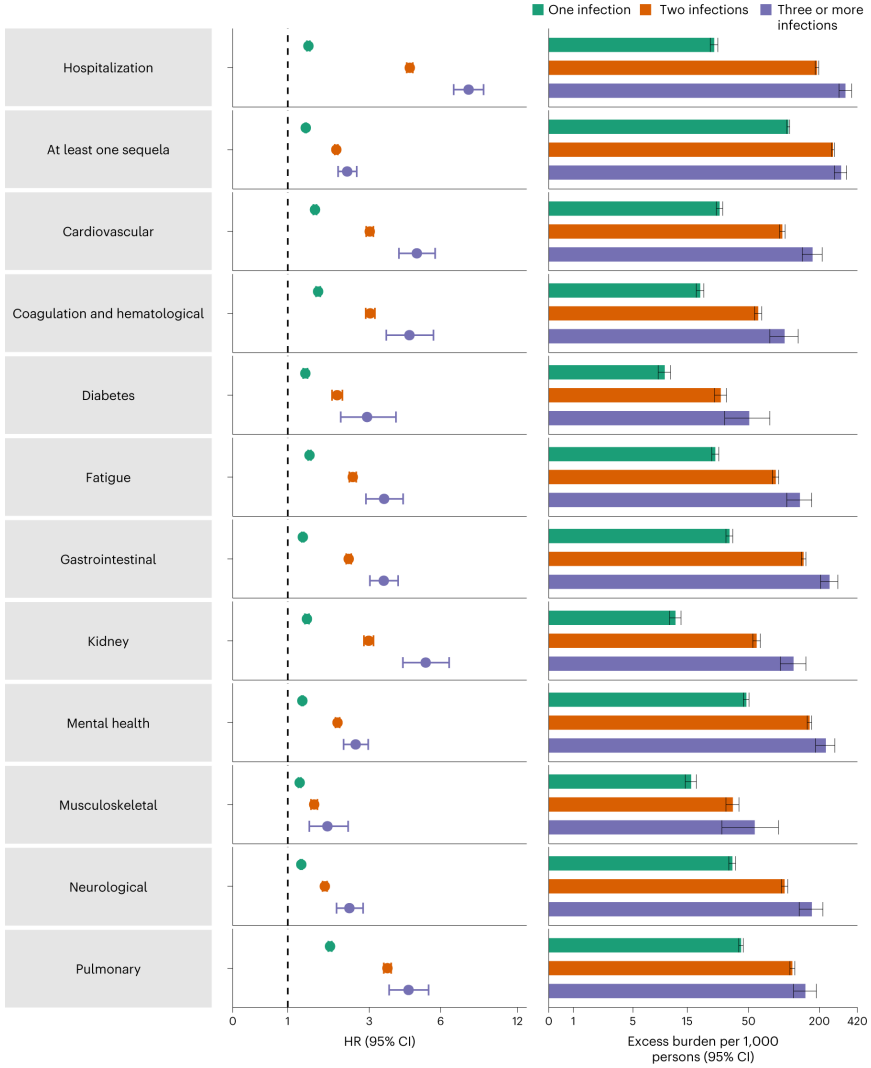

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Antigenic Imprinting (aka: ‘original antigenic sin’)

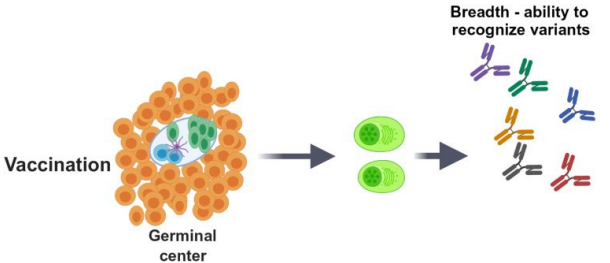
- Antigenic imprinting is the propensity of the immune system to preferentially use immunological memory based on a previous infection when a second slightly different version of that foreign pathogen (e.g., a virus or bacterium) is encountered.
- This leaves the immune system "trapped" by the first response it has made to each antigen, and unable to mount potentially more effective responses during subsequent infections. Antibodies or T-cells induced during infections with the first variant of the pathogen are subject to repertoire freeze, a form of original antigenic sin.

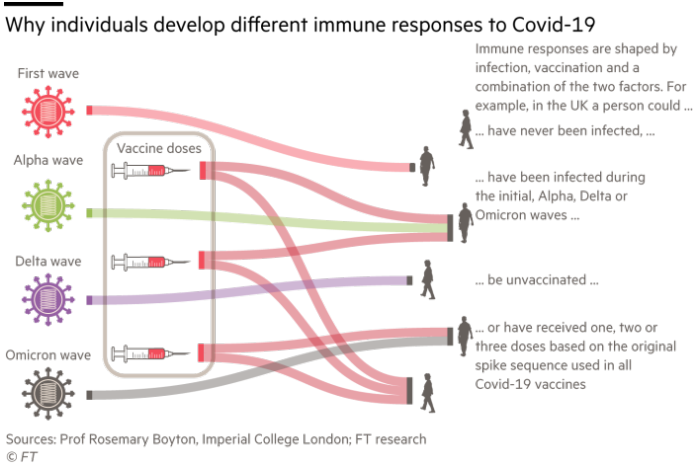
Antigenic Imprinting

- Concern - single-component vaccine could trap the immune system in just producing a response against this single-component. If the virus/bacteria changed vaccination could conceivably make an infection even worse than if no vaccination at all had occurred because the body wouldn't be able to mount an effective response against this new variant
- Antigenic imprinting can be a challenge when infectious agents change or have multiple 'strains':
  - Dengue Fever – vaccinated against one strain but when infected with another strain of Dengue - cytotoxic T cells (CTL) during a second infection by a different strain of dengue virus, the CTLs prefer to release cytokines instead of causing cell lysis. As a result, the production of these cytokines is thought to increase vascular permeability and exacerbate damage to endothelial cells, resulting in dengue hemorrhagic fever
  - HIV – vaccine against one variant of HIV may not protect against another variant
- Antigenic Imprinting is not consistent and varies also with each infectious agent vaccine, geographic location, and age
- Antigenic imprinting can be favorable, neutral, or negative

So, what does this mean for SARS-CoV2 infections and vaccines?

- The impact if any is not fully known and complicated by the fact there may also be immunogenic imprinting from infections with multiple variants
- Studies[1,2] suggested that the breadth of the immune response was greater from vaccination versus infections
- The ‘immune experience is different based on infections, with which variant and vaccination status/type and the order in which infections or vaccinations occured

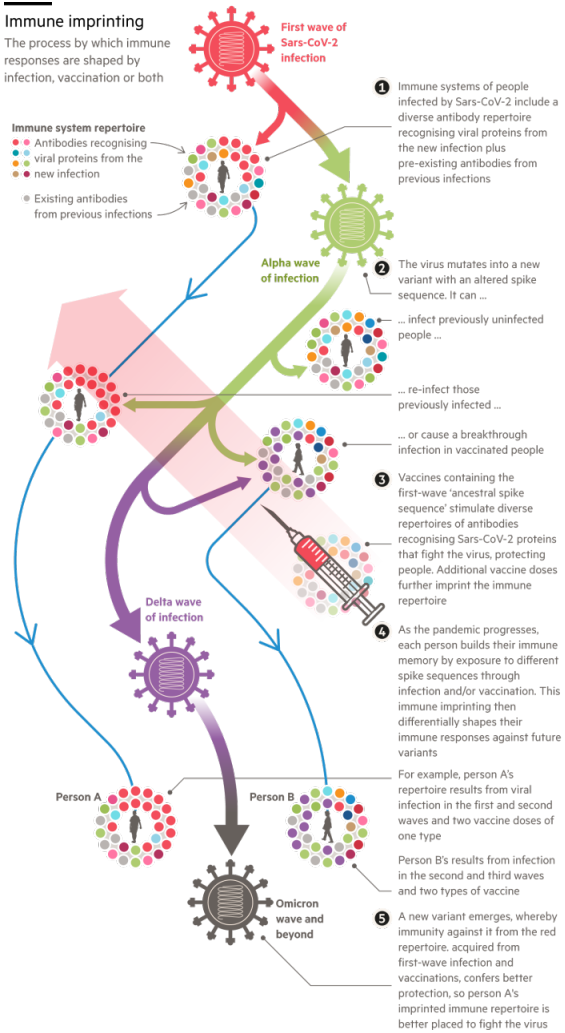




1. https://www.cell.com/trends/immunology/fulltext/S1471-4906%2822%2900048-5
2. https://www.cell.com/cell/fulltext/S0092-8674(22)00076-9?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867422000769%3Fshowall%3Dtrue

Immune imprinting

The process by which immune responses are shaped by infection, vaccination or both



Tracking and understanding immune imprinting of individuals and populations is thus important to counter new variants and inform next generation vaccine design

Sources: Prof Rosemary Boyton, Imperial College London; FT research

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Avoiding/Minimizing Immunogenic Imprinting

- Developed vaccines that result in immune response against multiple parts of the virus or against all β coronoviruses
- Extending the interval between jabs could help reduce the impact of immune imprinting
- Developing intra-nasal vaccines may also help by stopping infections at point of entry

"All the News That's Fit to Print"

The New York Times

LATE EDITION

Today, partly sunny and breezy, coldest day this season, high 39. Tonight, clear and cold, low 28. Tomorrow, plenty of sunshine, breezy, high 43. Weather map is on Page 32.

VOL. CLXXII . . . No. 59,613 © 2022 The New York Times Company NEW YORK, SUNDAY, NOVEMBER 20, 2022 $6.00

The Prosecutor About to Enter A Trump Storm

New Special Counsel Pursued Politicians

By CHARLIE SAVAGE and ALAN FEUER

When Jack Smith was appointed to lead the Justice Department's public integrity unit in 2010, he recommended closing a series of high-profile investigations into members of Congress without charges — attracting criticism that the division had lost its nerve. He rejected that idea.

"I understand why the question is asked," Mr. Smith said at the time. "But if I were the sort of person who could be cowed — 'I know we should bring this case, I know the person did it, but we could lose, and that will look bad' — I would find another line of work."

On Friday, Attorney General Merrick B. Garland appointed Mr. Smith to a role that is almost certain to test his fortitude like few others: As special counsel, he will oversee a pair of criminal investigations involving former President Donald J. Trump, thrusting

U.S. FALLS BEHIND ON COVID VACCINES AS FUNDS DRY UP

'WARP SPEED' SET BACK

Prospects Dim for Nasal Sprays and Universal Shots for Variants

By BENJAMIN MUELLER

Operation Warp Speed, the Trump-era program that poured billions of dollars into developing Covid shots, seemed to signal a new dawn of American vaccine making, demonstrating how decades of scientific grunt work could be turned into lifesaving medicine in a matter of months.

But as a third pandemic winter begins in the United States, its vaccine-making effort has lost steam. Efforts to test and produce next-generation Covid vaccines are bogged down by bureaucratic problems and funding shortfalls. Foreign rivals have raced ahead in approving long-awaited nasal

GANGS CRIPPLE CHOLERA CARE As the disease spreads through Haiti, armed groups are impeding victims from getting help. Page 10.

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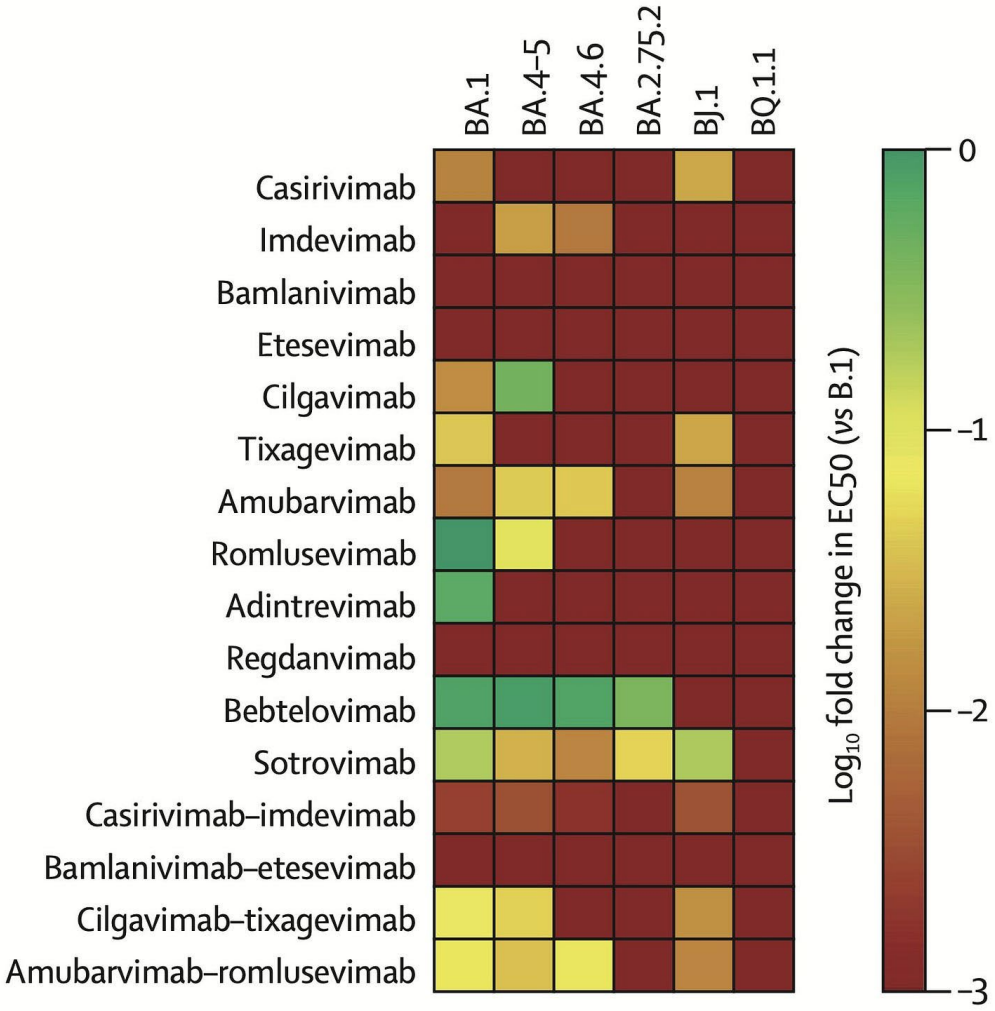
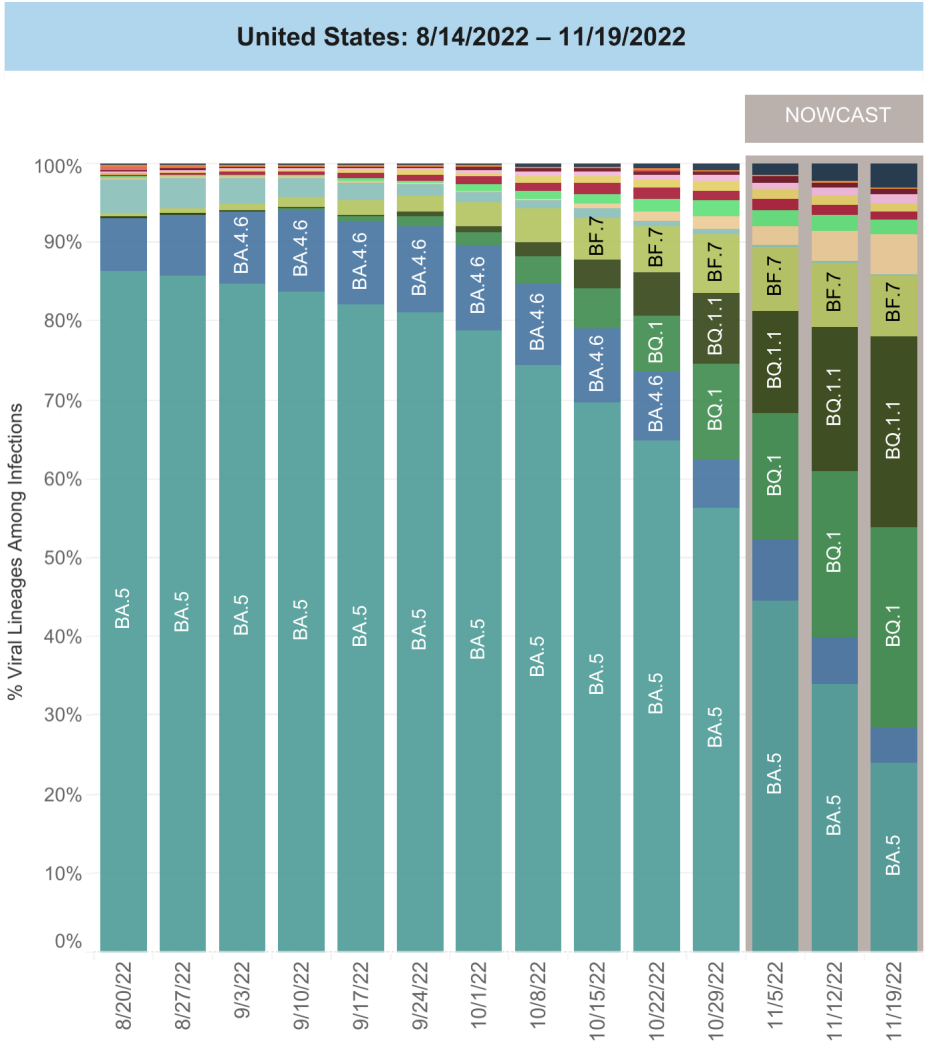
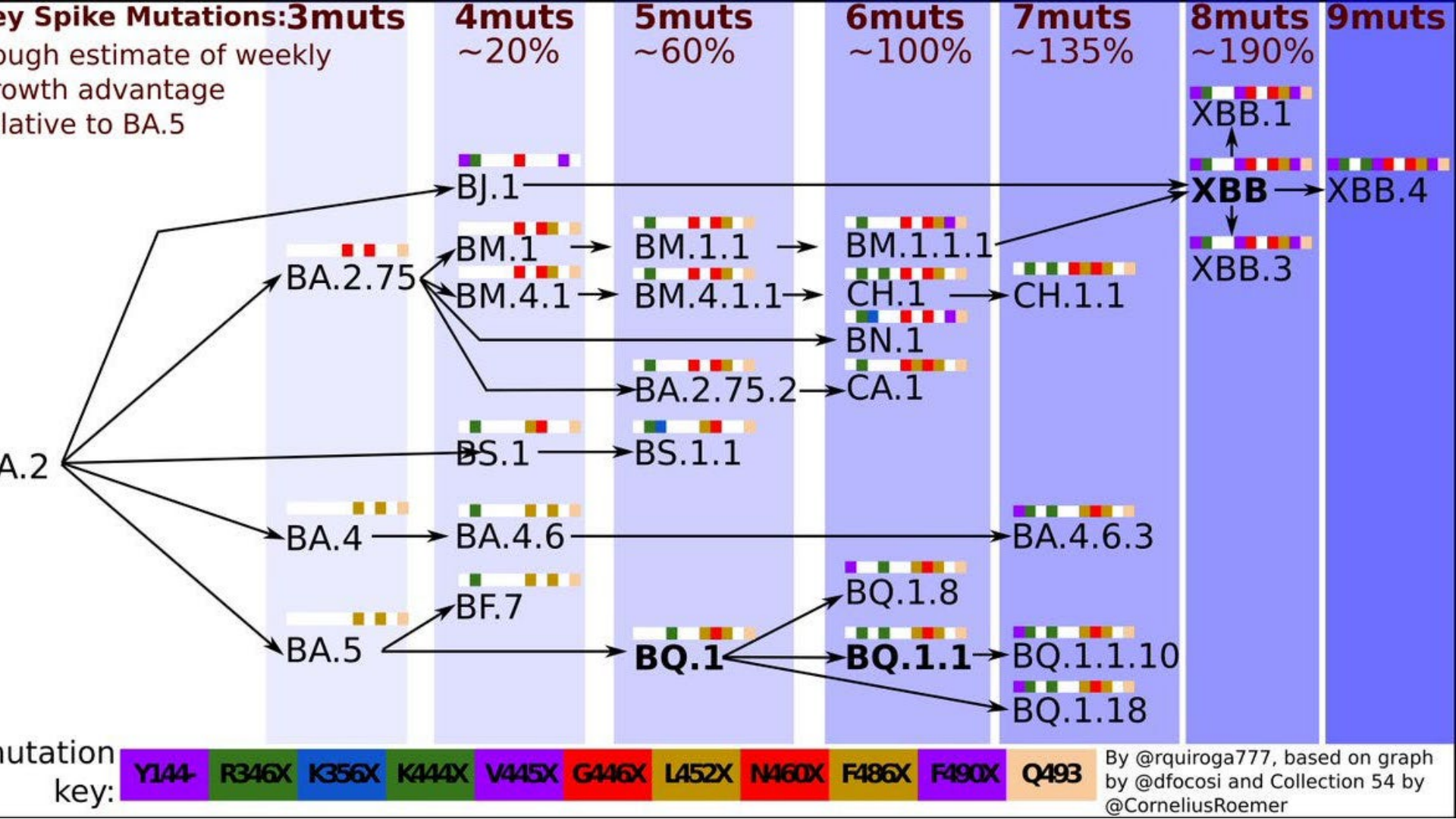

BA.1
BA.4–5
BA.4.6
BA.2.75.2
BJ.1
BQ.1.1
Casirivimab
Imdevimab
Bamlanivimab
Etesevimab
Cilgavimab
Tixagevimab
Amubarvimab
Romlusevimab
Adintrevimab
Regdanvimab
Bebtelovimab
Sotrovimab
Casirivimab–imdevimab
Bamlanivimab–etesevimab
Cilgavimab–tixagevimab
Amubarvimab–romlusevimab
Log10 fold change in EC50 (vs B.1)
0
–1
–2
–3

The Rise of BQ.1 and BQ 1.1

- BQ.1 and BQ.1.1 are the dominant 2 variants in the US
- BQ.1 and BQ.1.1 show extreme levels of immune invasion
- So what does this all mean for our potential winter wave?

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BA.2.75
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R346X
K356X
K444X
V445X
G446X
L452X
N460X
F486X
F490X
Q493
By @rquiroga777, based on graph
by @dfocosi and Collection 54 by
@CorneliusRoemer

A BQ or XBB future

- Several European countries had a small wave with BQ.1.1, Singapore had a significant wave of XBB but with little impact on serious disease.
- To date, BQ.1.1 has not been able to induce a new wave in 2 countries, a very positive sign … even with fewer and fewer controls such as masking and avoidance of indoor spaces
- This is the first time in the pandemic that a variant with clearcut, marked immune evasion has not induced a major new wave.
    - Examples of prior variants with increases in immune escape properties include Beta, Gamma, Omicron BA.1, BA.2, and BA.5. Each of these led to major waves globally or in specific continents (Beta in South Africa, Gamma in South America).
- A population-level immunity wall has been built up over 3 years, with all the infections and vaccinations

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Questions

Upcoming NEBGH virtual events:

- **Dec. 1 –** Getting the Bang out of Your Navigation Buck
- **Dec. 5** - Monday Bi-Weekly COVID-19 Update w/ Dr. Mark
- **Dec. 6 –** 28th Annual Tribute to Leadership
- **Dec. 8 –** The State of Women's Mental Health