

## Episode 268: Pathogenicity of BA.2 sublineages and RNA vaccines for young children

Dear colleagues,

Today, there are over 1000 COVID cases in Belgian hospitals (+ 13 % in one week). The number in ICU remains about 60 and daily deaths about 5-6. In this episode, I will present the emerging information, indicating that BA.4/BA.5/BA.2.12.1 are indeed still pathogenic.

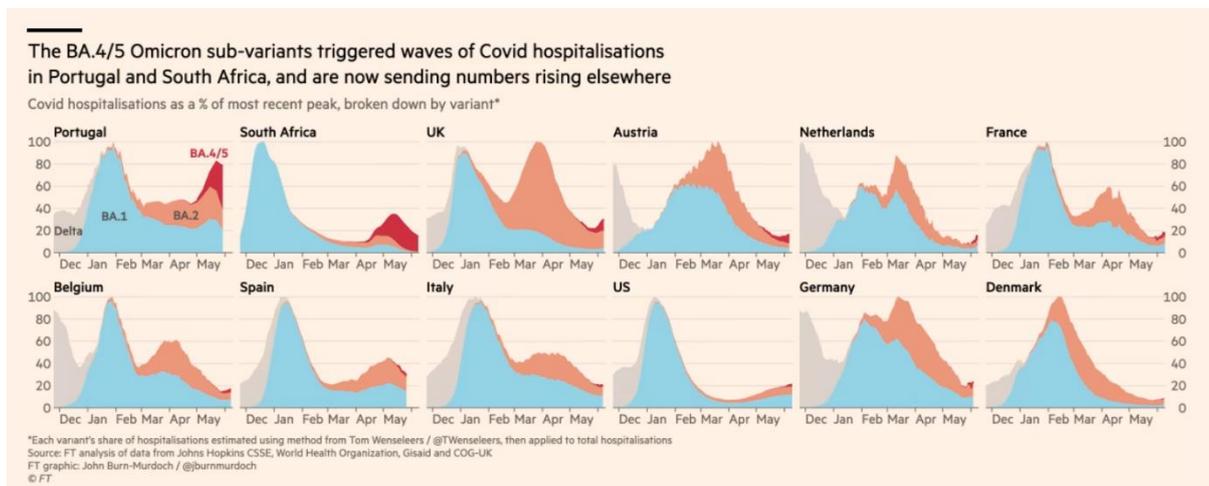
Afterwards, I will briefly discuss the recent approval of Pfizer and Moderna vaccines in US for children 6 mo-4 years.

See

### Pathogenicity of Omicron BA.2 sublineages

Ep 268-1: Analysis of the evolution in selected European countries, including Portugal, UK and Belgium suggests that BA.4/BA.5 wave is accompanied by increasing rates of hospitalization.

Ep 268-2: Article in the Guardian, based on analysis by our colleague Tom Wenseleers



European countries are experiencing a surge in Covid-19 hospital admissions driven by sub-variants of the highly infectious Omicron strain, threatening a fresh global wave of the disease as **immunity levels wane and pandemic restrictions are lifted**. Admissions have risen in several countries including France and England, according to data analysed by the Financial Times.

The BA.5 sub-variant of Omicron now accounts for more than 80 per cent of new infections in Portugal. In Germany, where admissions have been rising for over a week, the share of Covid-19 infections ascribed to BA.5 doubled at the end of last month.

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The potential power of one Omicron sub-variant, BA.5, is clearest in Portugal, where there has been a large surge in hospital admissions over the past month, rising almost as high as its original Omicron wave in January and driving higher excess mortality.

Ep 268-3: Short review on actual state of Belgian epidemic in NL (A) and FR (B).

- We are clearly heading towards BA-5 dominance
- High proportion of long sick leave amongst professional caregivers: about double to triple of general population: COVID fatigue?

Ep 268-4: Article in the Guardian, also pointing to rising hospitalizations in UK, with comment by Geert Molenberghs: in Portugal doubling of (registered) infections (BA.5) led to doubling of hospitalizations, while in NYC (BA.2.12.1) doubling of infections led to 50 % increase in hospitalization.

Ep 268-5: Similar situation in France, with an interesting comparison between BA.1 and BA.4/5 cases on pages 11 and 12

- Similar proportion of 14 % reported a previous infection, but significantly higher proportion of BA.4/5 cases reported 3 vaccine doses (38 %) as compared to BA.1 (only 4 %). This may (partly?) be due to the timing of vaccination, but it shows that even triple dose of vaccine does not protect very well against infection.
- BA.4/5 is more symptomatic than BA.1 and longer duration of symptoms

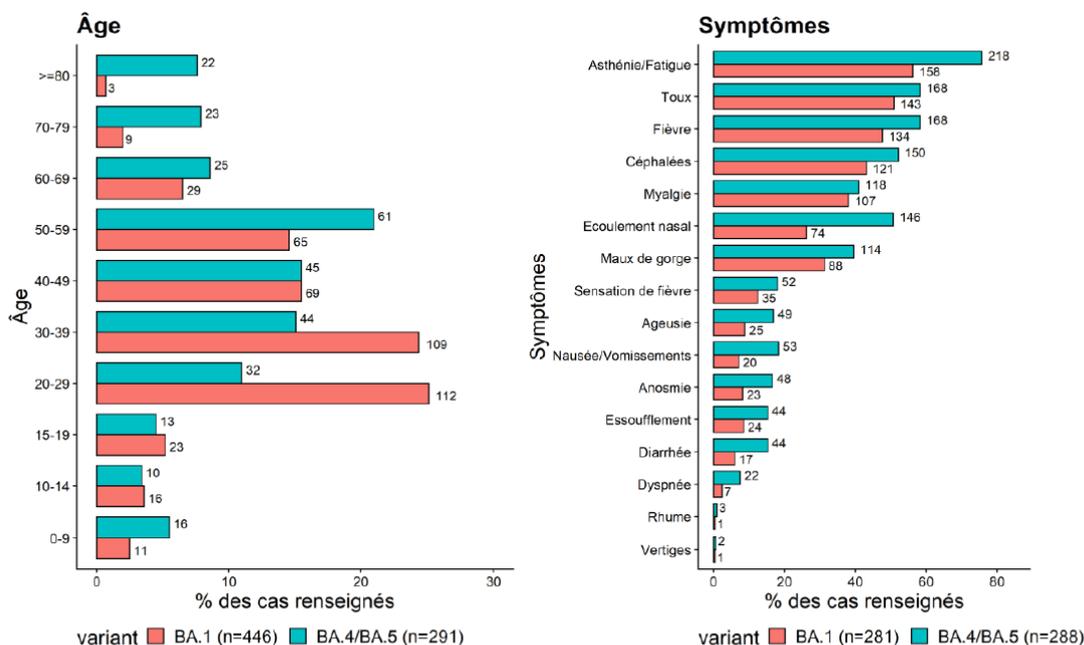


Figure 4 : Âge et symptômes des cas d'infection par BA.4 et BA.5 comparés aux cas d'infection par BA.1 précédemment investigués.

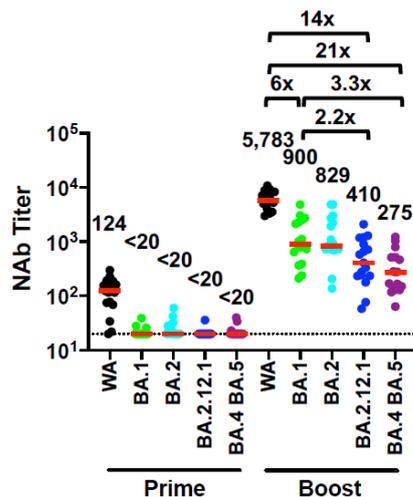
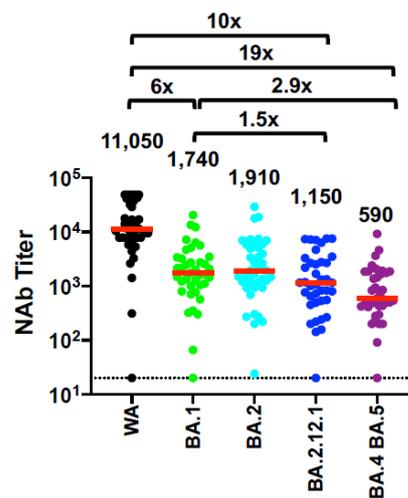
- The median age of the BA.4/5 cases was 47 versus 35 for BA.1
- Hospitalization rate was similar in BA.4/5 and in BA.1 cases (4%). 80 % of those showed elevated risk factors No ICU or deaths in this small series.

The conclusion of the Santé Publique de France is mixed:

*The moderate and time-limited impact of the epidemic waves associated with BA.4 and BA.5 in South Africa and Portugal is reassuring as to the consequences that BA.5 could have in France. Moreover, the sustained circulation of BA.2 in France, unlike South Africa and Portugal, could have a protective effect against BA.5 and further moderate its impact. However, it remains essential to continue to protect those at risk, through booster vaccinations as soon as necessary and respect for barrier gestures.*

With regard to the argument of cross-protection between BA.2 and BA.4/5, it is not so sure:

See Ep 266-11: Hachmann medRxiv 19 May 2022 **Neutralization Escape by the SARS-CoV-2 Omicron Variants BA.2.12.1 and BA.4/BA.5**

**B****C**

**B.** Neutralizing antibody (NAb) titers by a luciferase-based pseudovirus assay in individuals 6 months following initial BNT162b2 vaccination (Prime) and 2 weeks following BNT162b2 boost (Boost).

**C.** NAb titers in “hybrid immune” individuals following infection with BA.1 or BA.2. All were vaccinated (except for the one individual with negative NAb titers).

Ep 268-6: Evaluation by Robert Koch Institute (A = full text in German; B = English translation of summary)

***The Robert Koch Institute estimates the risk of COVID-19 for the health of the population in Germany to be high***

- *The incidence of **acute respiratory episodes** with COVID-19, was around 700 to 1,400 patients/100,000 inhabitants in week 23, and has thus increased by 75% compared to the previous week .*
- *The number of **outbreaks in old people's and nursing homes** as well as in medical treatment facilities has increased significantly compared to the previous week*
- *For the first time since week 14, there are signs of a renewed **increase in hospitalizations** for SARI cases with COVID-19 in week 23.*
- *The number of people treated in an **intensive care unit** with a COVID-19 diagnosis rose again compared to the previous weeks and was 668 cases on June 15, 2022.*

Remember also Ep 264-4 Kimura bioRxiv 26 May: **Virological characteristics of BA-2 subvariants**

- **Spike L452R/Q/M mutations** in BA.2.12.1 and BA.4/5 increase the effective reproduction number
- BA.4/5 is **resistant to the immunity induced by BA.1 and BA.2** infections
- BA.2.12.1 and BA.4/5 **more efficiently spread in human lung cells** than BA.2
- BA.4/5 is **more pathogenic than BA.2** in hamsters

**CONCLUSIONS: BA.4/5 is an intrinsically pathogenic SARS-CoV-2 variant that has higher affinity for the lung than other Omicron variants and partly escapes from immunity induced by vaccination and by BA.1 or BA.2 infection.**

Therefore, there is no room for complacency, especially not in old and/or vulnerable subjects: they can benefit from a second booster and, when at high risk, potentially from monoclonal antibodies Evusheld and Sotrovimab (with clearly reduced efficiency), but other non-pharmacological measures (such as face masks) remain indicated.

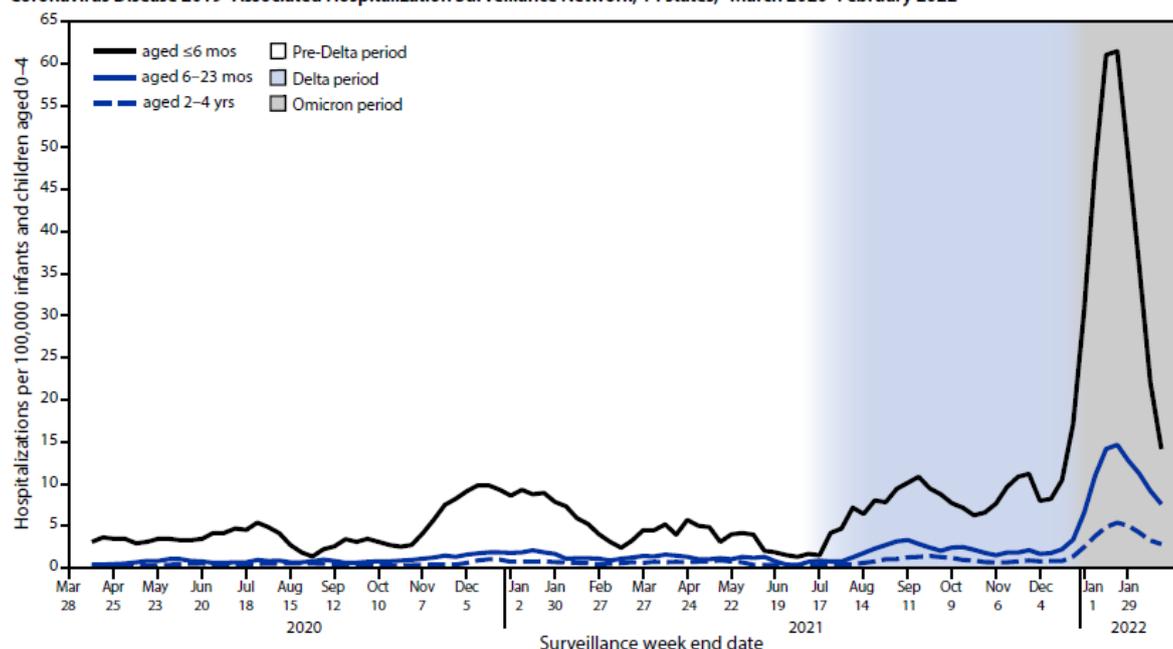
## Pfizer and Moderna vaccines approved for children 6 months-4 years in US

How big is the problem?

According to CDC <https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-Focus-on-Ages-0-18-Yea/nr4s-juj3>  
Between April 2020 and June 2022: **442 US children 0-4 year old have died from COVID** (out of > 1 million US deaths)

Ep 268-7: Marks MMWR March 2022 shows that especially the omicron (BA.1) wave resulted in a lot of hospitalizations in children 0-4 years.

FIGURE. COVID-19–associated hospitalization rates\* among infants and children aged 0–4 years, by age group (3-week moving average) — Coronavirus Disease 2019–Associated Hospitalization Surveillance Network, 14 states,† March 2020–February 2022<sup>§</sup>



Abbreviation: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network.

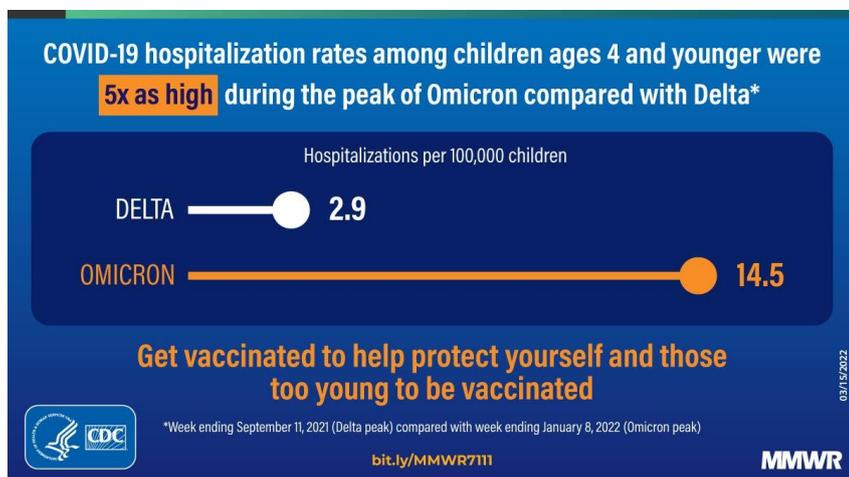
\* Number of patients with laboratory-confirmed COVID-19–associated hospitalizations per 100,000 population; rates are subject to change as additional data are reported.

† COVID-NET sites are in the following 14 states: California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah. Starting the week ending December 4, 2021, Maryland data are removed from weekly rate calculations.

<sup>§</sup> Periods of predominance are defined as follows: pre-Delta = March 1, 2020–June 26, 2021; Delta = June 27–December 18, 2021; Omicron = December 19, 2021–February 19, 2022.

According to the Table, about **35 % of those had an underlying condition and 18 % showed viral co-infection.**

Their message is clear:



Moderna is a two dose scheme of one quarter of adult dose, Pfizer a three-dose schema of one tenth of adult.

Main findings

## Pediatric COVID Vaccines

The trials, by the numbers

### Moderna: 2 doses

	Ages 2-5	Ages 6 months-23 months
Number of participants	3,031 vaccine group; 1,007 placebo	1,761 vaccine group; 589 placebo
Antibody response	Equal to adults'	Exceeds adults'
Efficacy against symptomatic illness	36.8% (12.5%-54%)	50.6% (21.4%-68.6%)
Efficacy including asymptomatic	31.5% (11.4%-46.7%)	40.5% (12.3%-59.2%)
Local reaction (i.e. injection site)	83.5% (versus 57.8% placebo)	65.3% (versus 44.6% placebo)
Systemic reaction (i.e. fever)	76.3% (versus 64.4% placebo)	88.5% (versus 84.4% placebo)
Serious adverse events related to vaccine	One possible; vomiting, fatigue, fever. Recovered within 1.5 hours.	One; febrile seizures, rash. Recovered.

Source: Emily Oster • Created with Datawrapper

### Pfizer: 3 doses

	Ages 2-4	Ages 6 months-23 months
Number of participants	606 vaccine group; 280 placebo	386 vaccine group; 184 placebo
Antibody response	Exceeds adults'	Exceeds adults'
Efficacy against confirmed illness	82.4% (-7.6% - 98.3%)	75.6% (-369.1% - 99.6%)
Local or systemic reaction, non-serious	18.7% (versus 18.7% placebo)	30.1% (versus 27.1% placebo)
Serious adverse events related to vaccine	One possible; fever, calf pain.	One possible; febrile seizure possibly related to vaccination.

Table: Emily Oster • Created with Datawrapper

### Conclusions:

- Both vaccines are safe
- Pfizer seems more efficacious, but the number of participants is low and confidence intervals are wide, especially for Pfizer.

Clearly, these results are much less convincing than in adults and it remains to be seen how efficaciously these vaccines will protect children at risk from severe disease.