Project No.: COVID1903003
Project Title: Long-term longitudinal comparisons of health status and immune responses in convalescent COVID-19 and vaccinated cohorts in Hong Kong

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COVID1903003

Oral presentation:

To investigate the SARS-CoV-2 specific cellular and humoral immune responses in community subjects who have received different types of COVID-19 vaccines.

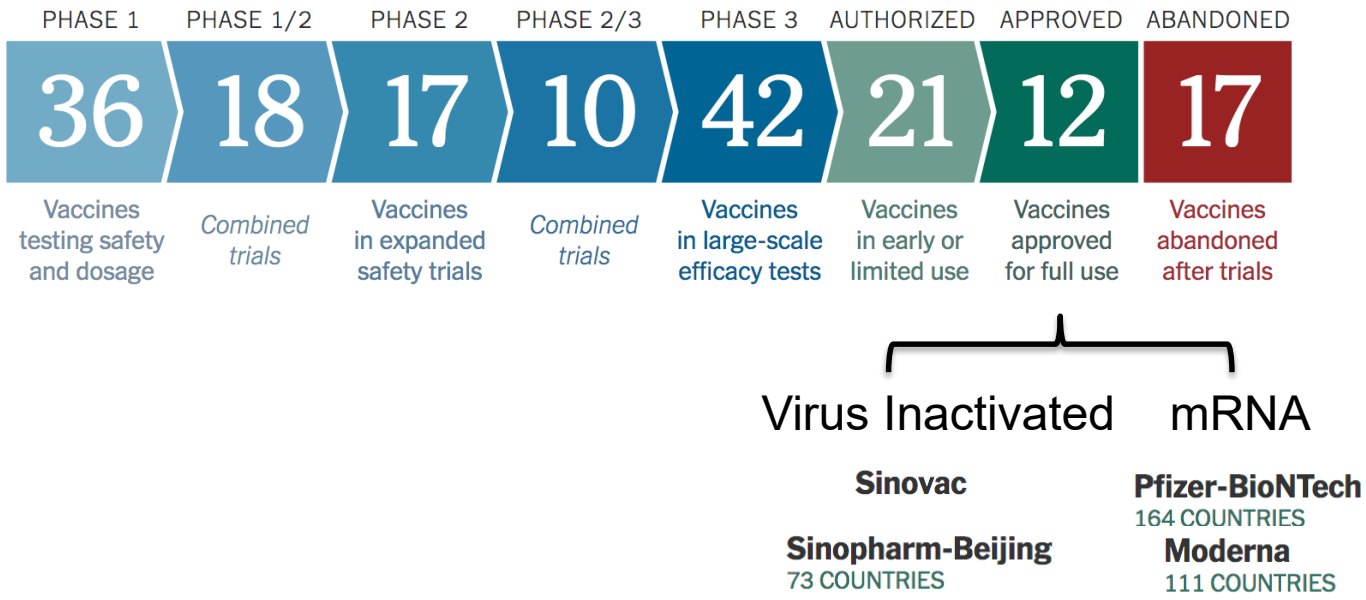
Posters x2:

- **To examine the health status of COVID-19 patients who have recovered from different levels of disease severity.** Ken KP CHAN [1,2], Susanna S NG [1], Grace LUI [3], HS LEUNG [4], KT WONG [4], Winnie CHU [4], Karen YIU [1], Eugene TSO [5], KW TO [1], Jenny NGAI [1], Tommy WH YIP [1], Rachel LO [1], Joyce NG [1], Fanny KO [1], David SC HUI [1]
- **Differential prolonged multiomic responses to mRNA and inactivated virus COVID-19 vaccines.** Chris KP Mok, Hein M Tun, Shilin Zhao, Chunke Chen, Yuzhou Chen, Ye Peng, David SC Hui

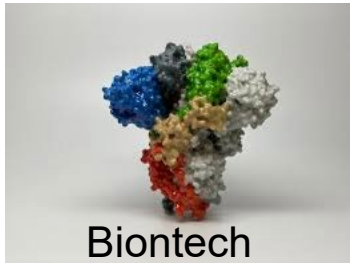
The New York Times

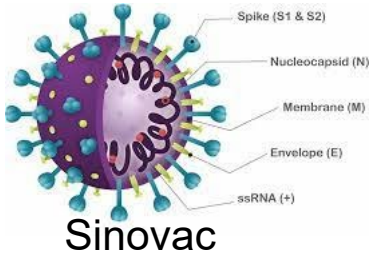
Coronavirus Vaccine Tracker

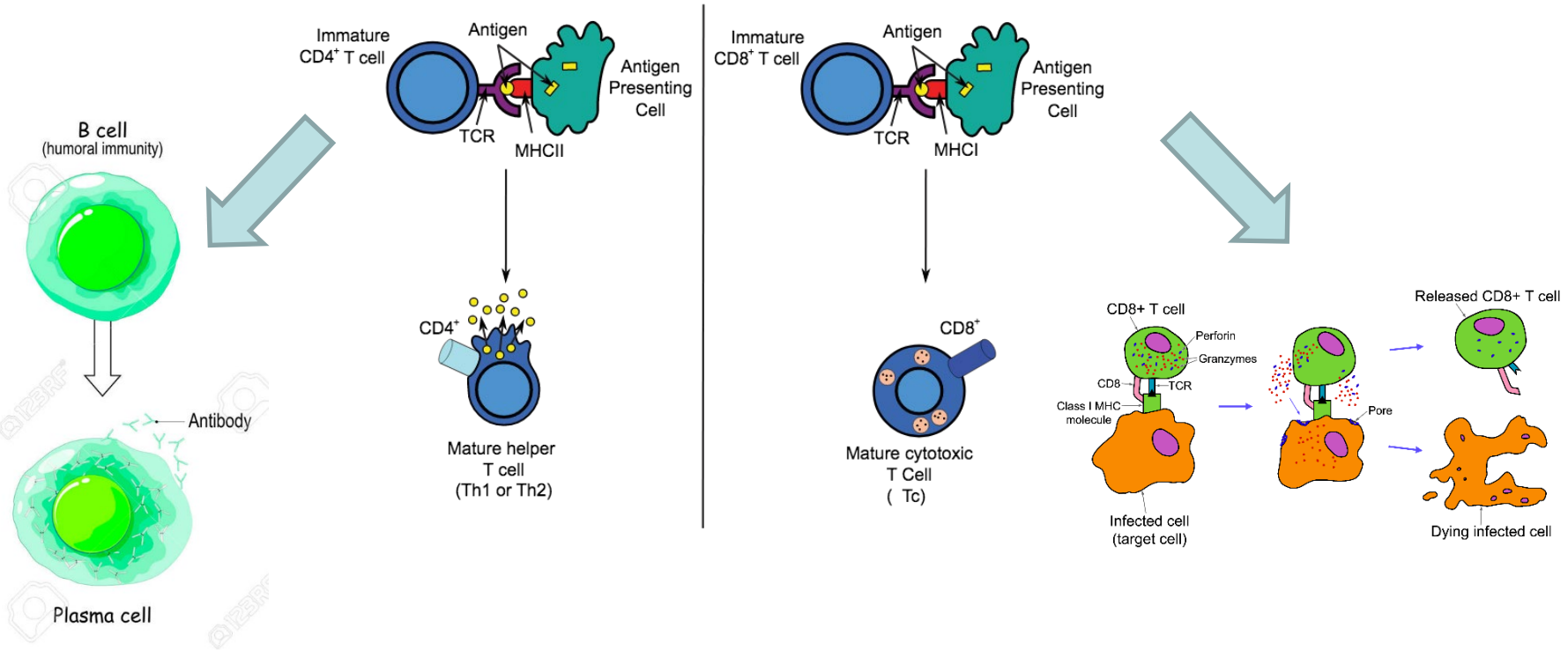
By Carl Zimmer, Jonathan Corum, Sui-Lee Wee and Matthew Kristoffersen Updated Aug. 31, 2022



Two arms of adaptive immunity: Antibody and T cells



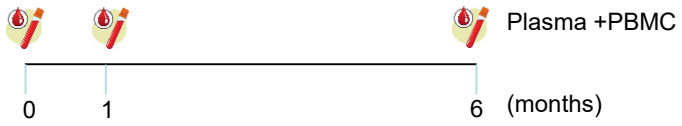




Subjects recruitment

Cohort 1: 2 doses
(10/3/2021-31/8/2021)

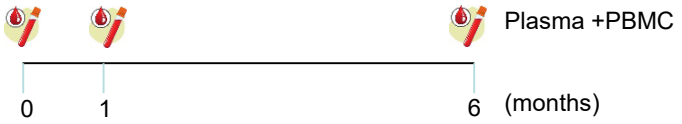
1) BioNTech:
mRNA vaccine x2
2) Sinovac:
Inactivated vaccine x2



Previous COVID-19 infection was excluded by ORF8 ELISA

Cohort 2: 3 doses
(18/8/2021-26/10/2021)

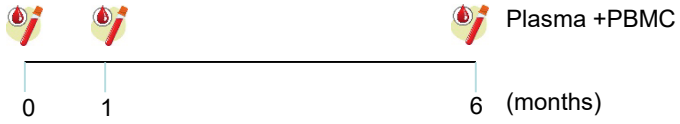
1) BioNTech:
mRNA vaccine x3
2) Sinovac:
Inactivated vaccine x3
3) Inactivated vaccine x2 +
mRNA vaccine x1



Previous COVID-19 infection was excluded by ORF8 ELISA

Cohort 3: 4/5 doses
(31/5/2022-6/7/2023)

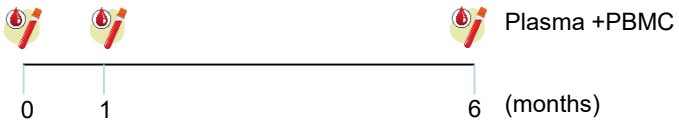
1) BioNTech:
mRNA vaccine x4
2) Sinovac:
Inactivated vaccine x4
3) Mix doses x3 +
mRNA vaccine x1
4) 3/4 doses
WT+Bivalent vaccine
x1



Previous COVID-19 infection was excluded by ORF8 ELISA

Cohort 4: XBB booster (BioNTech Vs Moderna)
(2/1/2024-3/2/2024)

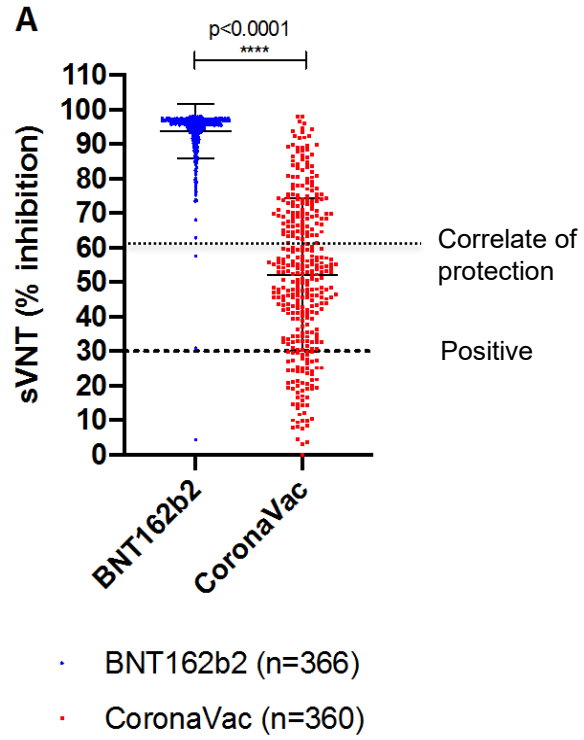
1) Previous
vaccination
+BioNTech XBB
vaccine
2) Previous
vaccination +Moderna
XBB vaccine



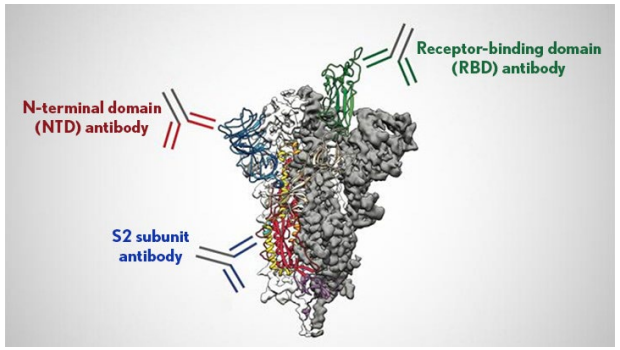
Previous COVID-19 infection was excluded by ORF8 ELISA

Two doses of CoronaVac (SinoVac) trigger lower antibody response than BNT mRNA vaccines (Cohort 1: 2 doses)

Mean 93.6% vs 52.1%

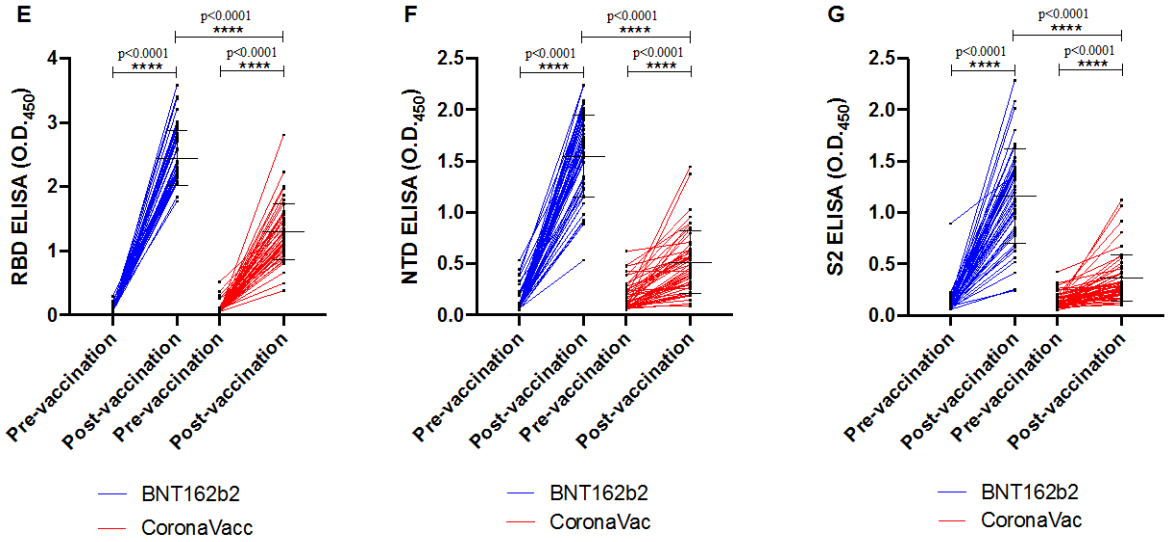


BNT162b2: ~100% vaccinees
CoronaVac: ~36.5% vaccinees



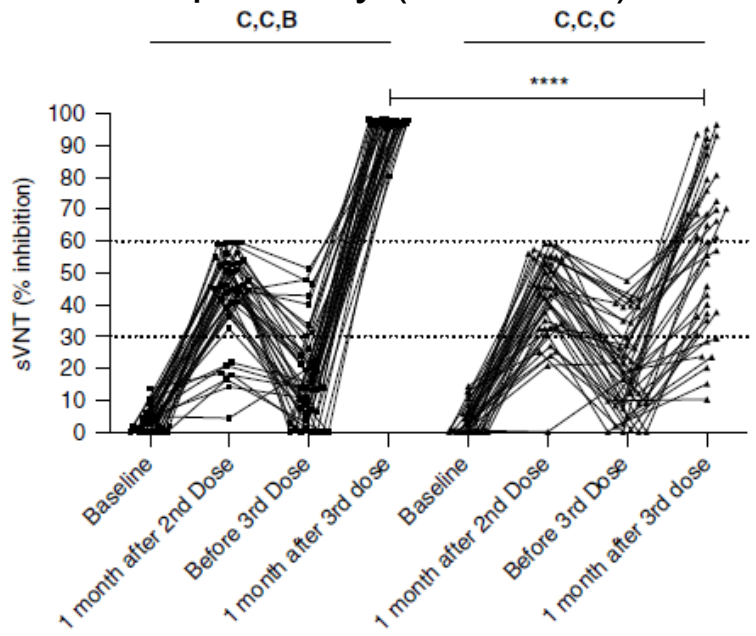
Antibodies against different regions of spike

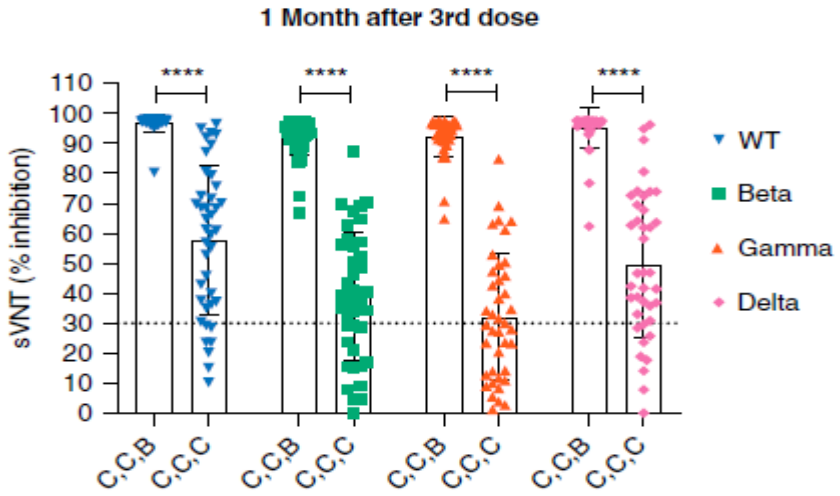
RBD NTD S2



Mok C, et al. Respirology 2022

RCT: One month after the 3rd dose of vaccination, the mean % of inhibition in the sVNT in the plasma for the BNT & CoronaVac groups was 96.8% vs 57.8%, respectively (P<0.0001)

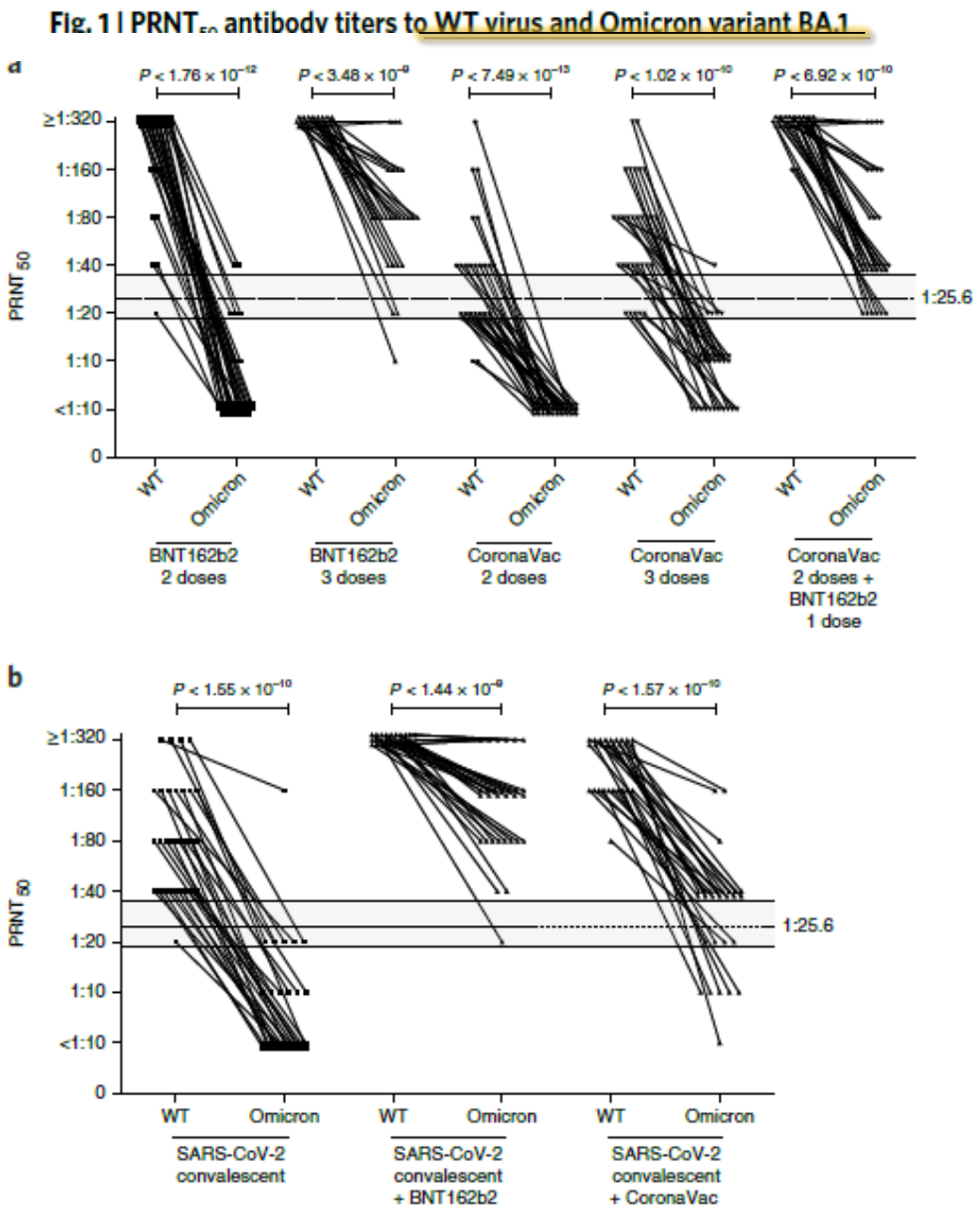


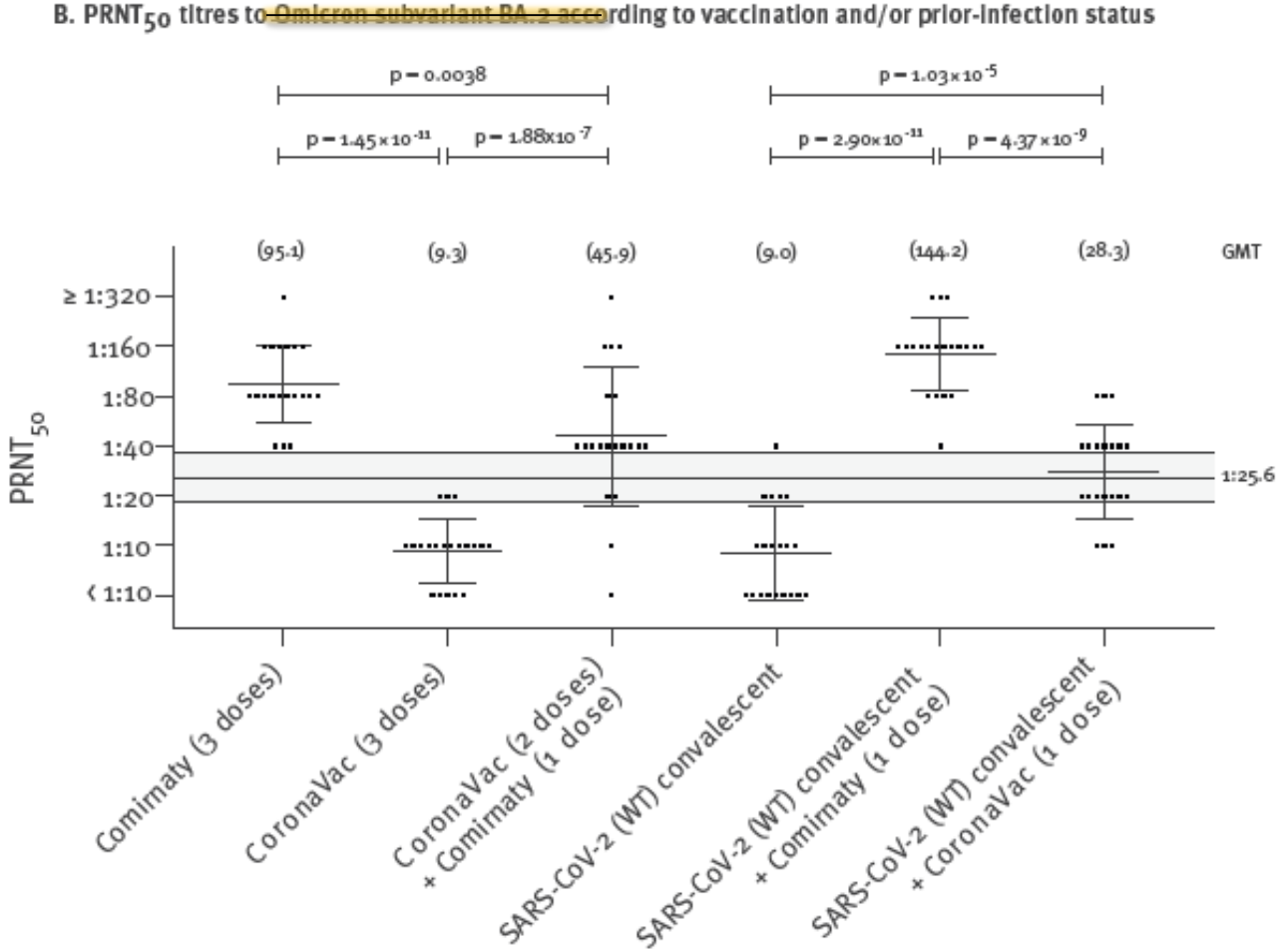


Adults vaccinated with 2 doses of CoronaVac

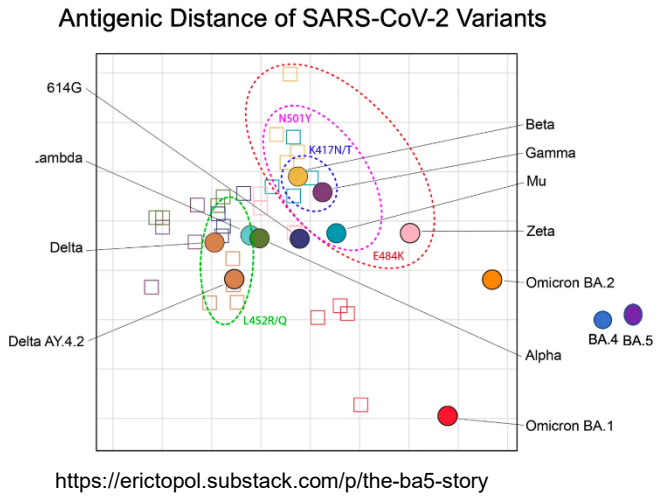
Side effects	After Third Dose		*P* Value
	C,C,B	C,C,C	
n	40	40	
Age (mean ± SD)	51.20 ± 8.79	51.50 ± 8.83	0.883*
Age (median, IQR)	51.50 (44.25–57)	50.00 (45.25–57)	0.969*
Male (female)	16 (24)	12 (28)	0.482*
Days between first and third dose	126.75	128.75	0.729*
Days between second and third dose	97.95	99.35	0.806*
Local reactions			
Pain	34	12	<0.001
Erythema	2	0	0.494
Pruritus	3	1	0.616
Swelling	14	4	0.014
Systemic reactions			
Fever†	7	1	0.057
Fatigue	24	10	0.003
Diarrhea	1	0	1
Muscle pain	13	4	0.027
Nausea	2	0	0.494
Headache	10	3	0.067
Cough	2	2	1
Anorexia	4	1	0.359
Hypoesthesia	4	0	0.116
Dizziness	6	2	0.264
Abdominal distention	1	0	1
Peripheral edema	1	0	1
Abdominal pain	1	0	1
Vomiting	0	0	N.A.
Drowsiness	11	8	0.601
Joint pains	6	3	0.482
Rash	2	0	0.494
Palpitation	5	2	0.432
Claimed no adverse effect	8	16	0.087

Mok C, et al. AJRCCM 2022



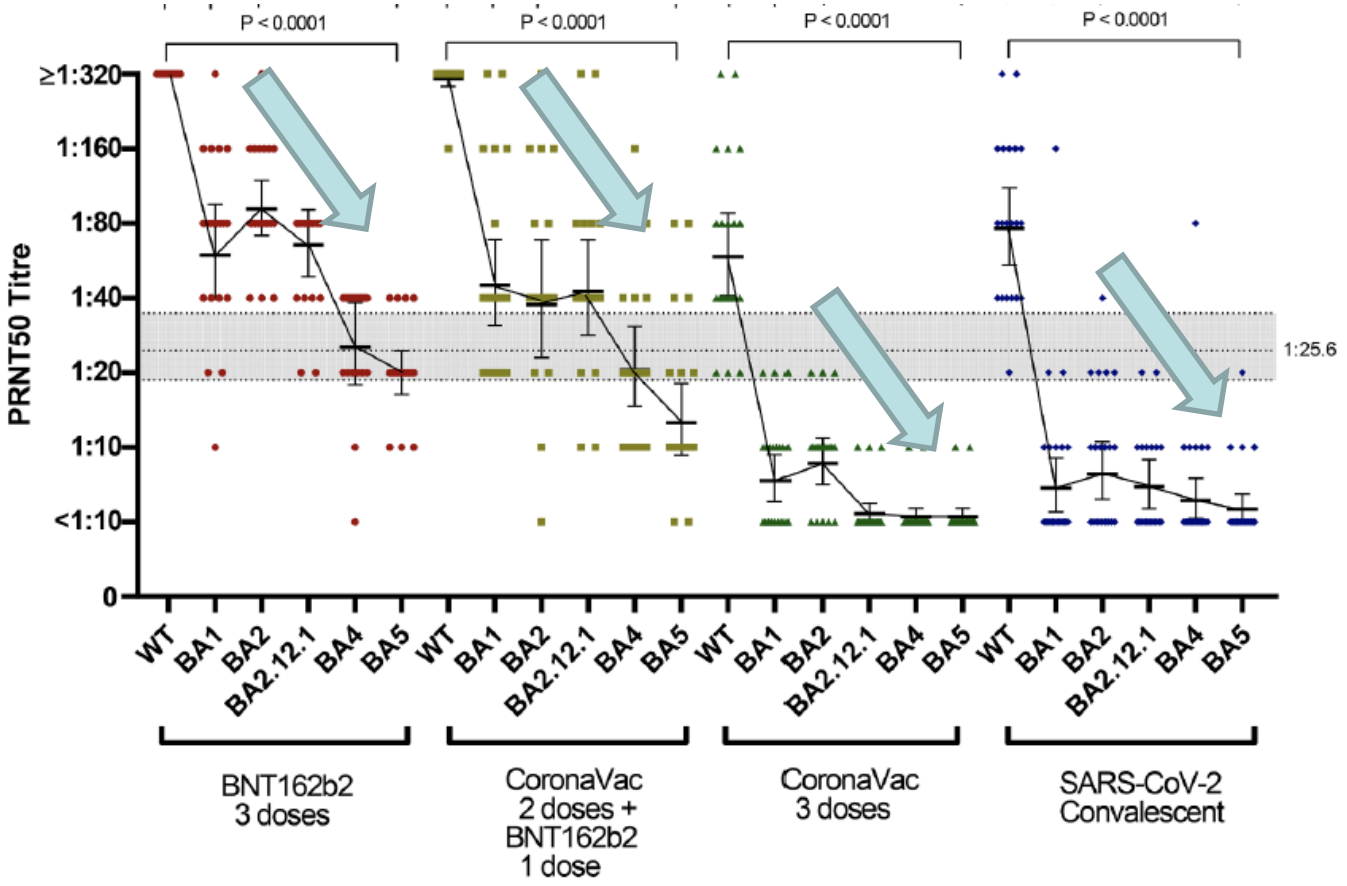


Countries/cities primarily using CoronaVac vaccines should consider mRNA vaccine boosters in response to the spread of Omicron. Cheng S, et al. Nature Med 2022 and EuroSurv 2022

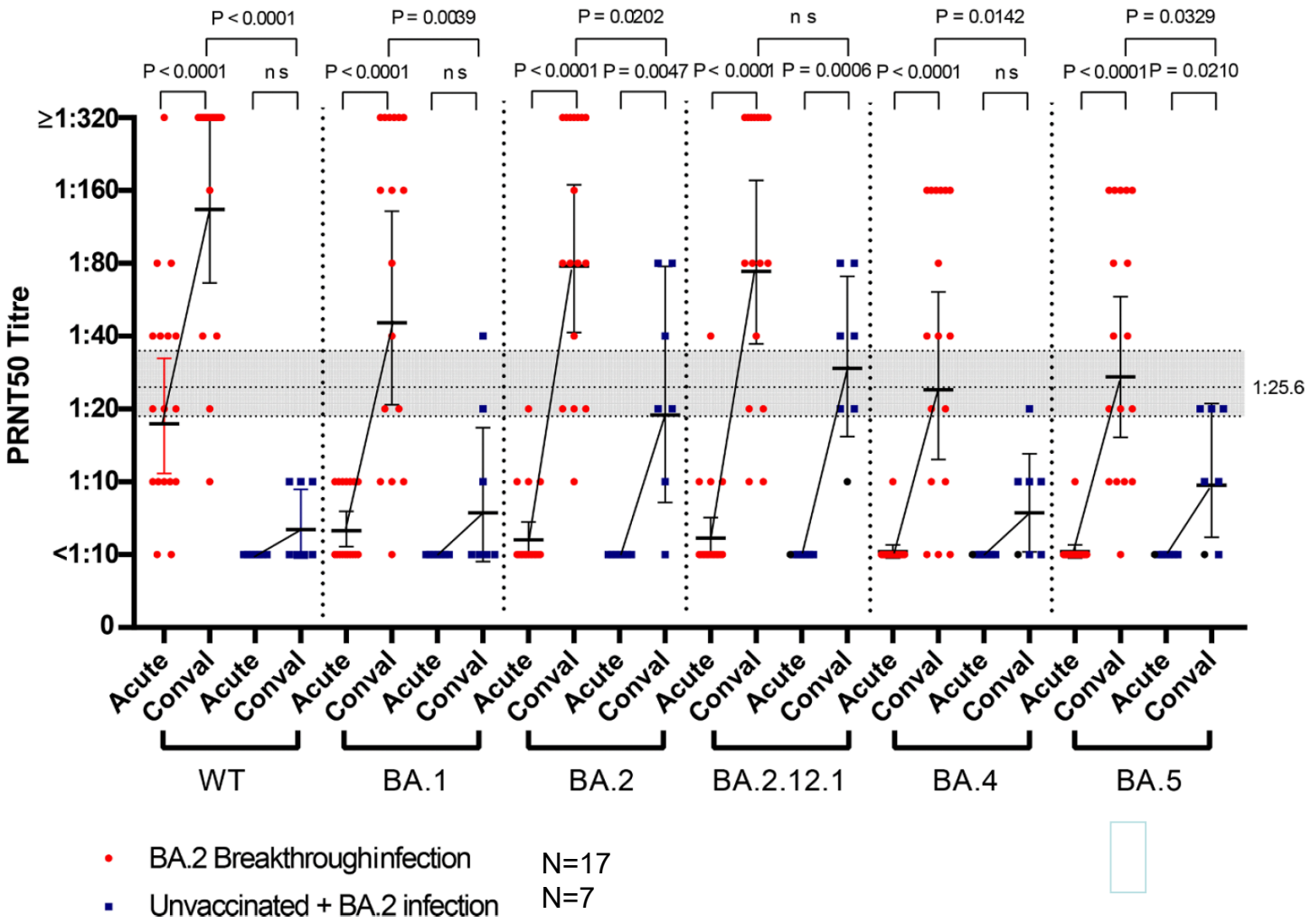


https://erictopol.substack.com/p/the-ba5-story

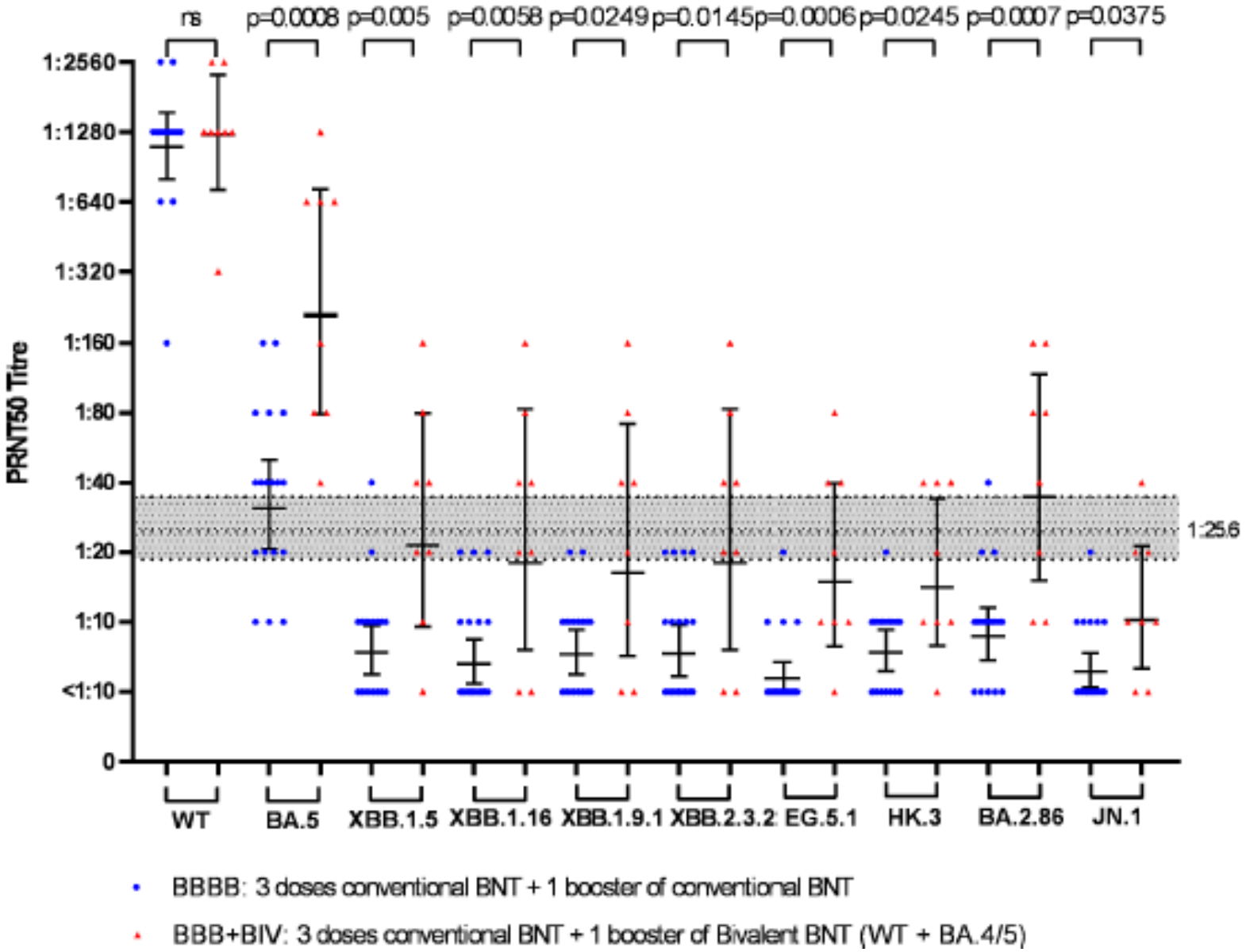
- BA.4 and BA.5 subvariants were less susceptible to BNT162b2 or CoronaVac vaccine elicited antibody neutralization than subvariants BA.1, BA.2 & BA.2.12.1.
- Nevertheless, 3 doses BNT162b2 or booster of BNT162b2 following 2 doses of CoronaVac elicited detectable BA.4 and BA.5 neutralizing antibody responses while those vaccinated with 3 doses of CoronaVac largely fail to do so.



Cheng S, et al. JCV, 2022



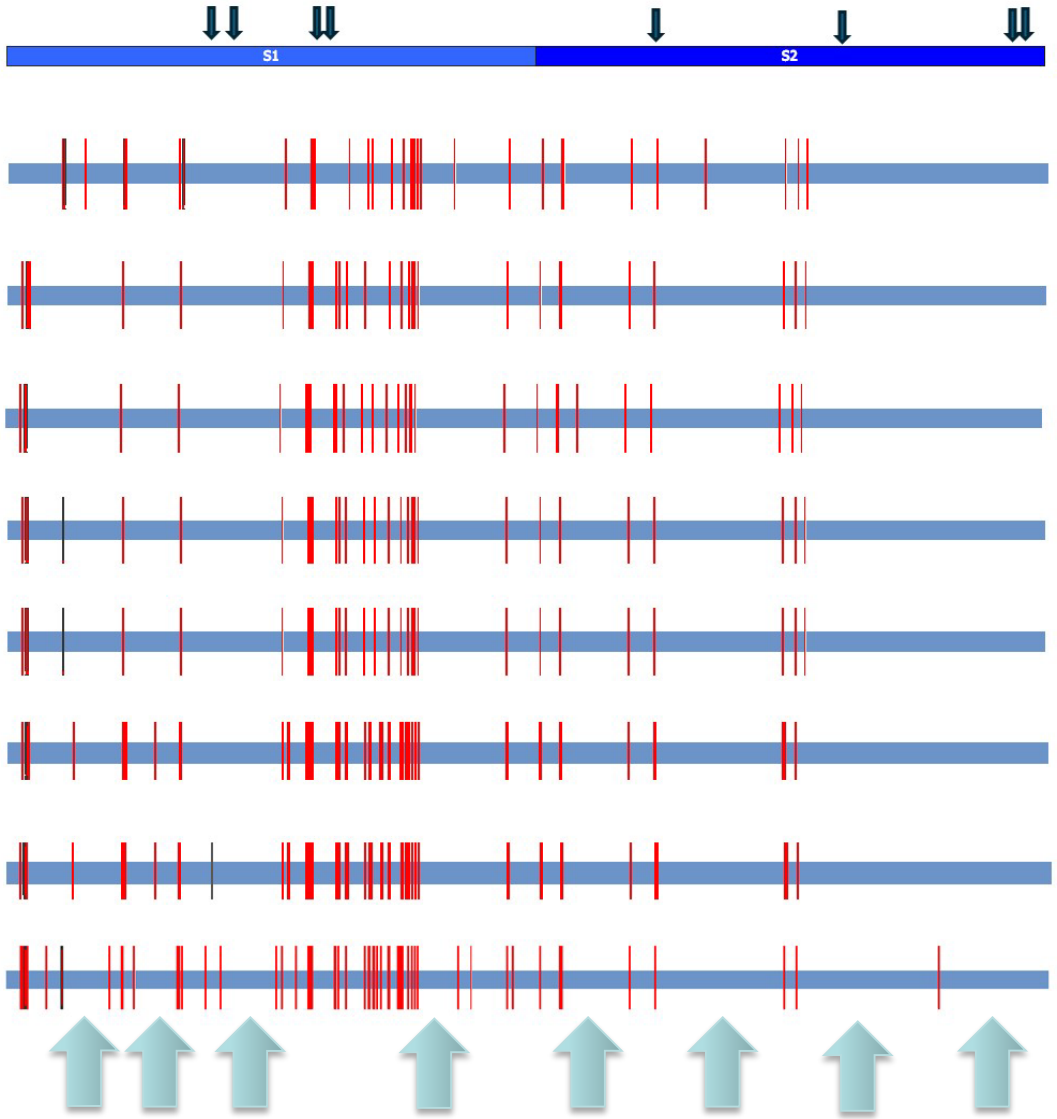
- BA.2 infections in vaccinated individuals led to higher levels of BA.4 or BA.5 neutralizing antibody compared to those who were vaccine-naive. Cheng SM, et al. JCV 2022



The bivalent WT+BA.4/5 mRNA vaccine elicited significantly higher neutralizing antibody levels to more recent omicron subvariants compared to boosting with the monovalent BNT162b2 vaccine.

T cells induced by both vaccines provide cross-reactive protection by recognizing important viral epitopes despite changes in viral Spike protein

Variants	Length of amino acid	Number of peptides	Number of peptides overlap
WT	1274aa	128	----
BA.1	1274aa	128	86
BA.2	1271aa	128	94
BA.2.12.1	1271aa	128	90
BA.4	1269aa	128	90
BA.5	1269aa	128	90
XBB	1270aa	128	85
XBB1.5	1270aa	128	83
JN.1	1266aa	128	72

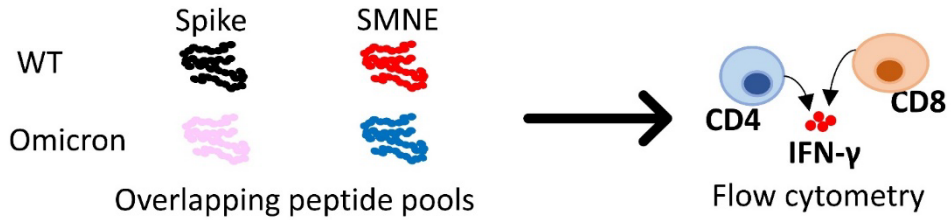


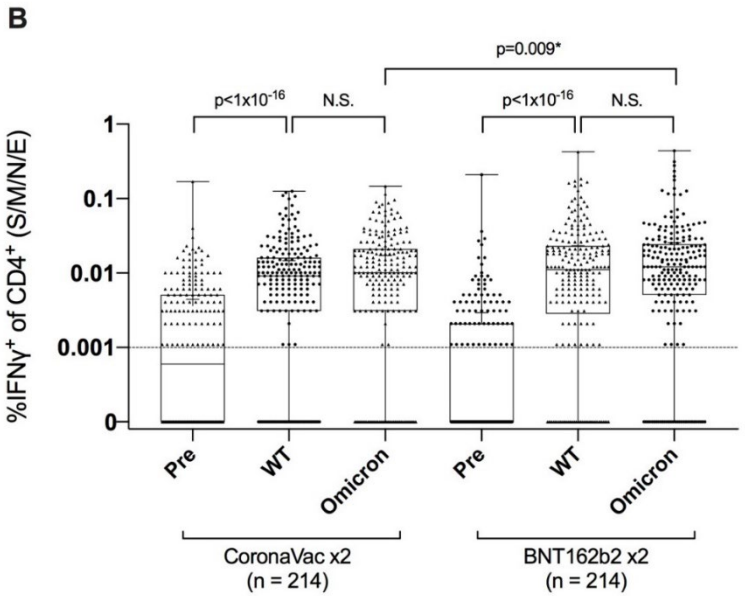
Cohorts

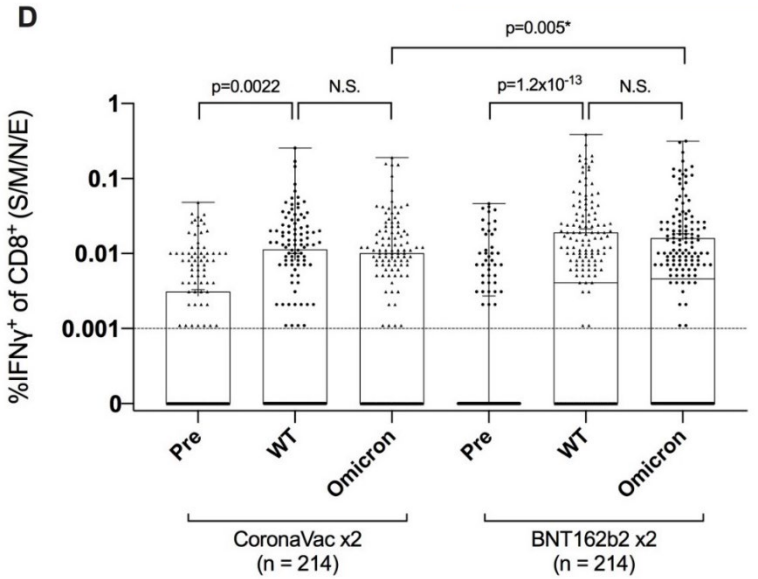
Cohort 1: SARS-CoV-2 naïve

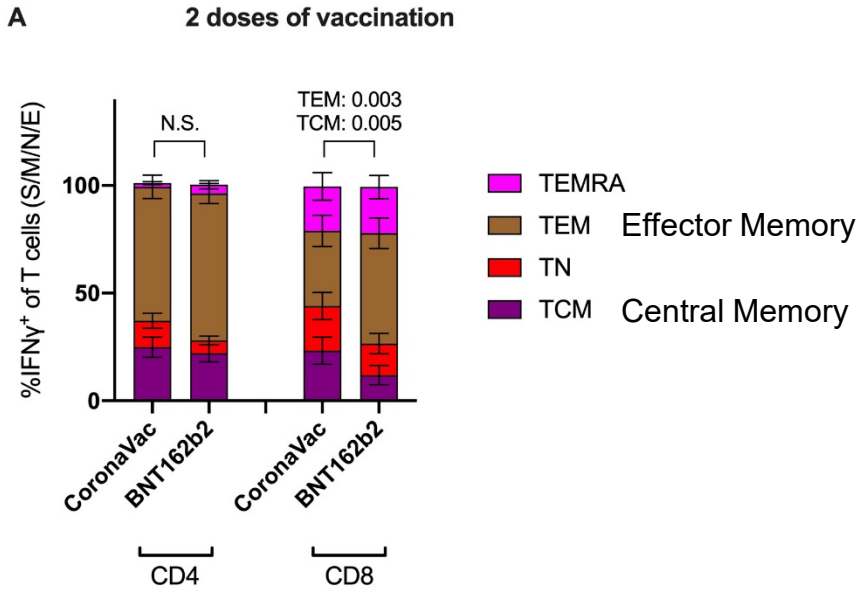
428 individuals → 2 doses of vaccination **856 samples**

Methods







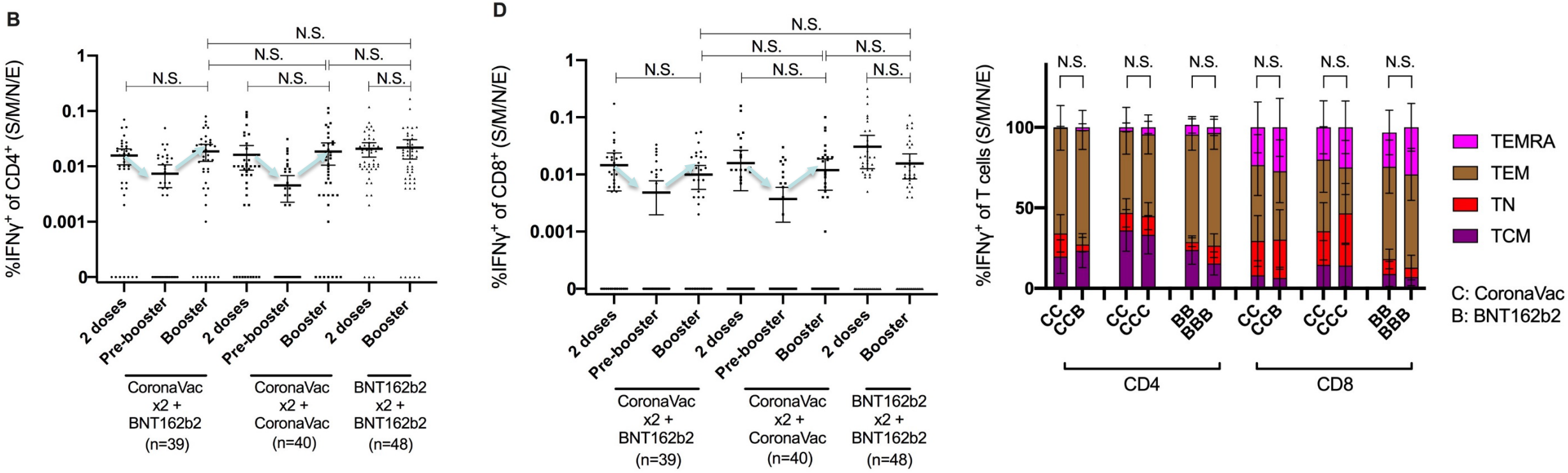


Both CoronaVac and BNT162b2 vaccines significantly induced CD4 and CD8 T response to WT and Omicron BA.1. These cells carried memory phenotypes suggesting long-term protection.

Mok C, et al. Lancet Microbe 2023

T cell response on 3 doses of vaccination

Omicron specific T cells



A third dose of either BNT162b2 or CoronaVac boosted waning T cell responses after 2 doses of CoronaVac but the levels did not exceed those seen 1 month after the second dose.

Mok C, et al. Lancet Microbe 2023

Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study

3 doses of either vaccines effective in preventing severe disease & deaths due to T cell response

McMenamin ME, et al. Lancet Infect Dis 2022; 22: 1435–43

Up to 16 March 2022

B cell response

T cell response

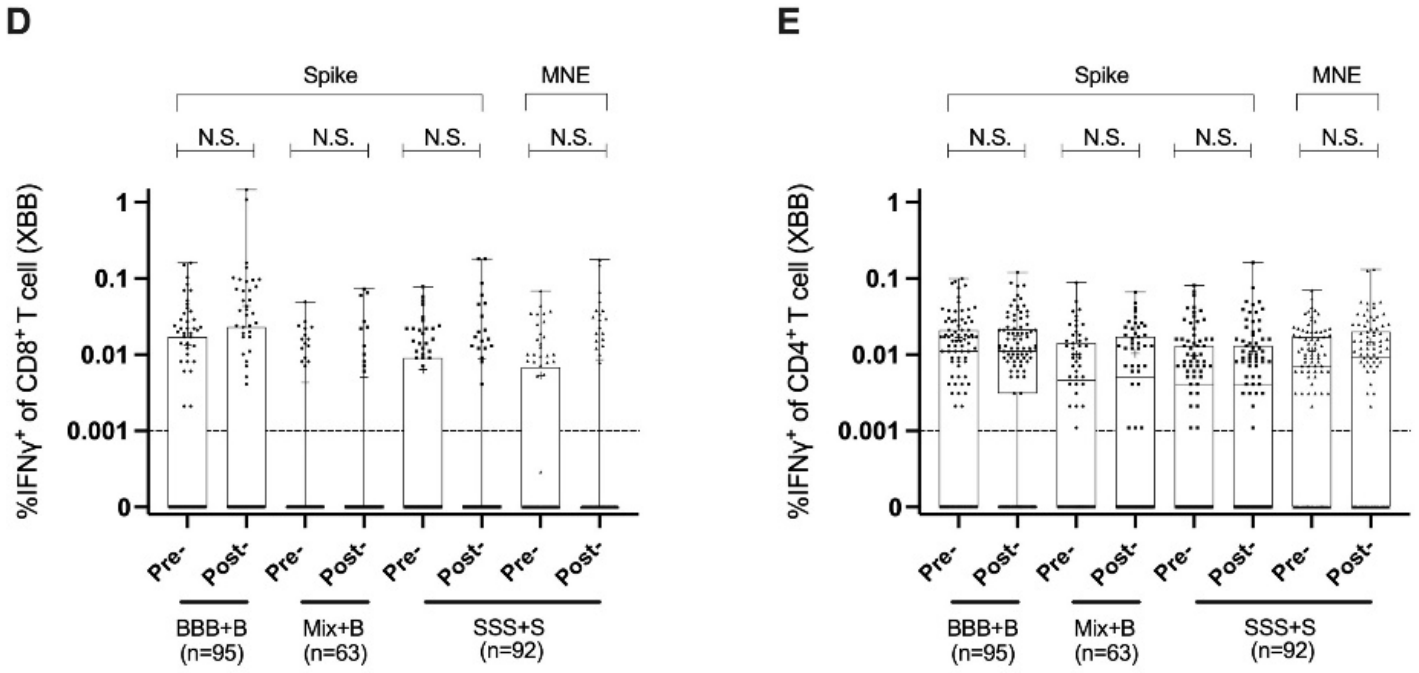
	One dose		Two doses		Three doses	
	BNT162b2	CoronaVac	BNT162b2	CoronaVac	BNT162b2	CoronaVac
Mild or moderate disease						
20–59 years	39·9% (24·8–52·3)	32·7% (14·4–47·6)	35·1% (26·6–42·5)	25·1% (14·7–34·3)	73·5% (66·6–79·2)	51·0% (39·6–60·4)
≥60 years	None*	None*	None*	None*	70·2% (53·3–82·0)	32·4% (8·3–51·0)
Severe or fatal disease						
20–59 years	95·4% (90·7–98·1)	74·8% (63·7–82·8)	96·3% (94·9–97·3)	91·7% (88·7–94·0)	98·6% (97·5–99·3)	98·8% (97·5–99·5)
60–69 years	70·0% (51·8–82·0)	54·2% (36·4–67·3)	91·1% (86·9–94·0)	79·3% (71·8–85·0)	98·9% (97·3–99·6)	97·4% (95·2–98·7)
70–79 years	72·2% (56·7–82·6)	29·2% (7·4–46·1)	89·8% (85·1–93·1)	74·3% (66·5–80·3)	99·0% (97·4–99·7)	95·4% (92·2–97·4)
≥80 years	75·0% (61·1–84·2)	39·0% (20·9–53·0)	86·9% (80·5–91·3)	58·2% (45·1–68·2)	97·1% (93·8–98·7)	97·3% (94·9–98·7)
Death						
20–59 years	96·7% (90·9–99·2)	78·2% (64·9–86·9)	96·8% (95·1–98·0)	93·3% (89·9–95·6)	99·2% (97·9–99·7)	99·4% (98·1–99·9)
60–69 years	77·6% (59·9–88·4)	65·6% (49·8–76·8)	92·7% (88·6–95·4)	84·3% (77·8–89·0)	99·0% (97·2–99·8)	99·0% (97·3–99·8)
70–79 years	80·5% (66·3–89·2)	45·3% (25·1–60·3)	92·3% (88·0–95·2)	76·7% (68·5–82·8)	99·4% (97·9–99·9)	97·0% (94·2–98·6)
≥80 years	78·7% (65·5–87·0)	44·8% (26·9–58·4)	90·3% (84·9–93·9)	63·0% (50·3–72·5)	97·5% (94·2–99·0)	97·9% (95·7–99·1)

Data are effectiveness (95% CI). *No evidence of protection based on a negative or very small positive point estimate and wide CIs.

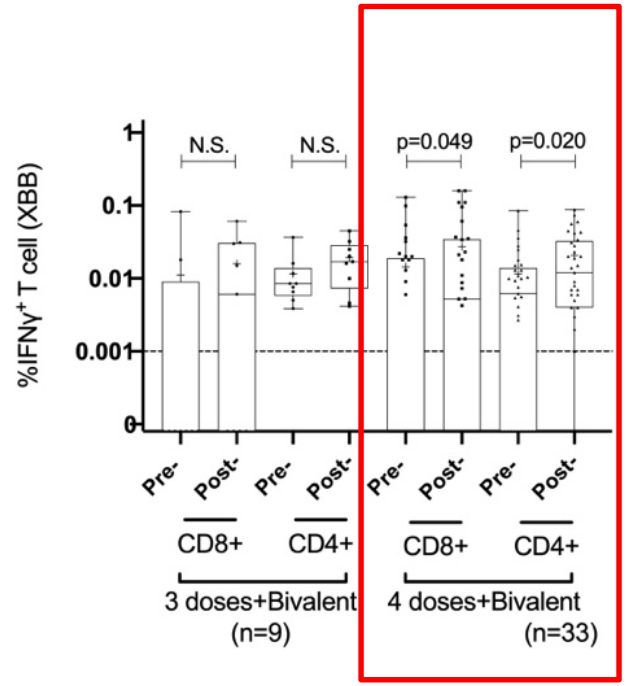
Table 2: Vaccine effectiveness by dose and vaccine type in all ages and within age categories against COVID-19

Among all vaccination strategies, only adults who had received the bivalent WT+BA.4/5 mRNA vaccine as the third booster dose significantly elicited T cell responses to the XBB variants. Tang YS, et al. IJID 2024

WT vaccine

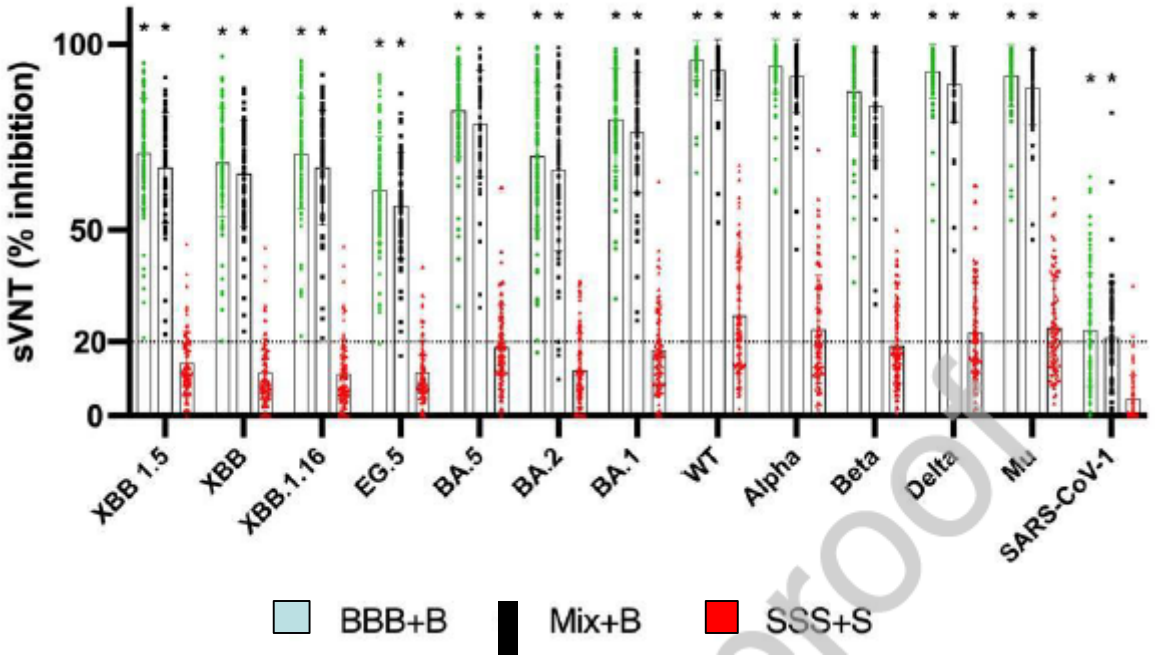


WT+BA4./5 mRNA vaccine

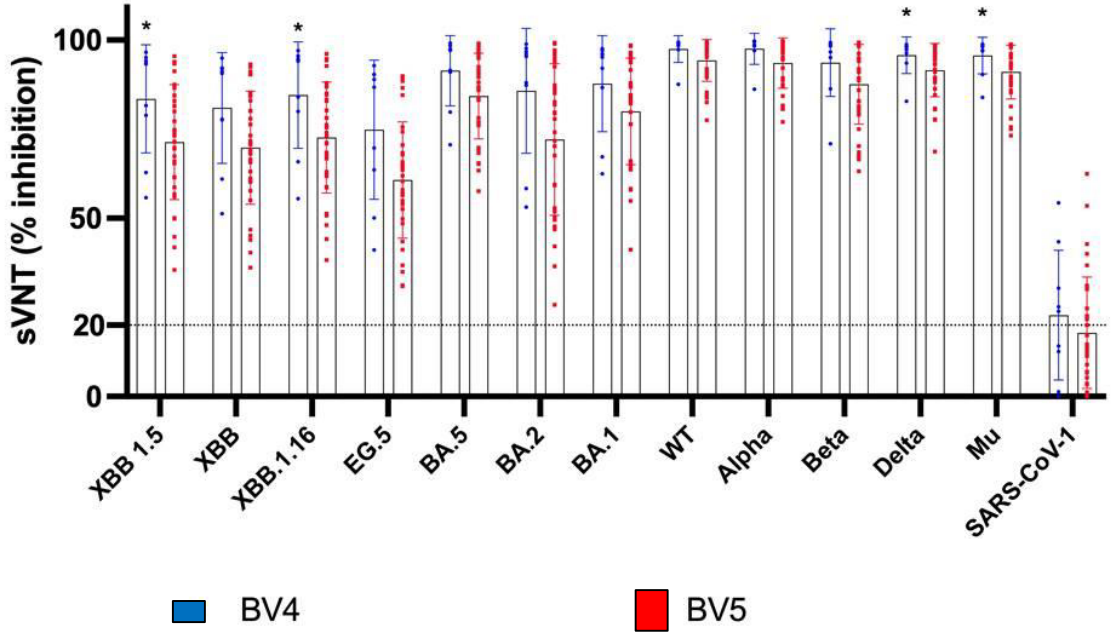


Either monovalent WT or bivalent WT+BA.4/5 mRNA but not inactivated virus vaccine as the second/third booster induced antibody against different XBB variants.

Monovalent vaccines



Bivalent BA.4/5 mRNA vaccines

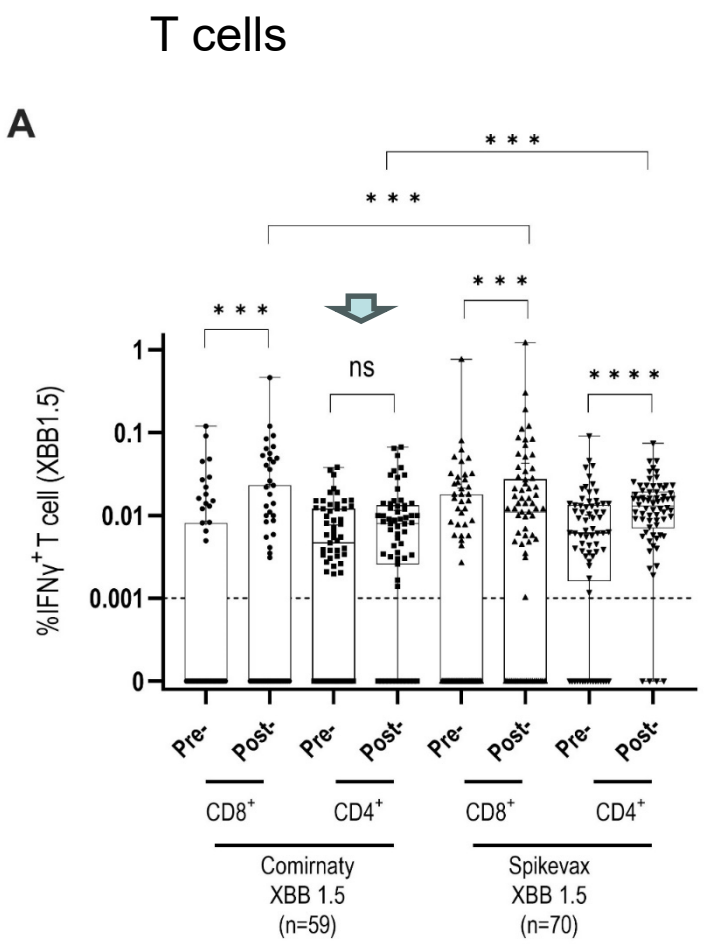


Tang YS, et al. IJID 2024

XBB.1.5 vaccines in the Elderly: Comirnaty (BioNTech) vs Spikevax (Moderna)

Recruitment period: 2 Jan -3 Feb 2024. N=129 Adults (60-91 yrs old)

Mok C, et al. J Infection (revision under review)

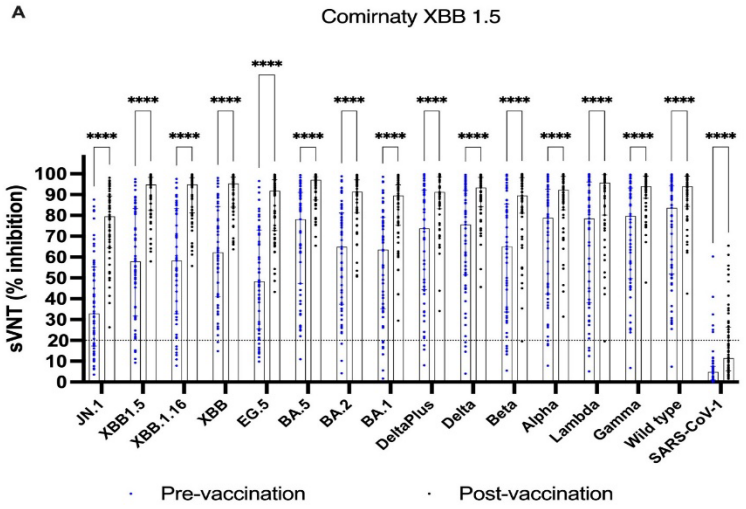


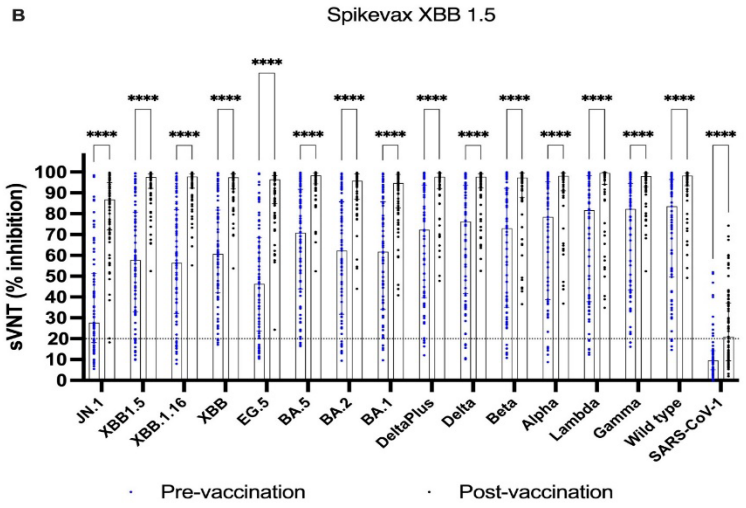
	Spikevax (n=70)	Comirnaty (n=59)	P-value
Local reactions			
Pain	34 (48.6%)	25 (42.4%)	0.595
Erythema	2 (2.9%)	0 (0.0%)	0.500
Pruritus	7 (10.0%)	2 (3.4%)	0.179
Swelling	11 (15.7%)	6 (10.2%)	0.438
None of the above	15 (21.4%)	22 (37.3%)	0.053
Systemic reactions			
Fever	11 (15.7%)	1 (1.7%)	0.006
Fatigue	18 (25.7%)	7 (11.9%)	0.072
Diarrhoea	0 (0.0%)	0 (0.0%)	-
Muscle pain	9 (12.9%)	5 (8.5%)	0.572
Nausea	0 (0.0%)	0 (0.0%)	-
Headache	7 (10.0%)	2 (3.4%)	0.179
Cough	2 (2.9%)	0 (0.0%)	0.500
Anorexia	3 (4.3%)	0 (0.0%)	0.250
Hypoesthesia	1 (1.4%)	0 (0.0%)	0.999
Dizziness	2 (2.9%)	2 (3.4%)	0.999
Abdominal distention	0 (0.0%)	0 (0.0%)	-
Peripheral oedema	1 (1.4%)	0 (0.0%)	0.999
Abdominal pain	0 (0.0%)	0 (0.0%)	-
Vomiting	0 (0.0%)	0 (0.0%)	-
Drowsiness	6 (8.6%)	2 (3.4%)	0.288
Joint pain	4 (5.7%)	3 (5.1%)	0.999
Rash	2 (2.9%)	0 (0.0%)	0.500
Palpitation	0 (0.0%)	1 (1.7%)	0.457
None of the above	36 (51.4%)	47 (79.7%)	<0.001

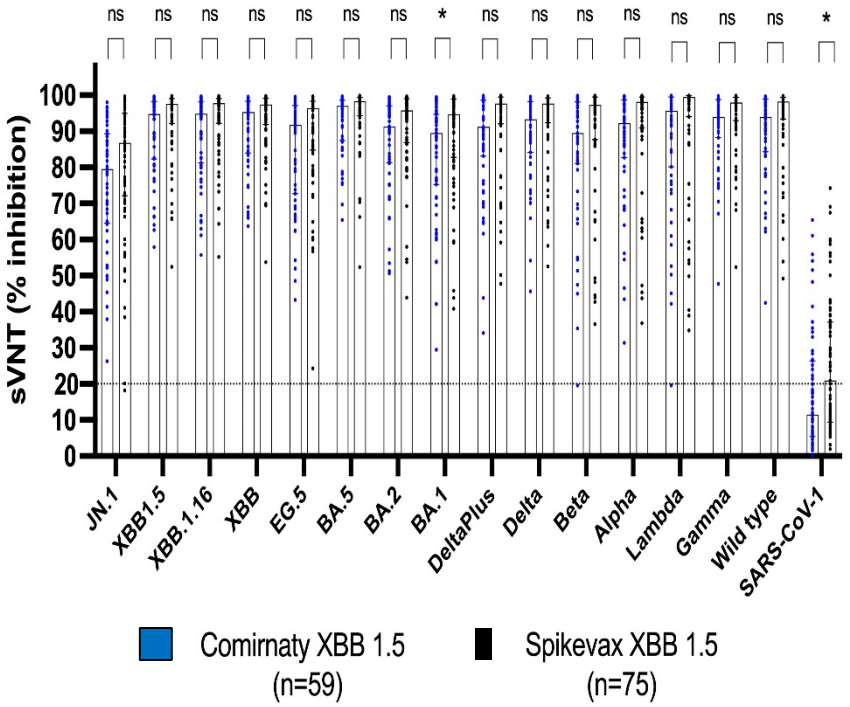
Both XBB vaccines induce T cell responses in the elderly, with relatively stronger response for Spikevax. More recipients of Spikevax showed fever vs those who had received Comirnaty

XBB vaccines in the Elderly: Comirnaty (BioNTech) vs Spikevax (Moderna)

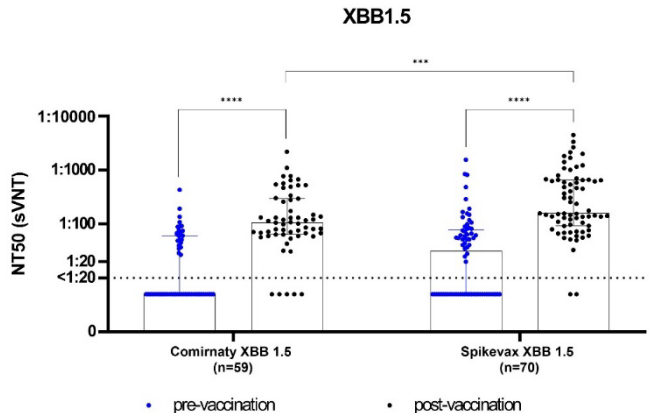
Recruitment period: 2 Jan -3 Feb 2024. N=129 Adults (60-91 yrs old)

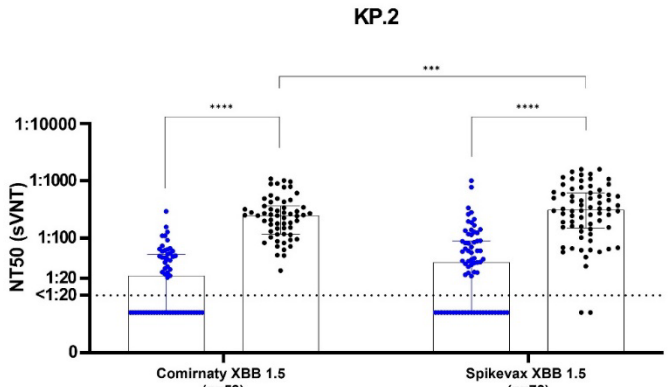


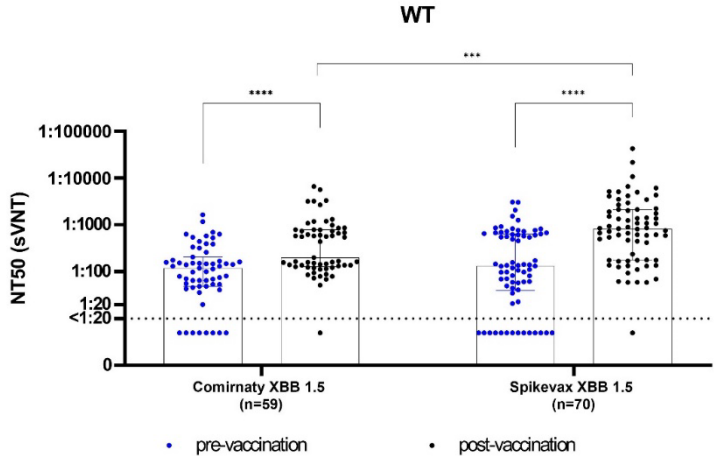




Both XBB vaccines confer antibody protection against the more recent variants JN.1 and KP.2. *Mok C, et al. J Infection (revision under review)*







Summary:

- CoronaVac (SinoVac) trigger lower antibody response than mRNA vaccines to WT and subsequent variants.
- Omicron subvariants show more immune evasion towards older generation vaccines but higher antibody levels in vaccinated individuals during breakthrough infection.
- The bivalent WT+BA.4/5 mRNA vaccine elicited significantly higher neutralizing antibody levels to omicron subvariants vs boosting with the monovalent BNT162b2 vaccine.
- Either BNT monovalent WT or bivalent WT+BA.4/5 mRNA but not inactivated virus vaccine as the second/third booster induced antibody against different XBB variants.
- Both BNT and CoronaVac vaccines significantly induced CD4 and CD8 T response to WT and Omicron BA.1. A third dose of either BNT162b2 or CoronaVac boosted waning T cell responses.
- Adults who had received the BNT bivalent WT+BA.4/5 mRNA vaccine as the third booster dose significantly elicited T cell responses to the XBB variants.
- XBB.1.5 vaccines made by BNT and Moderna confer antibody protection against the more recent variants JN.1 and KP.2 and induce T cell responses in the elderly, with relatively stronger response for Spikevax, with more recipients of Spikevax developing fever
- XBB.1.5 based vaccine recommended as the preferred initial or booster dose before the availability of JN.1 vaccines.

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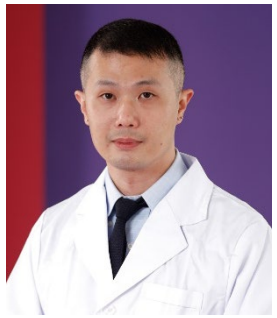
PWH vaccination center: Dr SV Lo, Dr Beatrice Cheng
Kowloon Bay vaccination center: Dr Ken Tsang
CUHKMC: Dr Fung Hong



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Thank You!