# Community based sero-epidemiological study of COVID-19 (Ref. No.: COVID190126)

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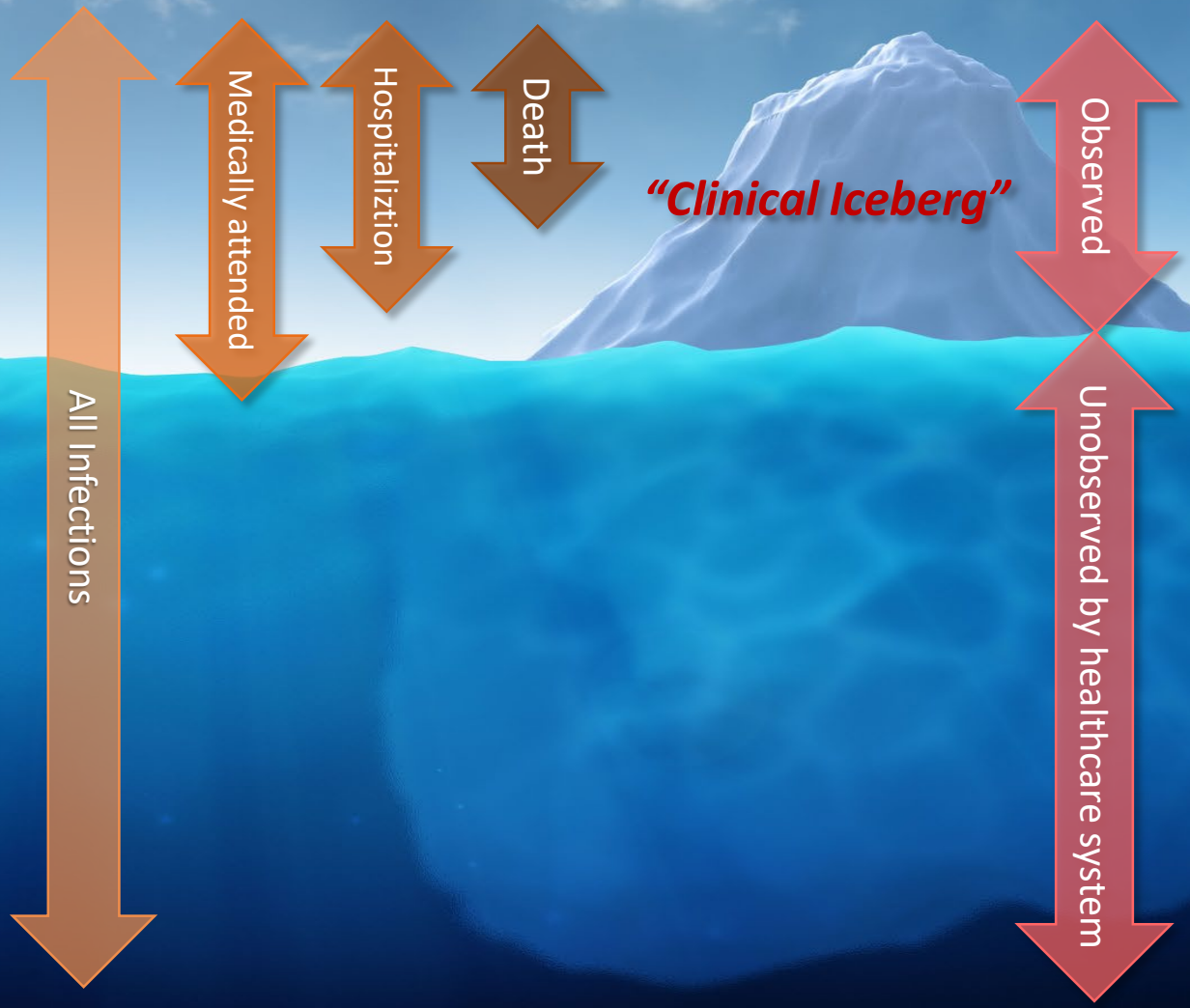
# Aim: To define SARS-CoV-2 infection attack rate to inform public health policy through population-based sero-epidemiology studies.

Morbidity and mortality observed in the clinical settings often constitute only a small proportion of all infections

Asymptomatic or subclinical infection carriers are common for many infectious diseases



## Phase 1 (April 2020-October 2021):

**Five cohorts with different levels of risk:**

A. Age stratified population based cohort (n=4,736)
B. Blood donors (n=14,164)
C. High risk occupations (excluding health care) (n=2,336)
D. COVID-19 contacts in quarantine (n=4,296)
E. COVID-19 convalescent cohort (n=622)

**Serological methods:**

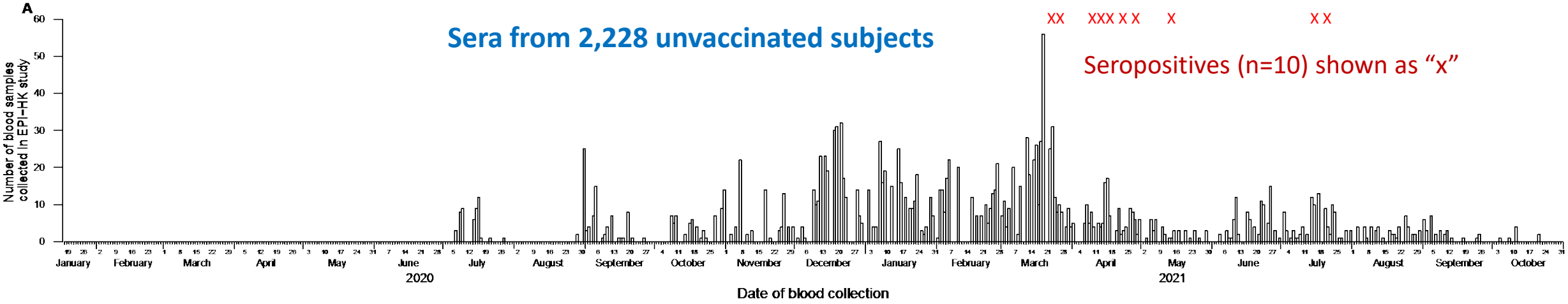
- RBD IgG ELISA→ surrogate neutralization→ Virus plaque neutralization tests

## Phase 2/3 (May 2022-July 2023)

- Blood donors (n=5,173); population based children (n=137)
- Same serological methods as in Phase 1 plus:
  - SARS-CoV-2 N and ORF8 IgG ELISA to differentiate vaccine elicited antibody from natural infection

# Cohort A: Population based cohort
# PI: Ben Cowling

Longitudinal cohort study with 4,736 individuals across all ages. Blood collection every 6 months. Serological methods for differentiating infection vs vaccination were still under development. Infection attack rate was estimated based on seropositivity among 2,228 unvaccinated subjects.




- Using a statistical model, we estimated that there had been 60,000 (95% CI: 12,000 – 140,000) unconfirmed SARS-CoV-2 infections in Hong Kong, i.e. cumulative incidence = 0.9%.
- Adding this to the 12,300 confirmed cases, the cumulative incidence = 1%.
- Case ascertainment = 17%.

# Cohort C: High occupational risk (excluding healthcare workers)
# PI: Michael Ni

Total recruited: 2,336

**<u>Unvaccinated sub-cohort</u>**
1,297 sera (including 2nd or 3rd visit follow up sera) from:
MTR front line staff (n=240); Bus drivers (n=139);
Courier delivery workers (n=66); Mini bus drivers (n=31);
Taxi drivers (n=258); Supermarket workers (n=45);
Wet market workers (n=44); Cross-border truck drivers (n=4); Foreign domestic helpers (n=8).

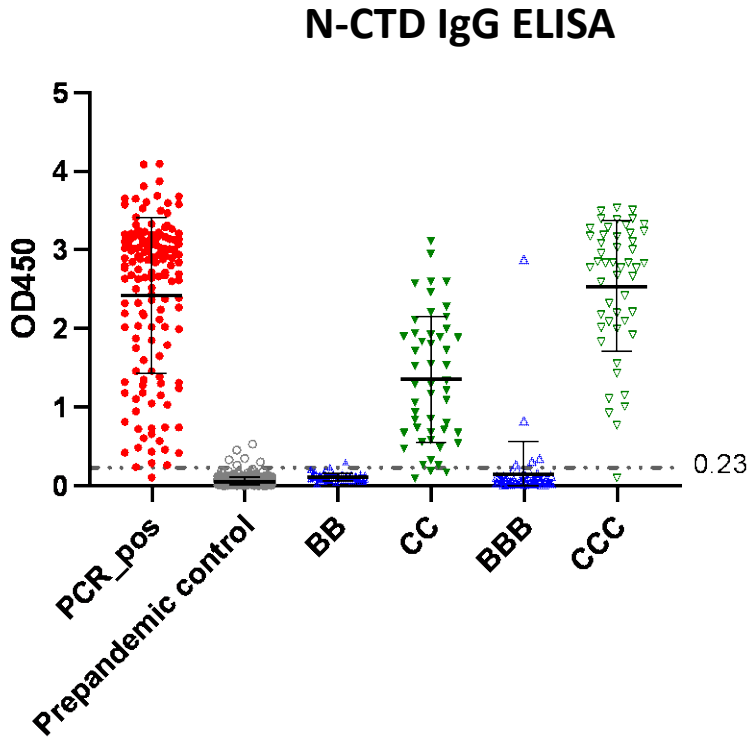
**Sero-positive proportion for:**
MTR workers 0.4%  (95% CI 0.02-2.3)
Bus drivers 0.7% (95% CI 0.04-3.9)

Not significantly higher than the general population

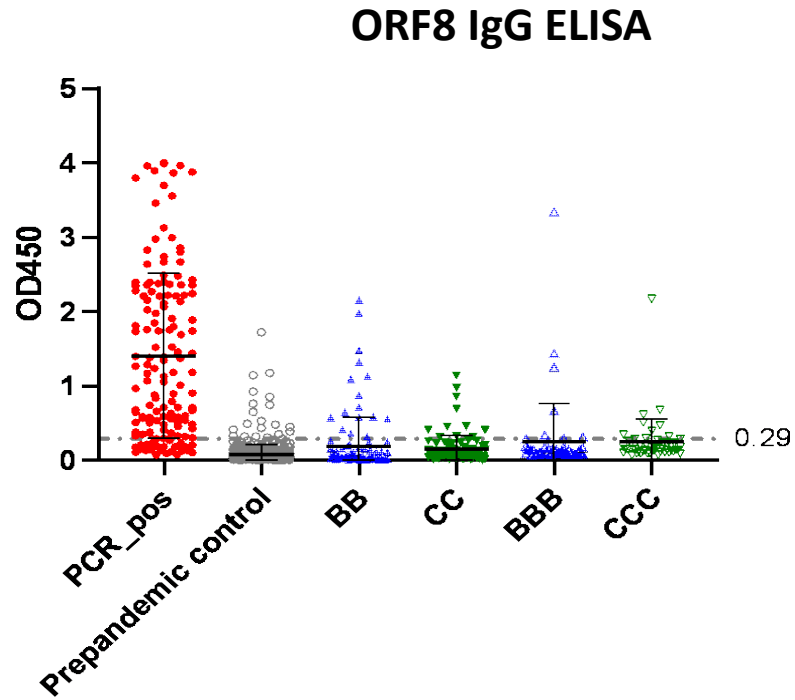
# Cohort D: Quarantined case-contacts
# PI: Dennis IP

- N= 4,044 quarantine confinees between June 2020 to July 2021 who completed mandatory isolation at government-designated quarantine centres, representing 8.02% of the total number of quarantined confinees and 8.91% of the overall close contacts as of 15 July 2021.
- The mean age of all recruited participants was 48 years (± 14.20), 45% being male. The mean lag time of serum sampling from COVID-19 exposure was 114 days (3 – 432 days). The recruitment trend was well distributed and covered the third and fourth waves of local COVID-19 epidemic wave in Hong Kong.
- Subjects with COVID-19 vaccine history prior to serum sampling (n=842; 21%) or reported RT-PCR positivity (n=251, 6%) were excluded from incidence analysis.
- Of the remaining 2,951 individuals, 28 (0.95%) had serological evidence of SARS-CoV-2 infection. 16 (57%) were from the household / family contact exposure group.
- Despite close medical surveillance during the quarantine period, including daily temperature and symptom monitoring and multiple deep-throat saliva collection for PCR testing against SARS-CoV-2, our data suggested that a minority of quarantine subjects had developed unsuspected infection.
  - Poor swabbing of quarantined subjects missed SARS-CoV-2 infection
  - Individuals acquired infected late during quarantine
  - Acquired infection after leaving quarantine.
- This finding was reported to the DH to inform swabbing and testing policies during quarantine.

# Differentiating natural infection from vaccine immunity
# RNA and inactivated whole virus vaccines




B= BionTech
C=CoronaVac



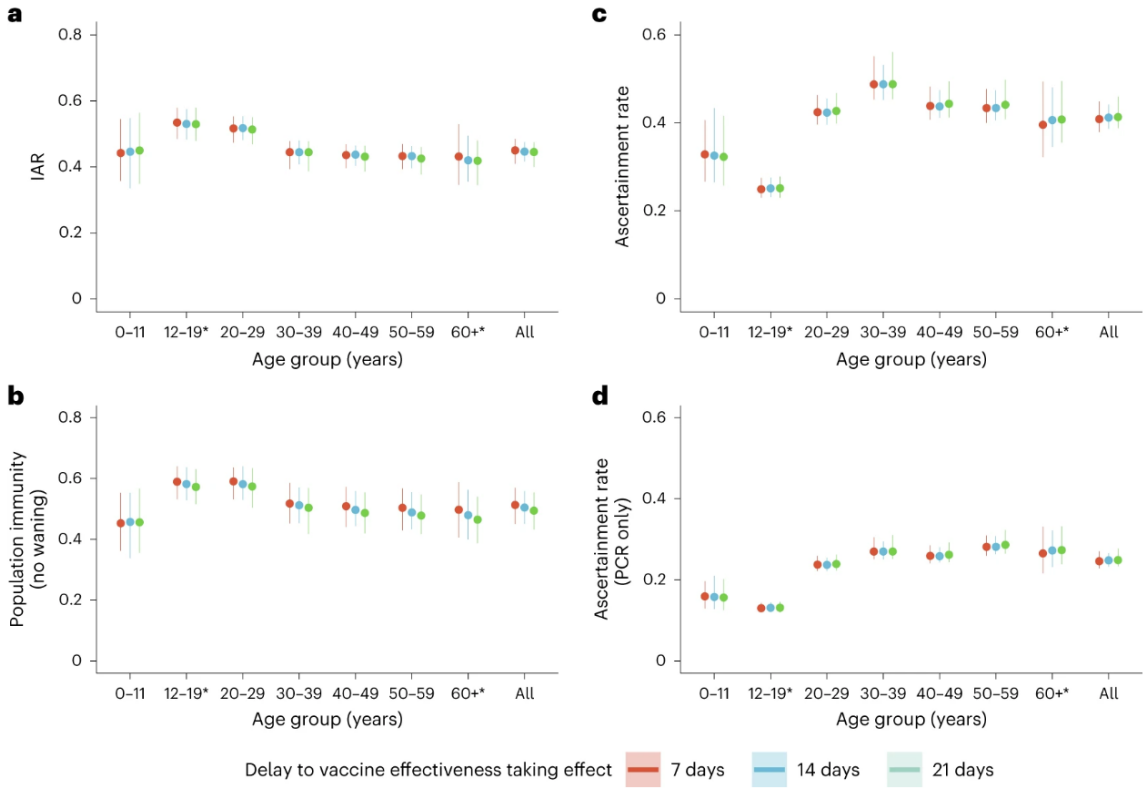

**N-CTD IgG ELISA differentiates natural infection from RNA vaccine immunity**
**ORF8 IgG ELISA differentiates natural infection from RNA or inactivated vaccine immunity (until recent variants which have mutated ORF8)**

*Cheng SMS et al. (Journal of Clinical Virology 2023)*

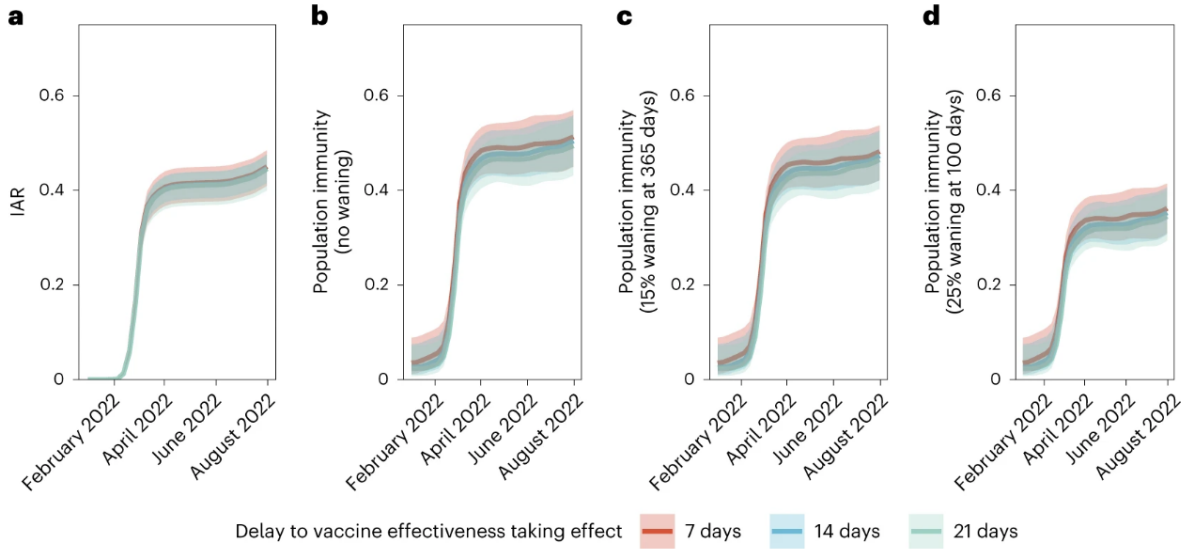
# Phase 2: Estimated IAR and population immunity during the 5th wave (Omicron BA.2)

**Omicron BA.2 infected 45% (41–48%) of the population between 1 January and 31 July 2022**

- 5,173 healthy adult blood donors recruited between 28 April and 30 July 2022; and 137 children aged 18 months to 11 years randomly recruited from the community.
- Used N and ORF8 antibody to distinguish infection from vaccination




Population immunity reached 52% (45–57%) by July 2022




*Lau JJ, et al. Nat Med. 2023 Feb;29(2):348-357.*

# Vaccine Effectiveness Against Omicron BA.2 Infection

13% (2–39%) on day 7
7% (1–21%) on day 100

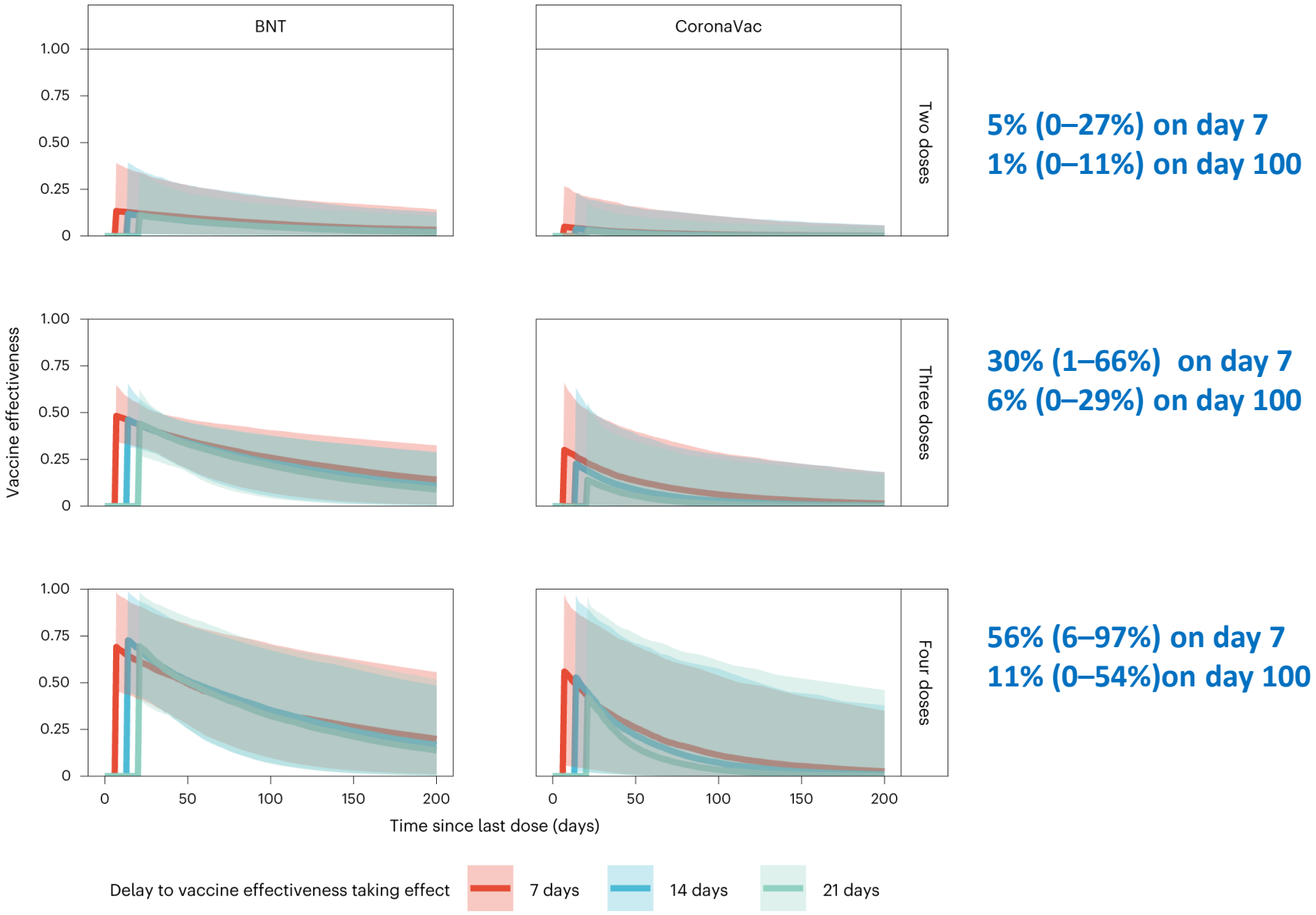
5% (0–27%) on day 7
1% (0–11%) on day 100

48% (34–64%) on day 7
26% (7–41%) on day 100

30% (1–66%) on day 7
6% (0–29%) on day 100

69% (46–98%) on day 7
35% (10–71%) on day 100

56% (6–97%) on day 7
11% (0–54%)on day 100



# Other key findings

- In contrast to previous reports, we showed that neutralizing and other antibody to the original SARS-CoV-2 are long lasting (Lau EHY et al. Nat Commun. 2021; Lau EH et al. EClinicalMedicine. 2021). But virus variants can evade neutralizing immunity.
- Omicron variants BA.1, BA.2, BA.5, XBB.1.5, EG.1.5 and JN.1 were progressively able to evade neutralizing antibody responses in those who had recovered from past infection (Cheng SMS et al Nat Med Nat Med. 2022; Cheng SM et al. Euro Surveill. 2022; Cheng SS et al. J Clin Virol. 2022; Cheng SMS et al. Virology J 2024).
- T cell responses were elicited following natural infection. Long term memory T cell responses were maintained up to 150 days after infection. Children mounted lower magnitude T cell responses than adults due to a higher threshold of baseline activation and lower pre-existing immune memory to related common cold viruses (Cohen CA et al. Nat Commun. 2021).
- Experimental animal studies with hamsters demonstrated that neutralizing antibodies by themselves can confer protection from infection and transmission (Su W et al. mBio. 2021 )
- As of July-Oct 2023, population immunity to variants such as BA.2 and BA.5 was ≥84%, while that to XBB.1.5 and EG.5.1 was ≤44%, indicating why BA.2 and BA.5 are no longer circulating while EG.1.5 and later variants continue to circulate in Hong Kong.
- The outputs of this research grant were communicated to Health Bureau in real-time and has led to 26 research papers in peer-reviewed scientific journals, cited over 940 times in the scientific literature.

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