Use of Electronic Health Registries to Estimate COVID-19 VE: The Experience of Qatar

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WCM-Q, Qatar Foundation

WHO EMRO COVID-19 Vaccine Effectiveness Study;
Status Update and Important Considerations
24 November 2022

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Overview

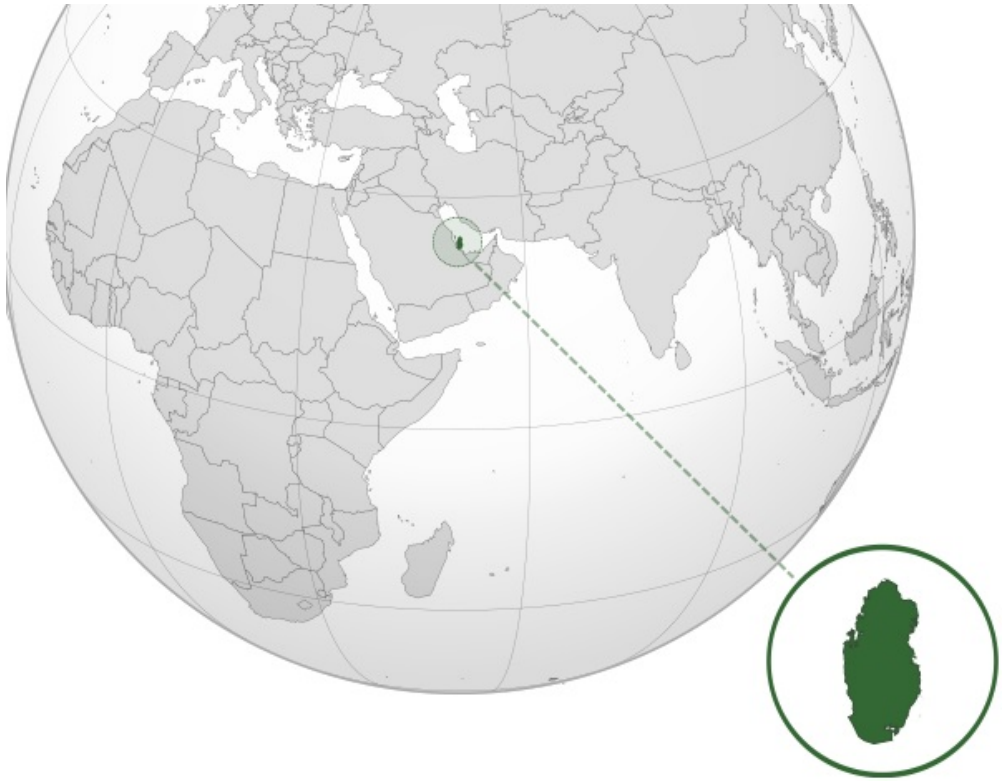
To provide an overall picture of the experience of COVID-19 vaccine effectiveness studies in Qatar

The diverse population of Qatar

Of 2.8 million people,

89% are expatriates from

over 150 countries.



Modernization of health care

Advanced digital health platforms: The Cerner system

Education City-Qatar Foundation

Infectious Disease Epidemiology Group

- **Scope of research:**
  - Infectious disease epidemiology
  - Diabetes epidemiology
- **Research focus:**
  - Epidemiology of HIV
  - Other sexually transmitted infections
  - Epidemiology of hepatitis C virus
  - Epidemiology of COVID-19
- **Regional focus**
  - Primarily Middle East and North Africa
  - Other world regions and globally

Weill Cornell Medicine-Qatar

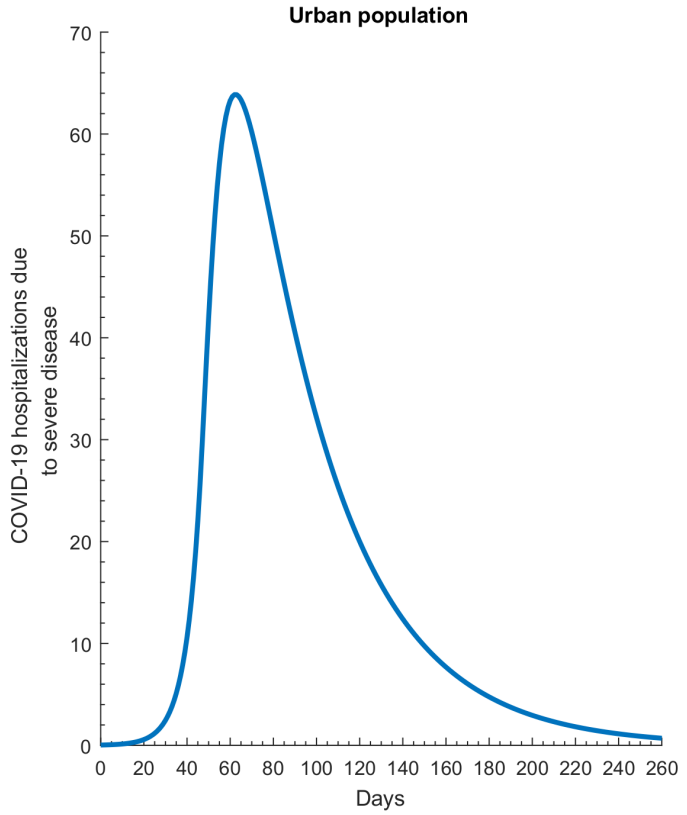
Infectious Disease Epidemiology Group

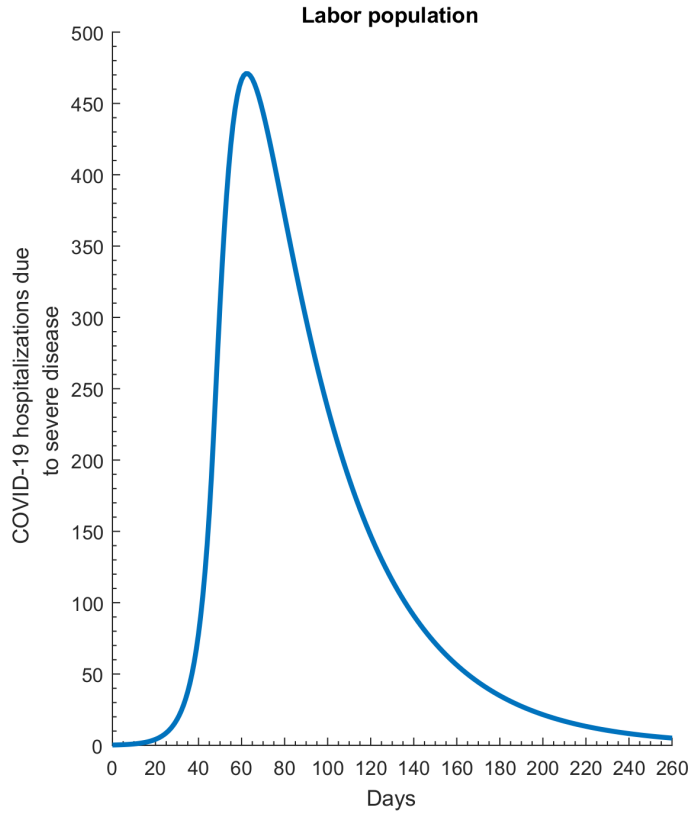
WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis

An effective partnership between the government and academic sectors

Forecasting healthcare needs

- Forecasting healthcare needs has been and continues to be a major engagement.





National, federated databases for COVID-19 that include all SARS-CoV-2-related data such as PCR testing, rapid antigen testing, vaccinations, hospitalizations, and infection severity and mortality classifications per WHO guidelines

National COVID-19 databases

- Completeness of data
- Inclusion of reason for testing
- COVID-19 severity, criticality, and fatality strictly per WHO definitions

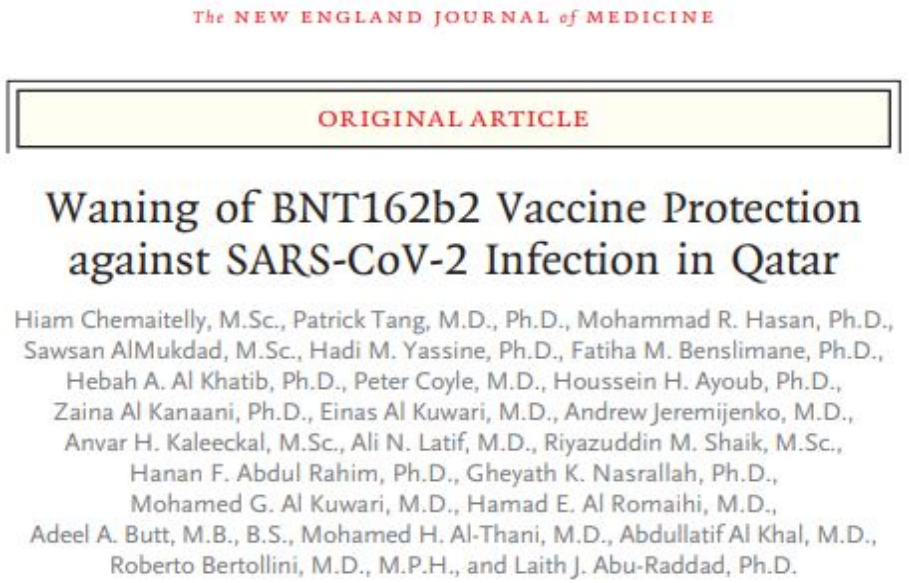
Study designs

- Test-negative case-control designs
- Other case-control designs
- Cohort designs
- Target trial designs
- Cross sectional designs

>15 major frontline COVID-19 discoveries

COVID-19 national response accomplishments

- 82 COVID-19 papers published since pandemic onset
  - 12 papers published in the *New England Journal of Medicine* ranked at the 99th percentile and were the most viewed at NEJM website
  - 3 papers published in *Nature Medicine*
  - 2 papers published in *the Journal of American Medical Association* (*JAMA*)
  - 5 studies published in *Lancet journals*


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar

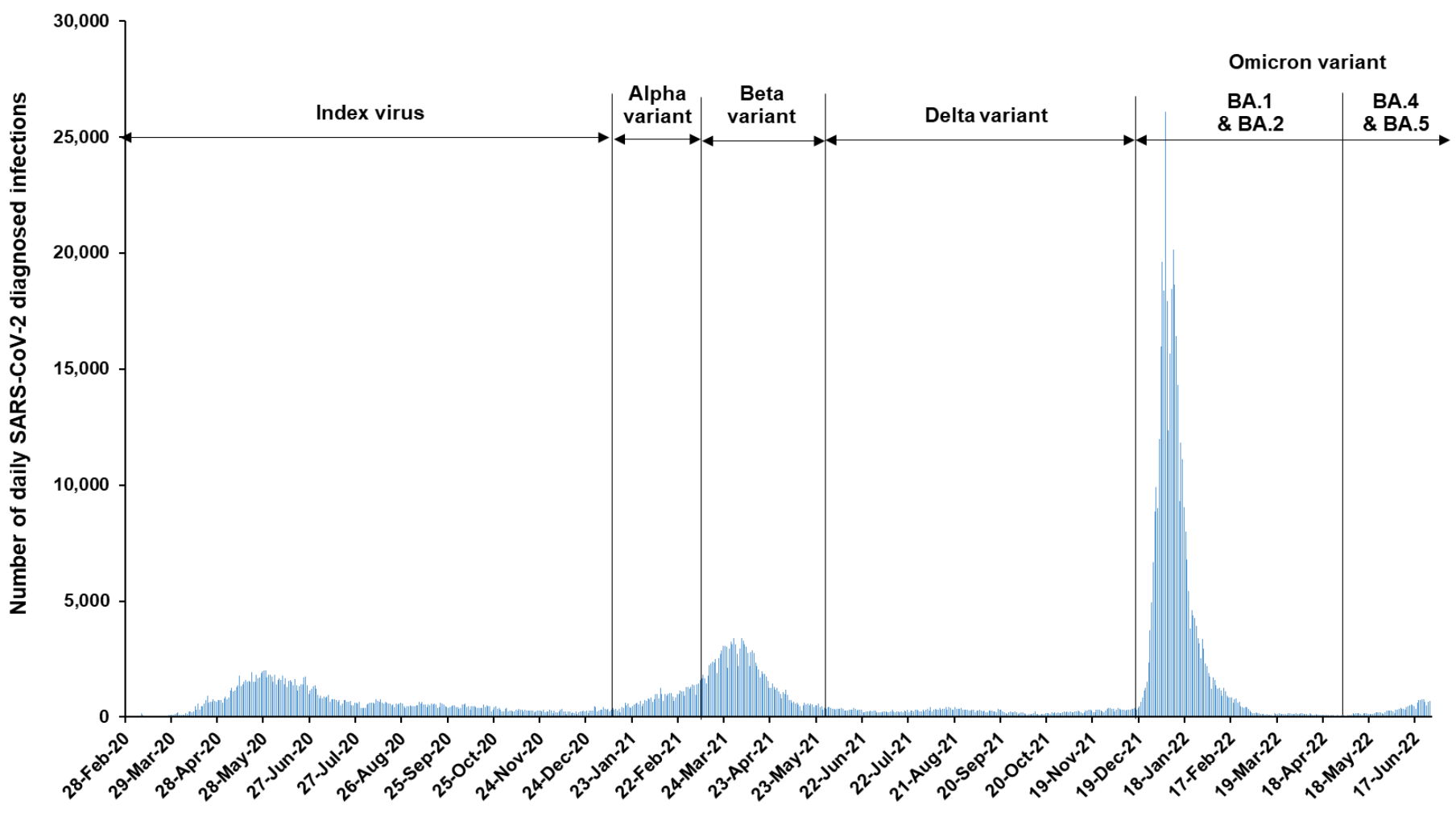
Hiam Chemaitelly, M.Sc., Patrick Tang, M.D., Ph.D., Mohammad R. Hasan, Ph.D., Sawsan AlMukdad, M.Sc., Hadi M. Yassine, Ph.D., Fatiha M. Benslimane, Ph.D., Hebah A. Al Khatib, Ph.D., Peter Coyle, M.D., Houssein H. Ayoub, Ph.D., Zaina Al Kanaani, Ph.D., Einas Al Kuwari, M.D., Andrew Jeremijenko, M.D., Anvar H. Kaleeckal, M.Sc., Ali N. Latif, M.D., Riyazuddin M. Shaik, M.Sc., Hanan F. Abdul Rahim, Ph.D., Gheyath K. Nasrallah, Ph.D., Mohamed G. Al Kuwari, M.D., Hamad E. Al Romaihi, M.D., Adeel A. Butt, M.B., B.S., Mohamed H. Al-Thani, M.D., Abdullatif Al Khal, M.D., Roberto Bertollini, M.D., M.P.H., and Laith J. Abu-Raddad, Ph.D.

- These accomplishments are exceptionally unique within the context of the modern history of medical scholarship in our region.

COVID-19 national response accomplishments

- Informed guidelines at WHO and different country guidelines
- Presented numerous times at high level meetings such as by Dr. Anthony Fauci in his White House press briefing and in US Senate testimony.
- Covered widely in international press and media such as at New York Times, Washington Post, CNN among others.
- This all shows the potential we have to excel in EMRO with the right investment on science.

Five epidemic waves in Qatar



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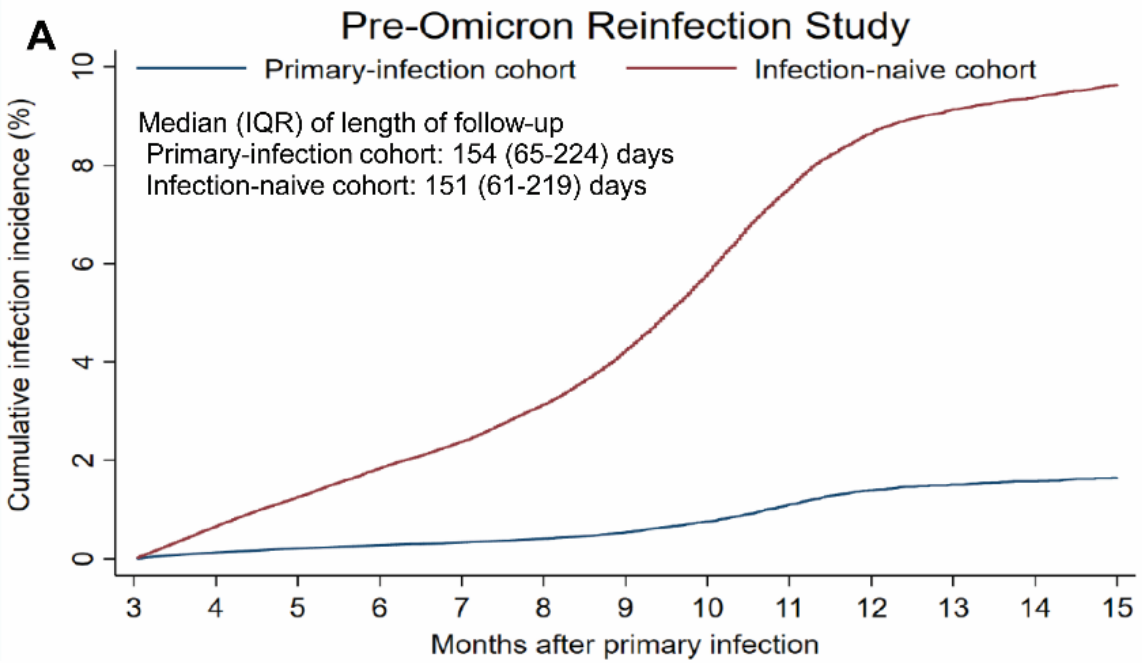
Natural immunity

Protection of natural immunity before Omicron

Incidence of index virus, Alpha, Beta, and Delta



Effectiveness of primary infection against reinfection is 85.5% (84.8-86.2%)

Chemaitelly H, Nagelkerke N, Ayoub HH, et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection. J Travel Med 2022 Sep 30:taac109. doi: 10.1093/jtm/taac109. Epub ahead of print.

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Protection of an Omicron subvariant against another Omicron subvariant

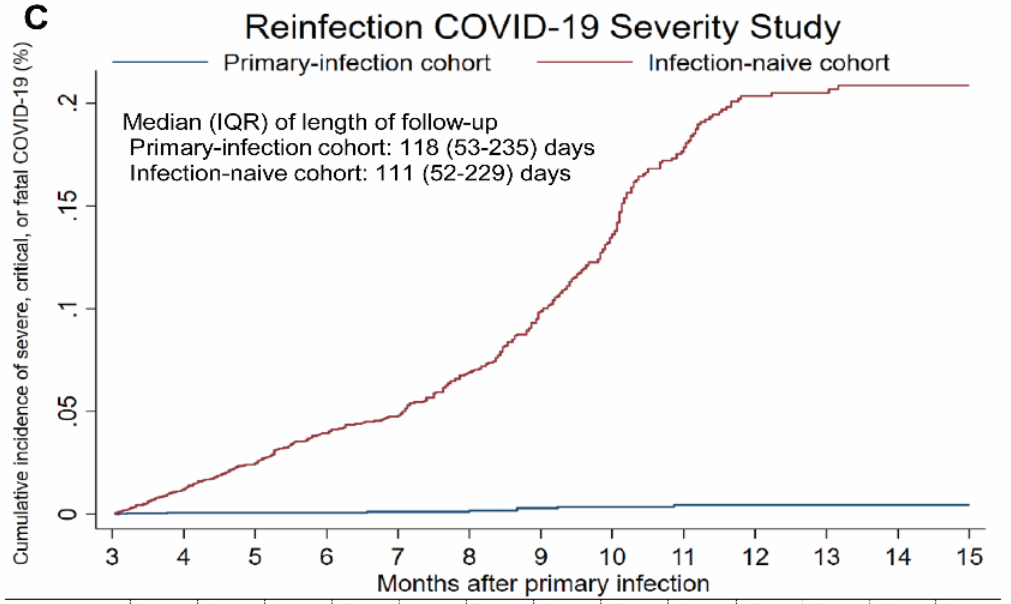
Omicron subvariant	Effectiveness (95% CI)
BA.1 against BA.2[1]	94.2% (89.2-96.9)
BA.2 against BA.1[1]	80.9% (73.1-86.4)
BA.1/BA.2 against BA.4/BA.5[2]	79.7% (74.3-83.9)

[1]*Chemaitelly H, Ayoub HH, Coyle P, et al. Protection of Omicron sub-lineage infection against reinfection with another Omicron sub-lineage. Nat Commun 2022;13:4675.*

[2]*Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Protective effect of previous SARS-CoV-2 infection against Omicron BA.4 and BA.5 subvariants. N Engl J Med 2022;387:1620-2.*

Protection against severe COVID-19 at reinfection

Incidence of all variants since pandemic onset



Month	0	4	5	6	7	8	9	10	11	12	13	14	15
No. at risk													
Primary infection	407,214	358,362	277,911	223,686	202,658	184,047	160,341	128,304	97,882	75,050	59,624	44,908	28,872
Infection naive	407,214	356,746	274,899	219,782	197,994	178,744	154,355	122,121	92,191	70,449	55,996	42,213	27,123

Effectiveness of primary infection against severe, critical, or fatal COVID-19 at reinfection is 97.3% (95.0-98.6%)

Chemaitelly H, Nagelkerke N, Ayoub HH, et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection. J Travel Med 2022 Sep 30:taac109. doi: 10.1093/jtm/taac109. Epub ahead of print.

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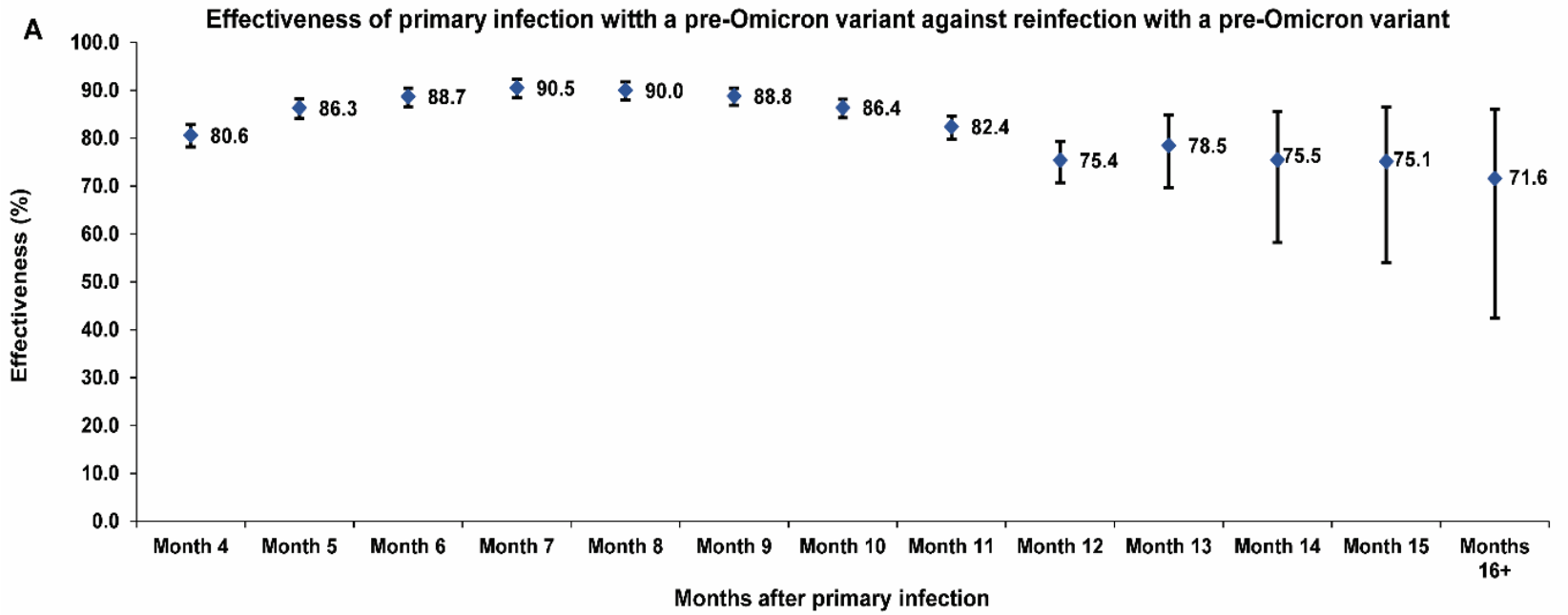
Waning of natural immunity before Omicron

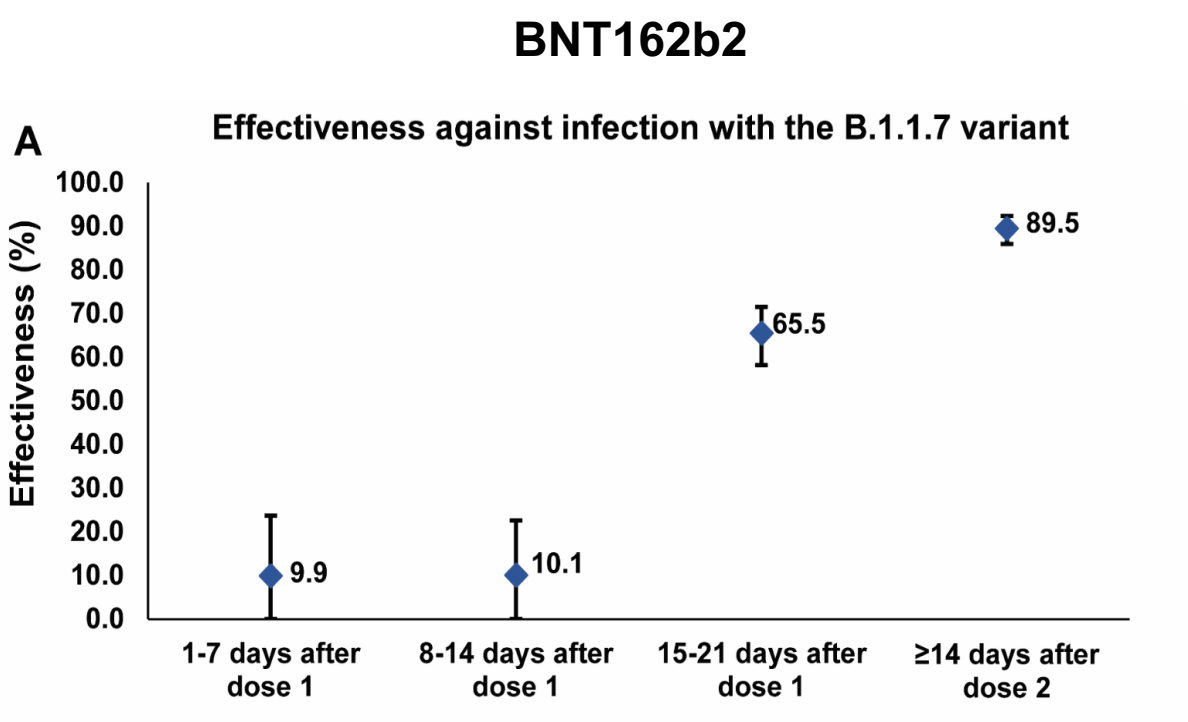


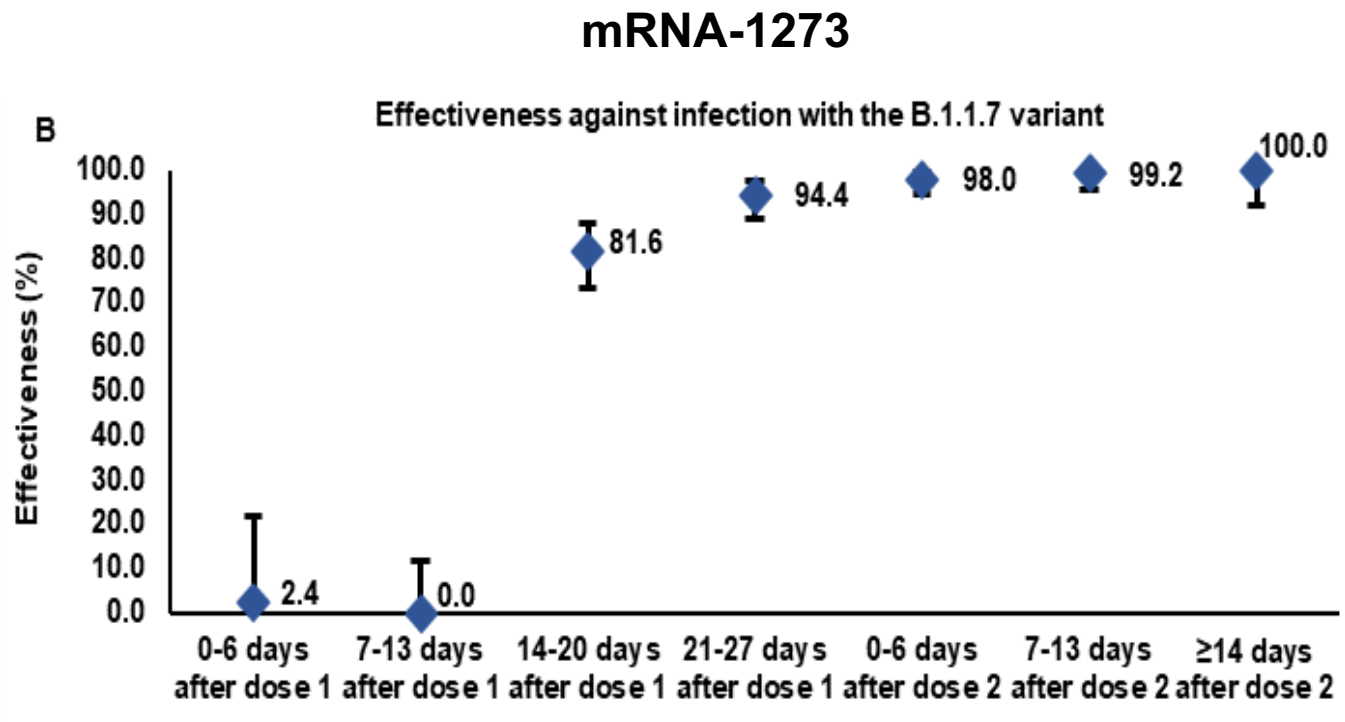
Evidence for waning of protection over time

Chemaitelly H, Nagelkerke N, Ayoub HH, et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection. J Travel Med 2022 Sep 30:taac109. doi: 10.1093/jtm/taac109. Epub ahead of print.

Vaccine immunity

BNT162b2 vaccine protection against Alpha variant

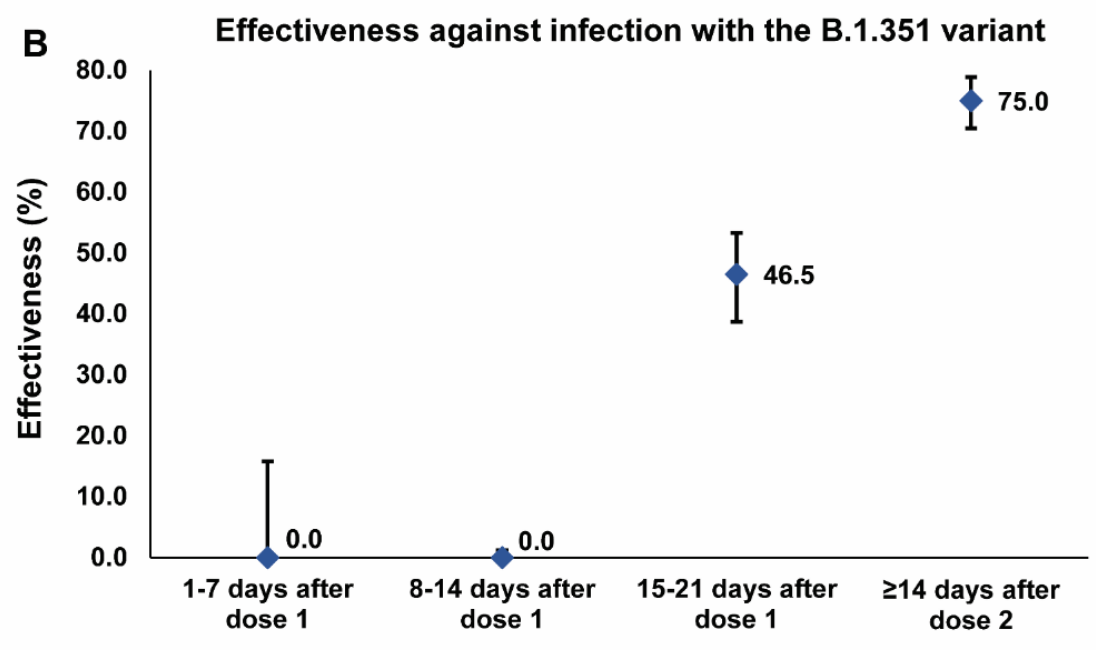




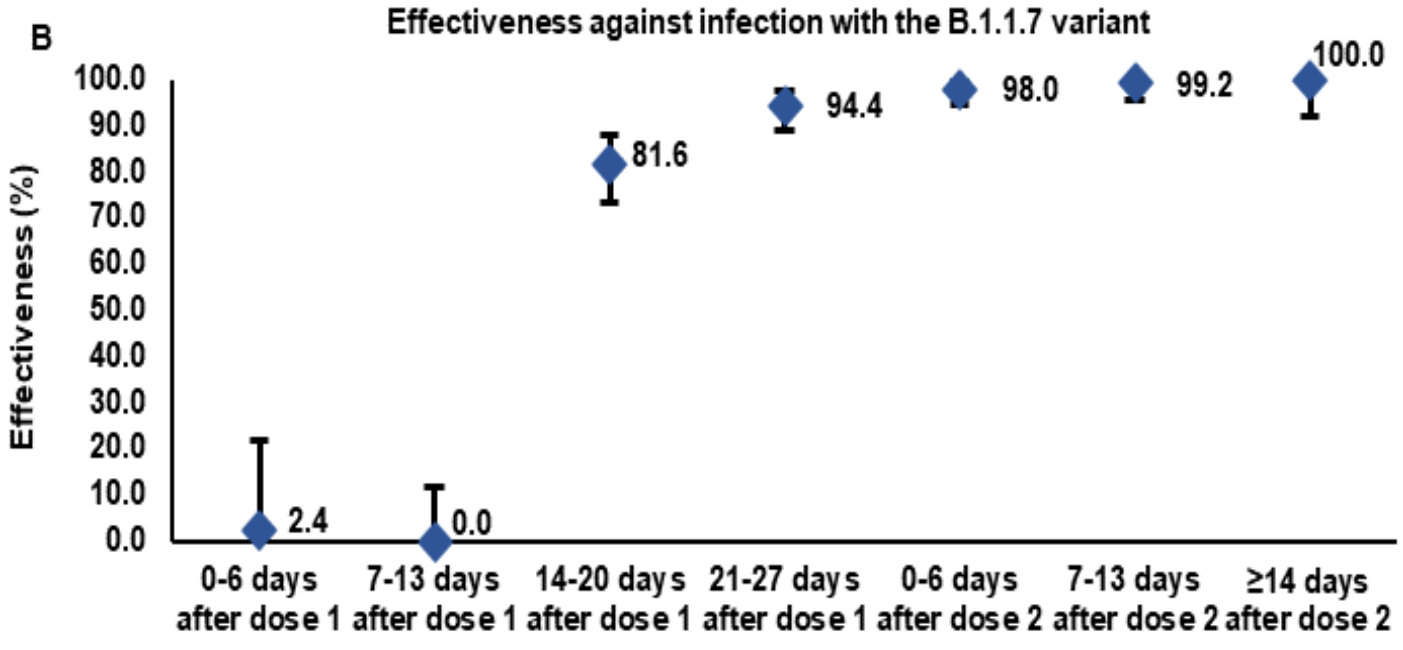
Abu-Raddad LJ, Chemaitelly H, Butt AA, National Study Group for C-V. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. N Engl J Med 2021;385:187-9.
Abu-Raddad LJ, Chemaitelly H, Yassine HM, et al. Pfizer-BioNTech mRNA BNT162b2 Covid-19 vaccine protection against variants of concern after one versus two doses. J Travel Med. 2021 May 28:taab083. doi: 10.1093/jtm/taab083.

BNT162b2 vaccine protection against Beta variant

BNT162b2



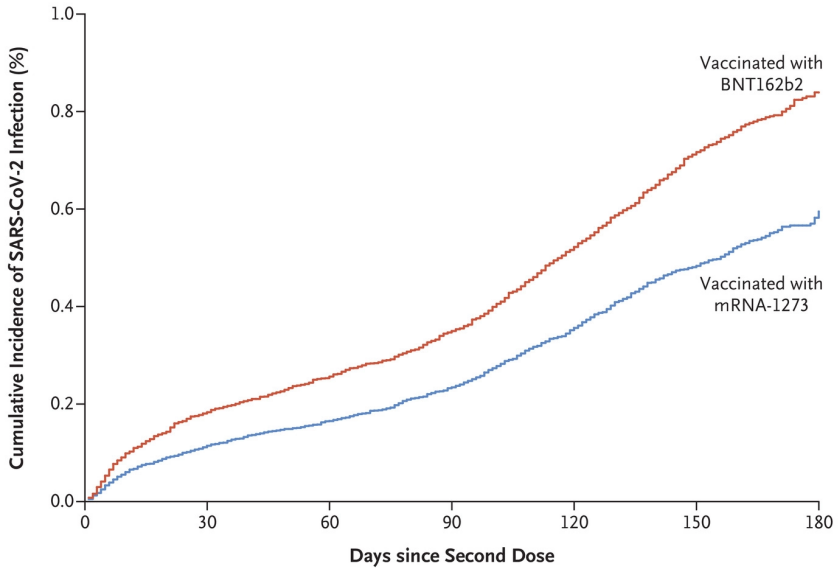
mRNA-1273



Abu-Raddad LJ, Chemaitelly H, Butt AA, National Study Group for C-V. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. N Engl J Med 2021;385:187-9.
Abu-Raddad LJ, Chemaitelly H, Yassine HM, et al. Pfizer-BioNTech mRNA BNT162b2 Covid-19 vaccine protection against variants of concern after one versus two doses. J Travel Med. 2021 May 28:taab083. doi: 10.1093/jtm/taab083.

mRNA-1273 versus BNT162b2 effectiveness: A retrospective controlled target trial

mRNA-1273 is associated with 30% less incidence of breakthrough infection than BNT162b2

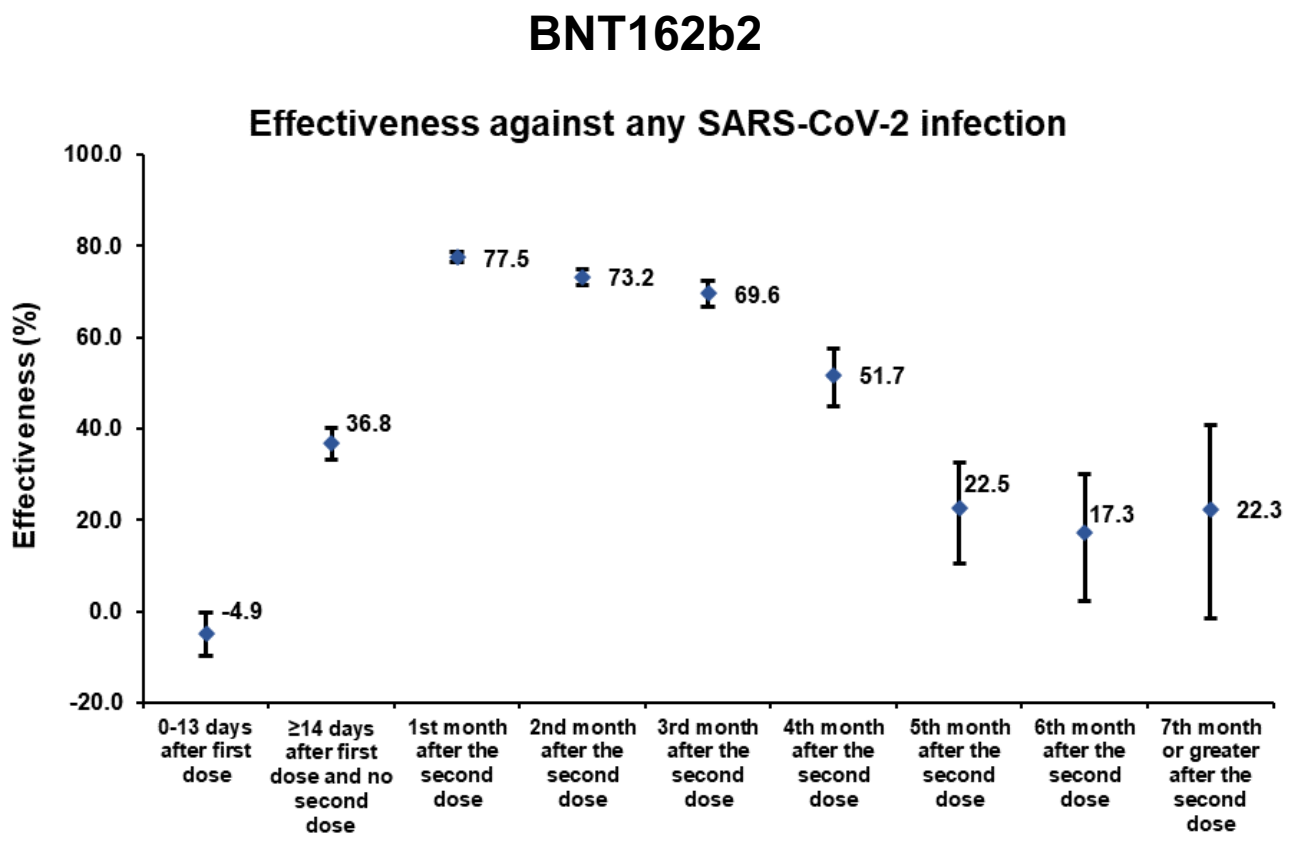


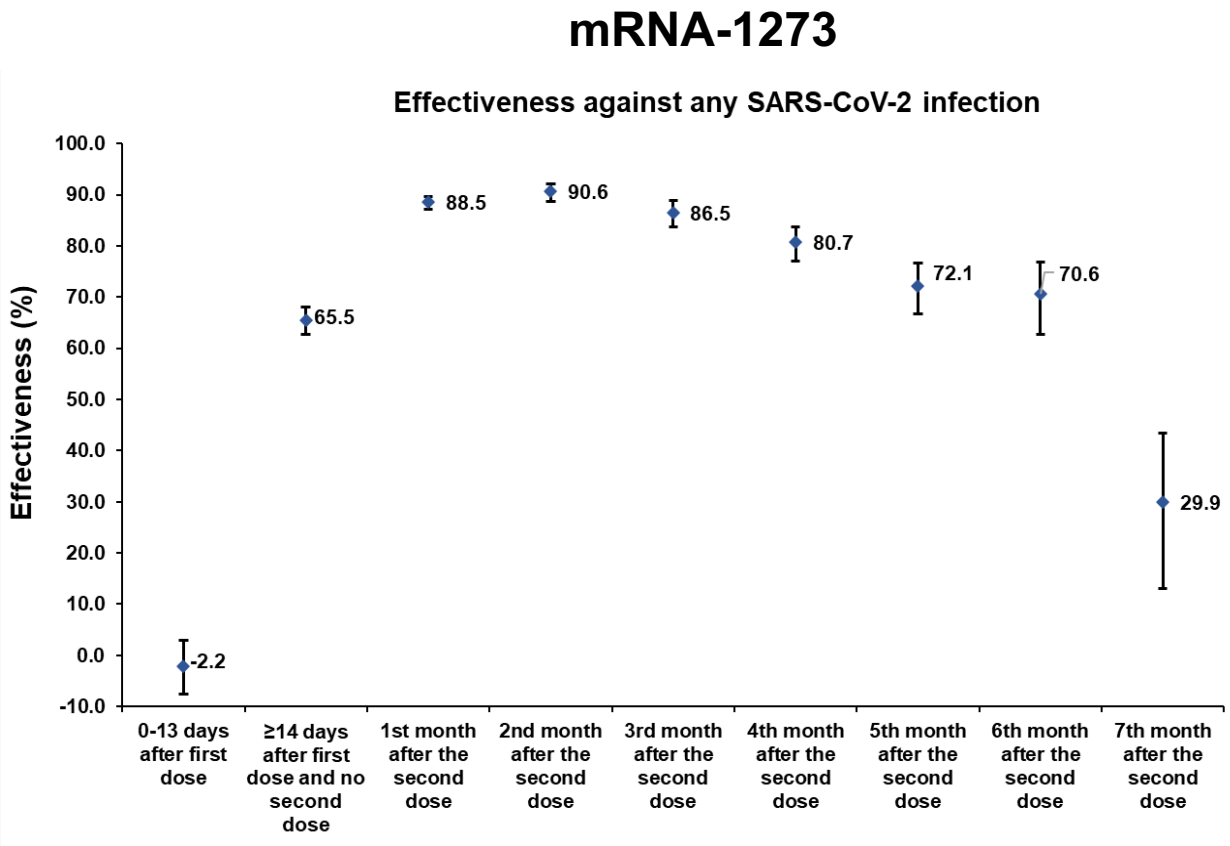
No. at Risk							
Vaccinated with BNT162b2	192,123	191,761	181,987	169,544	146,717	113,813	23,013
Vaccinated with mRNA-1273	192,123	191,890	182,265	171,164	146,223	114,672	23,400

Month of Follow-up after Second Dose	Vaccinated with mRNA-1273		Vaccinated with BNT162b2		Absolute Difference in Cumulative Incidence (95% CI)	Unadjusted Hazard Ratio for Breakthrough Infection (95% CI)	Adjusted Hazard Ratio for Breakthrough Infection (95% CI)
	No. of persons	Cumulative incidence (95% CI)	No. of persons	Cumulative incidence (95% CI)	Percentage points		
1	191,890	0.11 (0.10–0.13)	191,761	0.18 (0.16–0.20)	0.07 (0.04–0.10)	0.62 (0.52–0.73)	0.62 (0.52–0.73)
2	182,265	0.17 (0.15–0.18)	181,987	0.26 (0.23–0.28)	0.09 (0.06–0.12)	0.73 (0.57–0.95)	0.73 (0.57–0.95)
3	171,164	0.23 (0.21–0.26)	169,544	0.35 (0.32–0.38)	0.12 (0.09–0.15)	0.72 (0.57–0.91)	0.72 (0.57–0.91)
4	146,223	0.36 (0.33–0.38)	146,717	0.52 (0.49–0.56)	0.16 (0.12–0.20)	0.70 (0.58–0.85)	0.70 (0.58–0.85)
5	114,672	0.48 (0.45–0.52)	113,813	0.72 (0.68–0.76)	0.24 (0.18–0.30)	0.67 (0.55–0.81)	0.67 (0.55–0.81)
6	23,400	0.59 (0.55–0.64)	23,013	0.84 (0.79–0.89)	0.25 (0.18–0.32)	0.81 (0.59–1.10)	0.82 (0.60–1.12)

Abu-Raddad LJ, Chemaitelly H, Bertollini R, National Study Group for Covid Vaccination. Effectiveness of mRNA-1273 and BNT162b2 Vaccines in Qatar. N Engl J Med 2022: 386:799-800.

Waning of BNT162b2 and mRNA-1273 vaccine effectiveness against infection





Chemaitelly H, Tang P, Hasan MR, et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. N Engl J Med 2021. 385:e83.
Abu-Raddad LJ, Chemaitelly H, Bertollini R, et al. Waning mRNA-1273 Vaccine Effectiveness against SARS-CoV-2 Infection in Qatar. N Engl J Med 2022. 386(11): 1091-1093.

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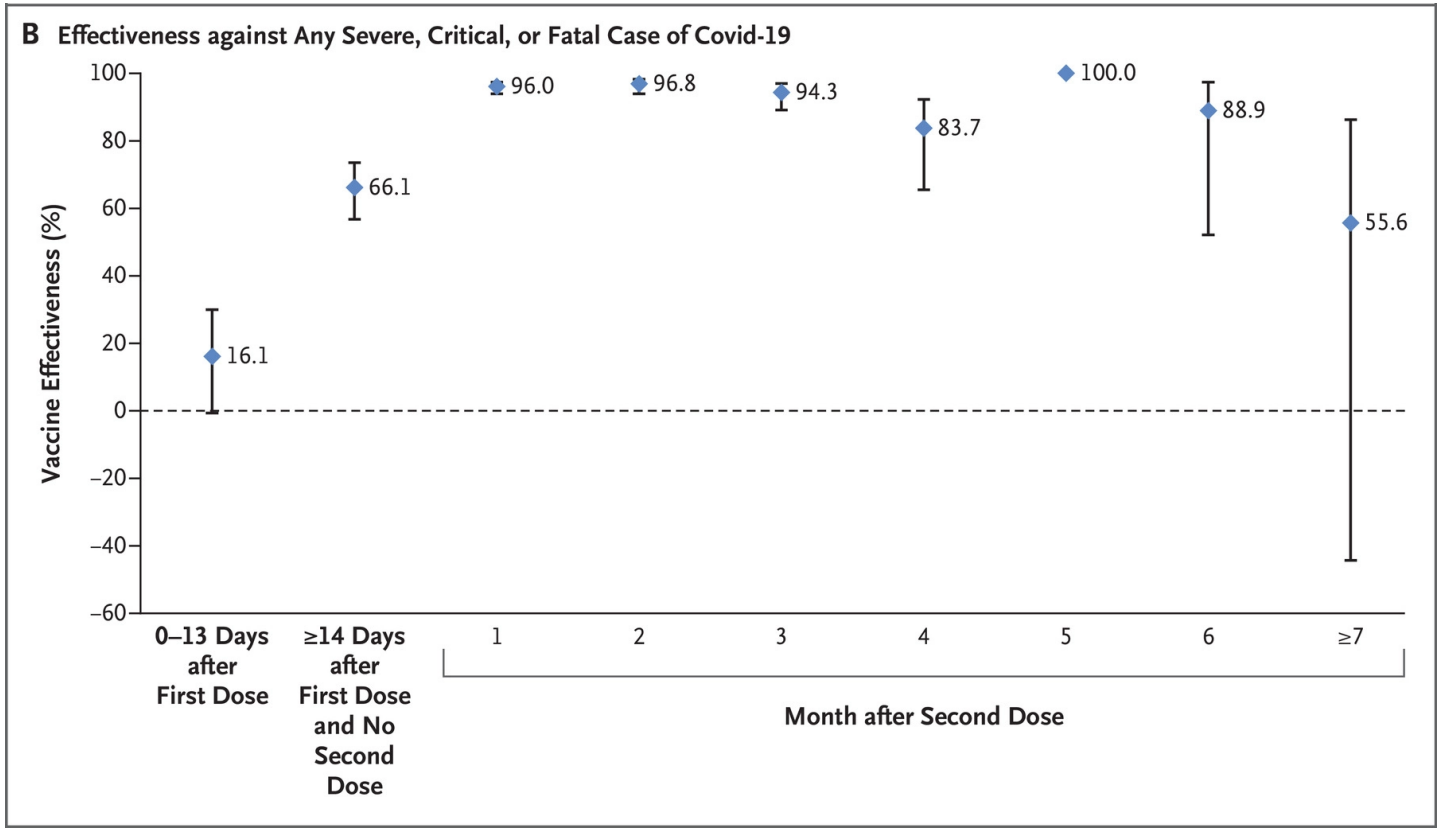
Waning of BNT162b2 vaccine effectiveness against hospitalization and death



No evidence for major waning of protection against hospitalization and death

Chemaitelly H, Tang P, Hasan MR, et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. N Engl J Med 2021. 385:e83.

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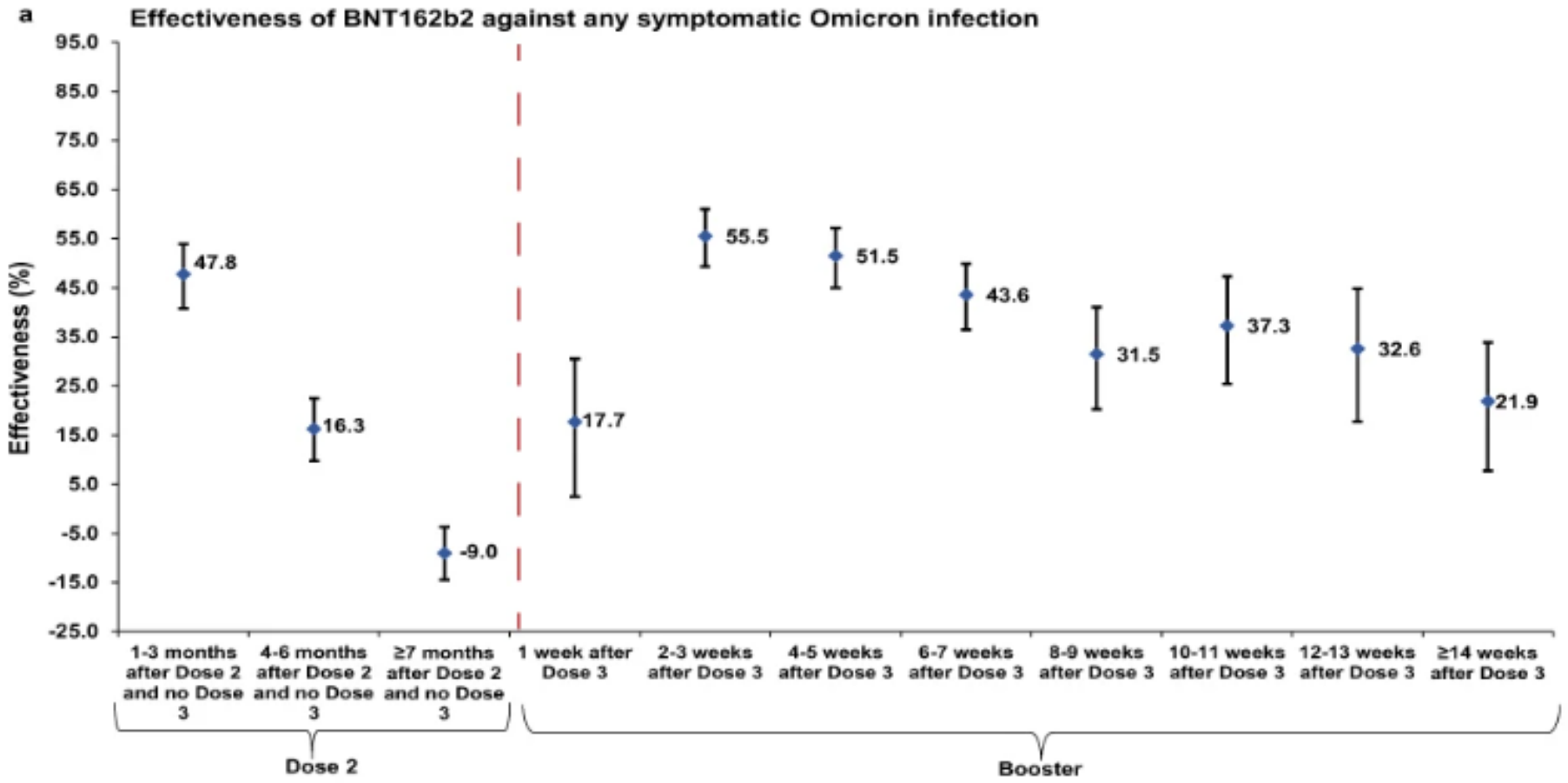
Effectiveness of BNT162b2 against symptomatic Omicron infection

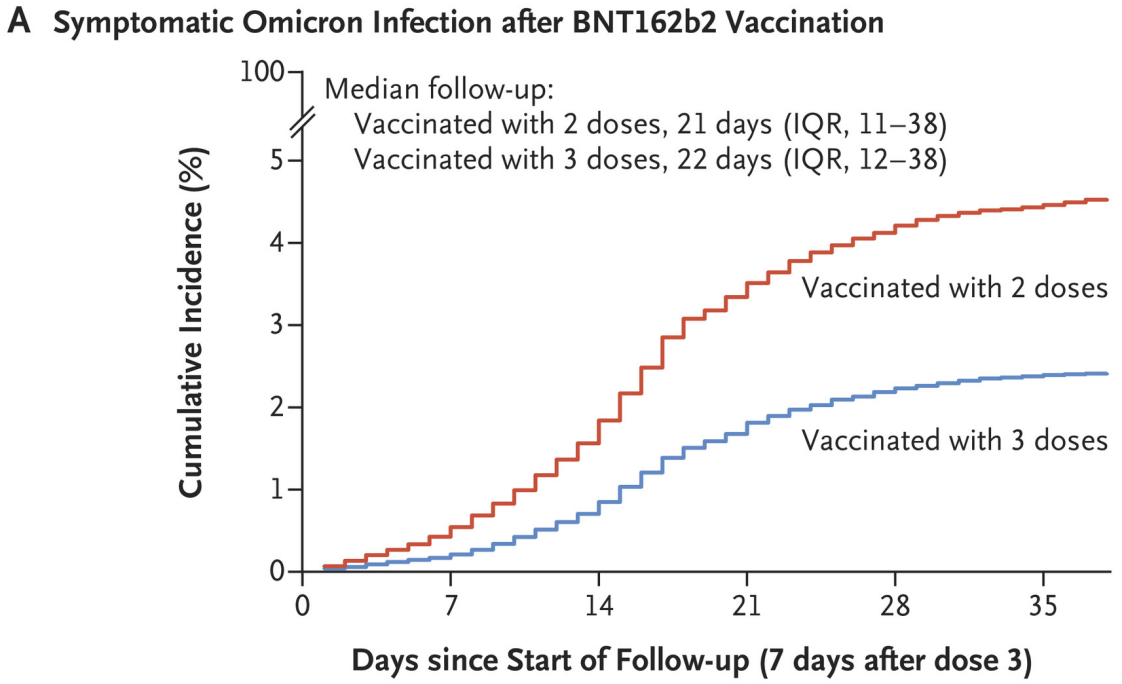


Chemaitelly H, Ayoub HH, AlMukdad S, et al. Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. Nat Commun 2022;13:3082.

Effectiveness of BNT162b2 booster against symptomatic Omicron infection

Booster effectiveness against symptomatic Omicron infection relative to primary series was
49.4% (95% CI: 47.1-51.6%)

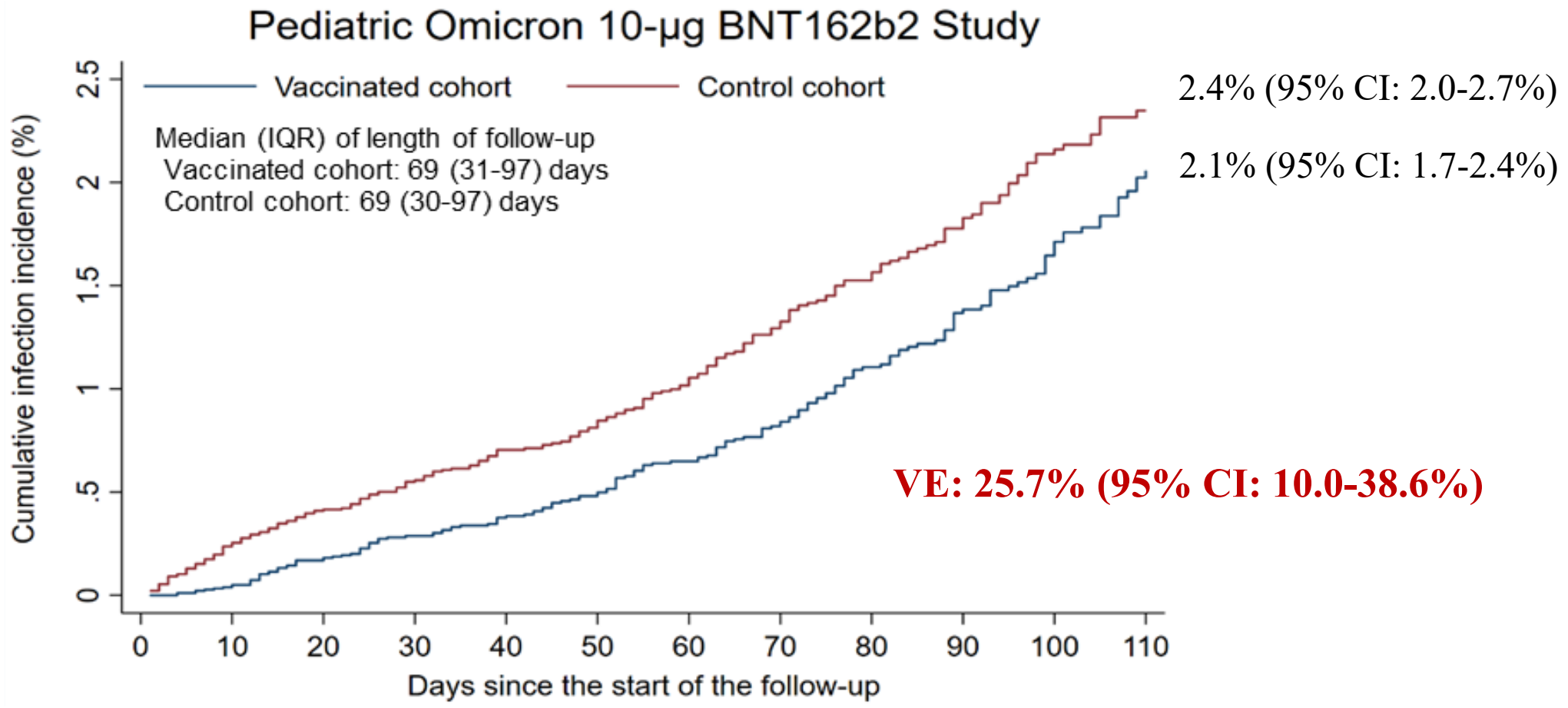
Booster effectiveness against COVID-19 hospitalization and death due to Omicron infection, relative to primary series, was
76.5% (95% CI: 55.9-87.5%)



No. at Risk						
Vaccinated with 2 doses	189,483	162,896	131,625	97,210	74,544	59,598
Vaccinated with 3 doses	189,483	163,851	135,279	103,404	81,558	66,302

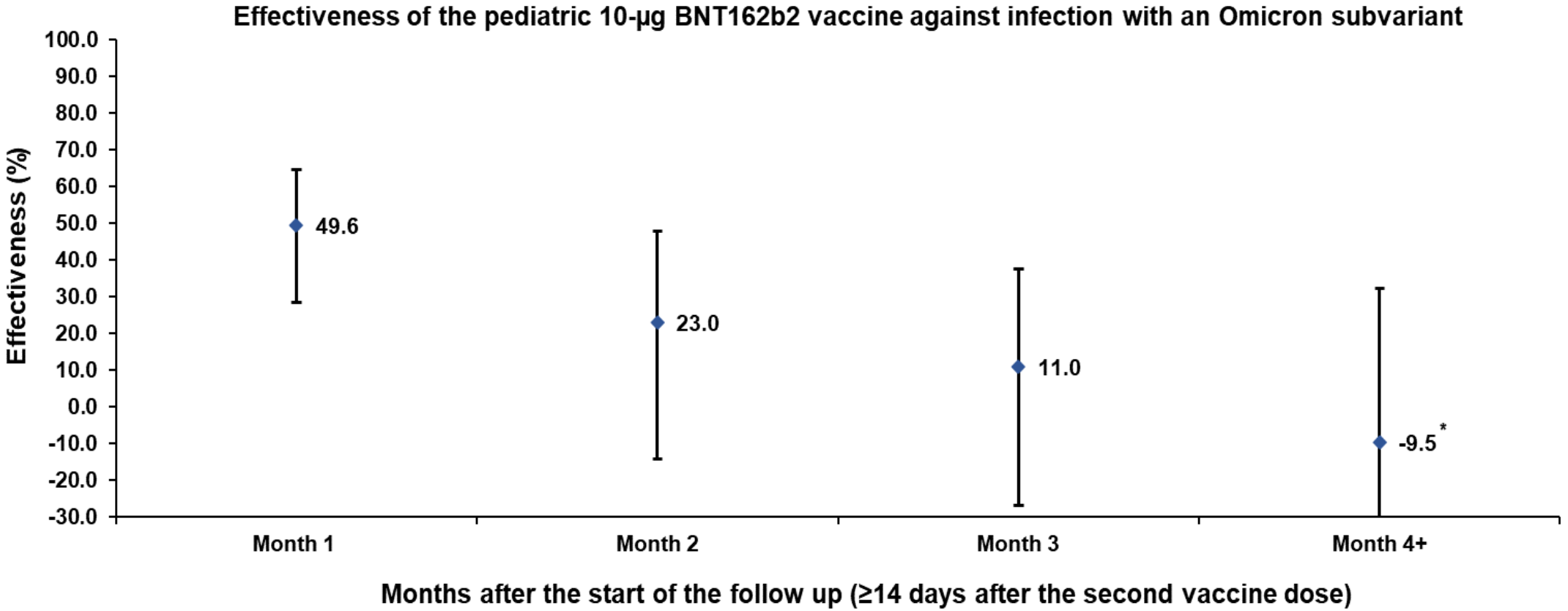
Abu-Raddad LJ, Chemaitelly H, Ayoub HH, et al. Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar. N Engl J Med 2022;386:1804-16.

Effectiveness of the pediatric 10-µg BNT162b2 vaccine against infection with Omicron in children 5-11 years old



Chemaitelly H, AlMukdad S, Ayoub HH, et al. Covid-19 Vaccine Protection among Children and Adolescents in Qatar. N Engl J Med 2022;387:1865-76.

Waning of effectiveness of the 10-µg BNT162b2 vaccine against infection in children 5-11 years old



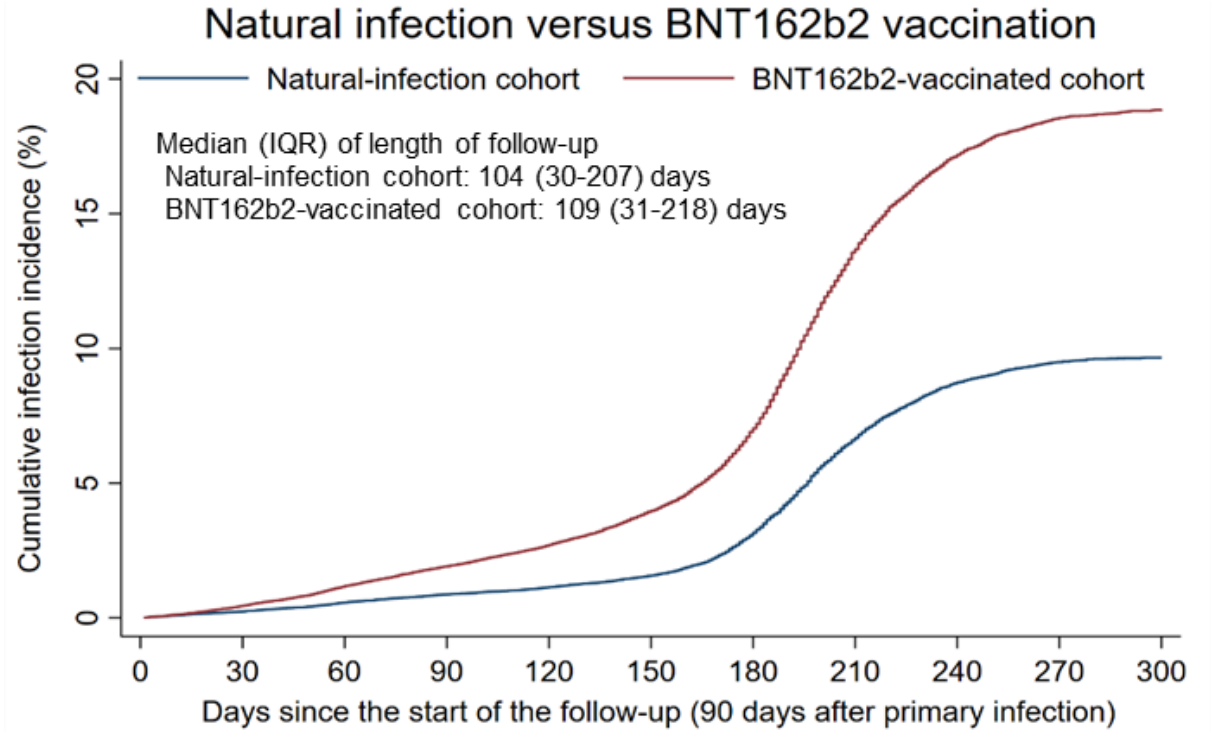
Chemaitelly H, AlMukdad S, Ayoub HH, et al. Covid-19 Vaccine Protection among Children and Adolescents in Qatar. N Engl J Med 2022;387:1865-76.

Natural immunity versus Vaccine immunity

Protection of prior natural infection compared to vaccination with BNT162b2

Adjusted hazard ratio for SARS-CoV-2 infection: 0.47 (95% CI: 0.45-0.48)

Adjusted hazard ratio for severe COVID-19: 0.24 (95% CI: 0.08-0.72)

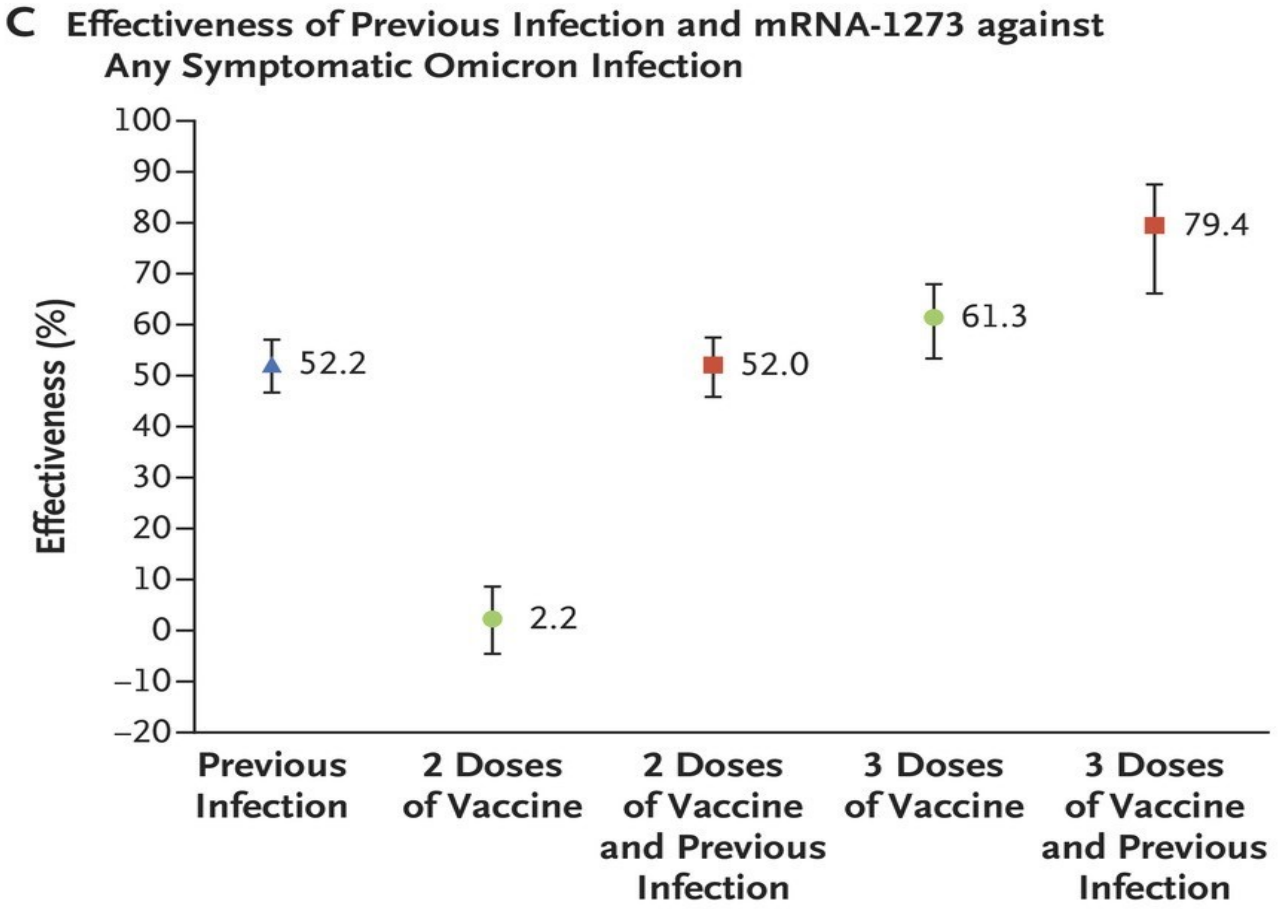


Time (days)	0	30	60	90	120	150	180	210	240	270	300
No. at risk											
Natural-infection cohort	104,500	79,187	62,980	55,459	50,483	44,462	35,989	27,901	22,565	18,104	12,093
BNT162b2-vaccinated cohort	104,500	79,066	62,640	54,898	49,681	43,399	34,458	25,513	19,923	15,620	10,139

Chemaitelly H, Ayoub HH, AlMukdad S, et al. Protection from previous natural infection compared with mRNA vaccination against SARS-CoV-2 infection and severe COVID-19 in Qatar: a retrospective cohort study. Lancet Microbe 2022;doi: 10.1016/s2666-5247(22)00287-7:Epub ahead of print.

Hybrid immunity

Effectiveness of hybrid immunity against Omicron



Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of previous infection and vaccination on symptomatic Omicron infections. N Engl J Med 2022;387:21-34.

Immune imprinting

What is immune imprinting?

Immune imprinting is a phenomenon in which specific sequence of immunological events (due to infection and/or vaccination) can enhance or compromise a person's future immune response against variants of the infection (or vaccination).

What is immune imprinting?

A key concept is that a specific sequence of immunological events can "trap" the immune system so that it is unable to mount a more effective response against a new infection/variant.

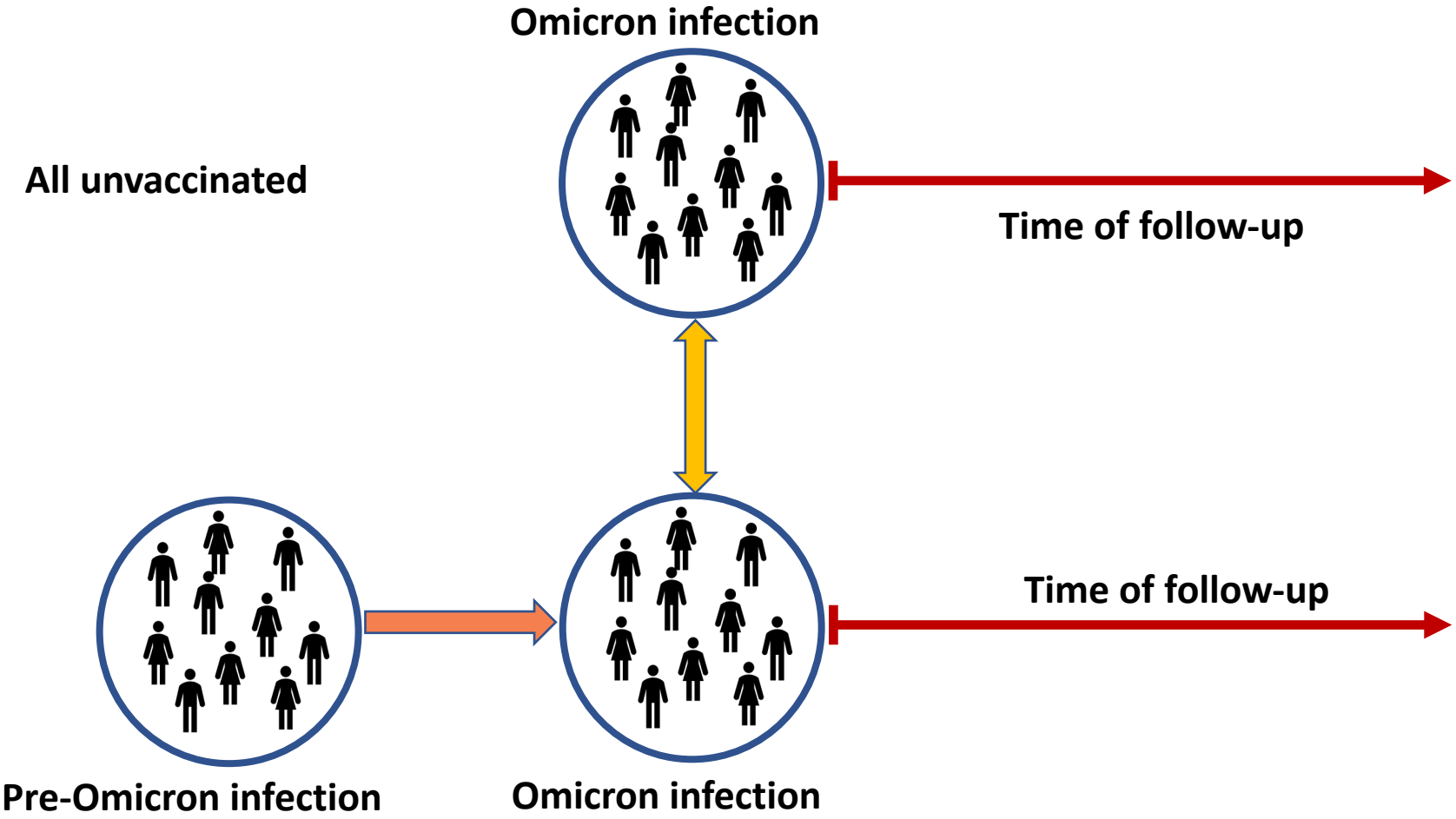
Basic science evidence

Evidence at the level of binding and neutralizing antibodies, B cell, and T cell immunity suggests that previous SARS-CoV-2 infection history can imprint a negative impact on subsequent protective immunity.

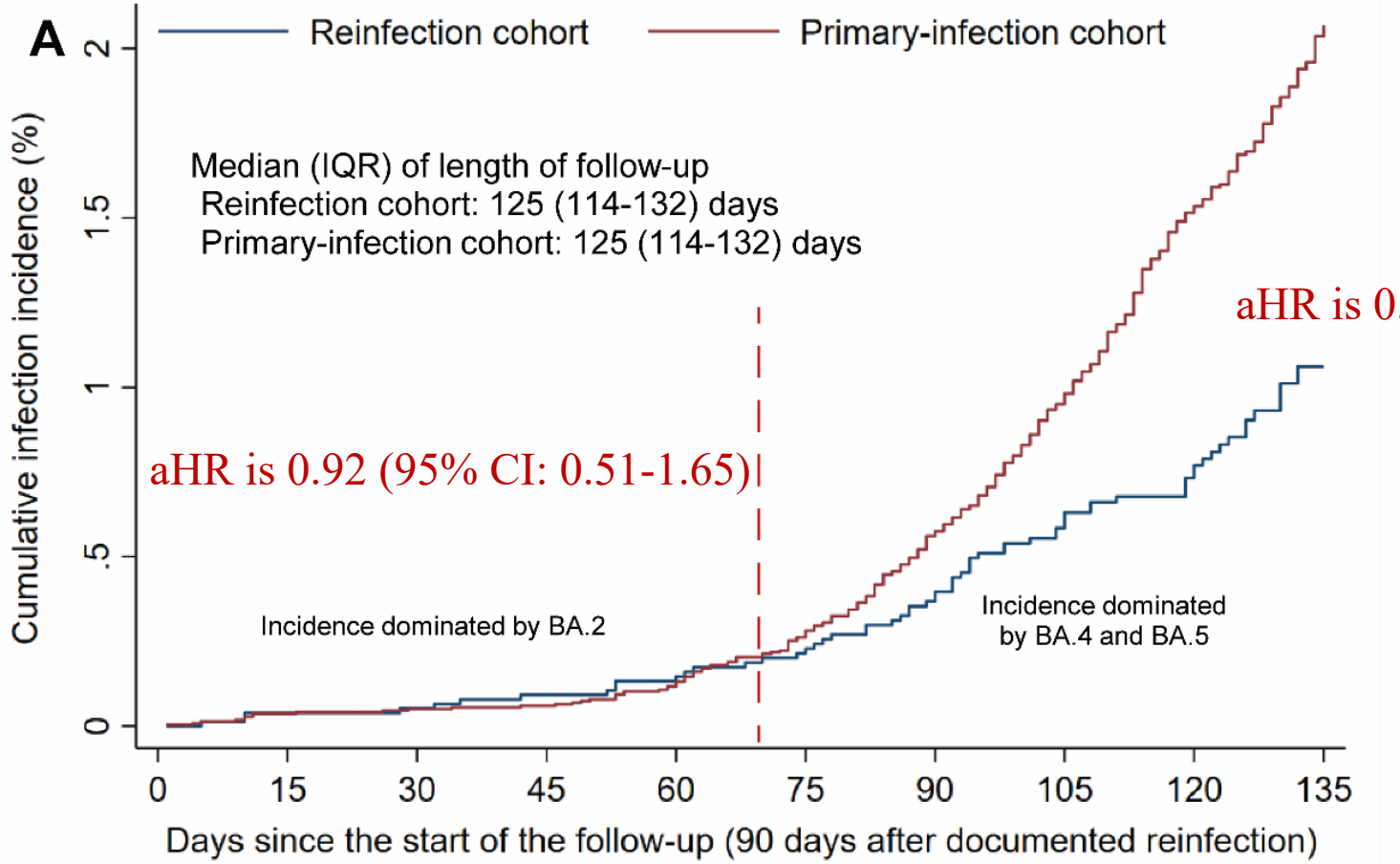
Reynolds CJ, Pade C, Gibbons JM, et al. Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure. Science 2022:eabq1841.

Investigation of epidemiological evidence for immune imprinting related to natural immunity.

Two matched cohorts of those with Omicron infections at the same time



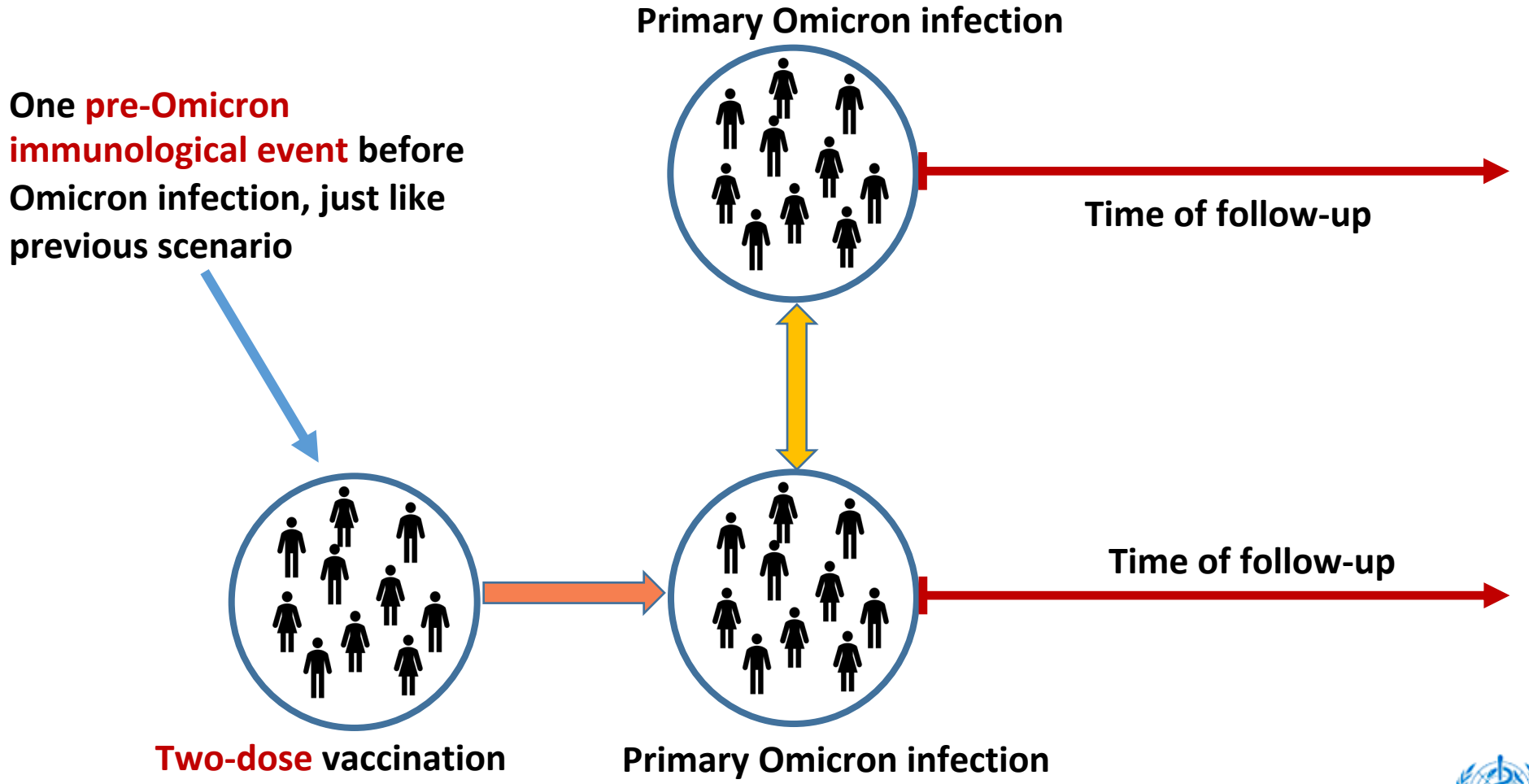
Epidemiology of re-reinfections and immune protection of having two infections compared to only one infection



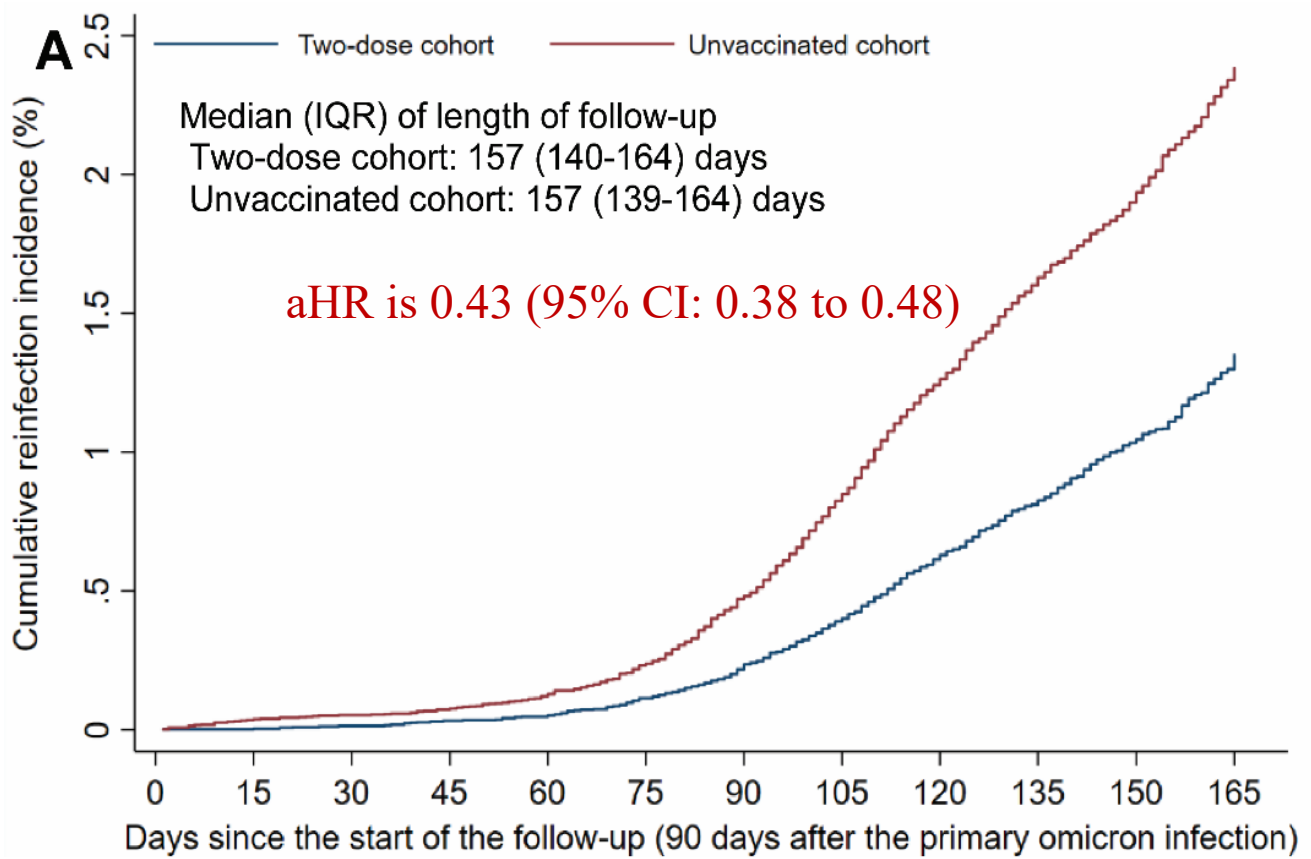
Chemaitelly H, Ayoub HH, Tang P, et al. Immune imprinting and protection against repeat reinfection with SARS-CoV-2. N Engl J Med 2022;387:1716-8.

Investigation of epidemiological evidence for immune imprinting related to vaccine immunity.

Two matched cohorts with primary Omicron infection at the same time: Comparing history of two-dose vaccination to no vaccination

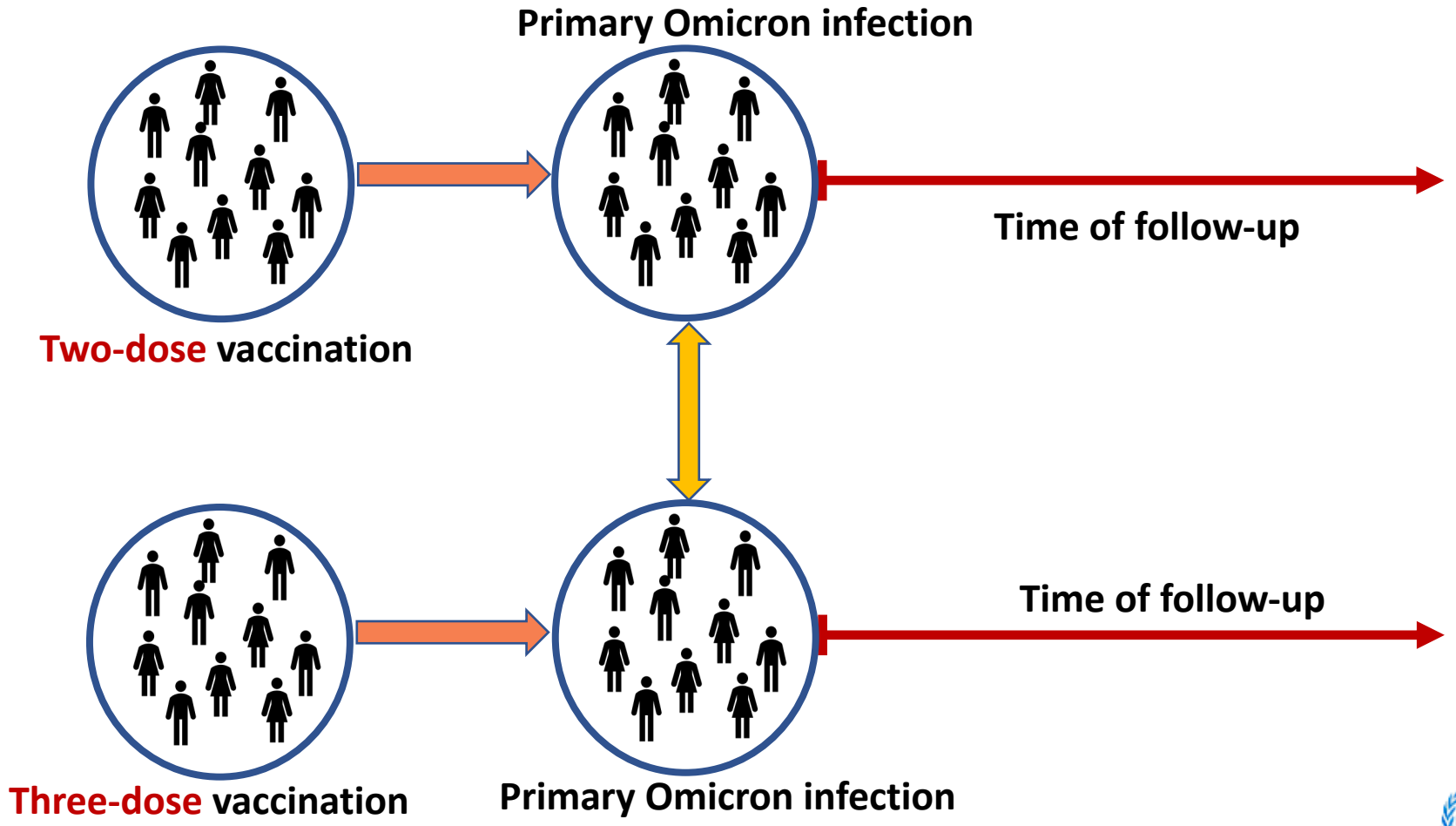


Epidemiology of reinfections and immune protection of having two-dose vaccination before primary Omicron infection compared to no vaccination

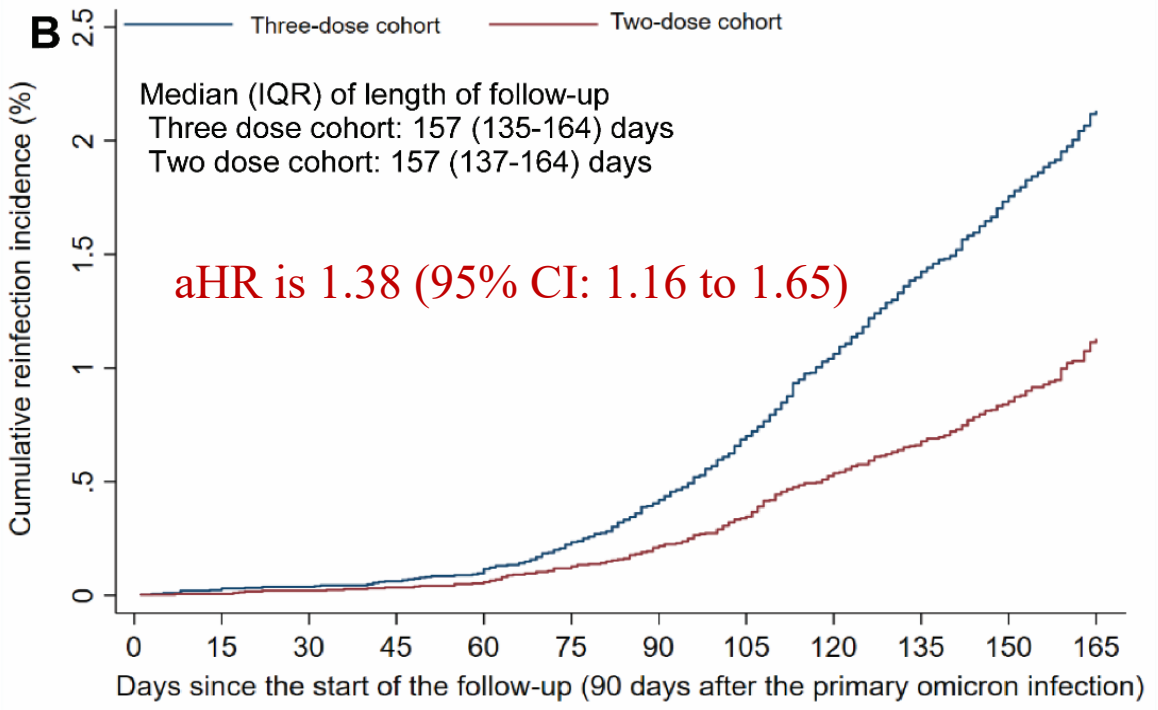


Chemaitelly H, Ayoub HH, Tang P, et al. COVID-19 primary series and booster vaccination and immune imprinting. medRxiv 2022:2022.10.31.22281756.

Two matched cohorts with primary Omicron infection at the same time: Comparing history of three-dose vaccination to two-dose vaccination



Epidemiology of reinfections and immune protection of having three-dose vaccination before primary Omicron infection compared to two-dose vaccination



Time (days)	0	15	30	45	60	75	90	105	120	135	150	165
No. at risk												
Three-dose cohort	30,541	28,947	28,043	27,147	26,335	25,624	25,022	24,563	23,881	22,923	20,343	6,116
Two-dose cohort	30,541	28,952	28,044	27,150	26,341	25,643	25,062	24,639	23,996	23,083	20,528	6,202

IQR denotes interquartile range

Chemaitelly H, Ayoub HH, Tang P, et al. COVID-19 primary series and booster vaccination and immune imprinting. medRxiv 2022:2022.10.31.22281756.

It appears that two consecutive immunological events of the same kind (pre-Omicron) contribute to negative immune imprinting against a new kind of immunological event (Omicron).

It appears that some immune histories could be associated with compromised protection while others could be associated with stronger and more broad protection.

Immune imprinting was observed when booster effectiveness has fully waned and at time when incidence was dominated by BA.4/5 and recently BA.2.75.2.

Short-term effects of boosters appear different from their long-term effects.

Key ingredients for vaccine effectiveness studies using electronic health records

- Structure, completeness, and quality of the databases.
- Strong and effective partnership between the academic and governmental sectors.

THANK YOU

- *Ministry of Public Health*
- *Hamad Medical Corporation*
- *Infectious Disease Epidemiology Group & WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis*
- *Biomedical Research Program at Weill Cornell Medicine-Qatar*

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