Frontline Worker Safety in the Age of COVID-19

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Immune protection of COVID-19 vaccination and natural infection: Findings of two years of COVID-19 epidemiology research in Qatar

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WCM-Q, Qatar Foundation

Weill Cornell Medicine-Qatar

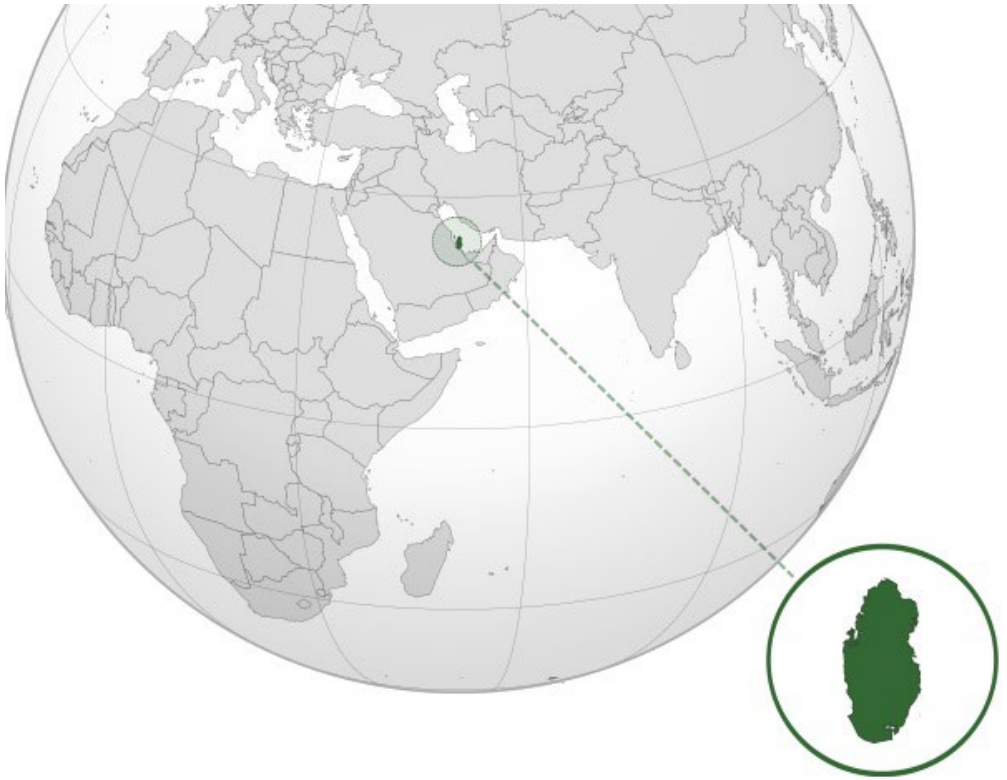
WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis

The diverse population of Qatar

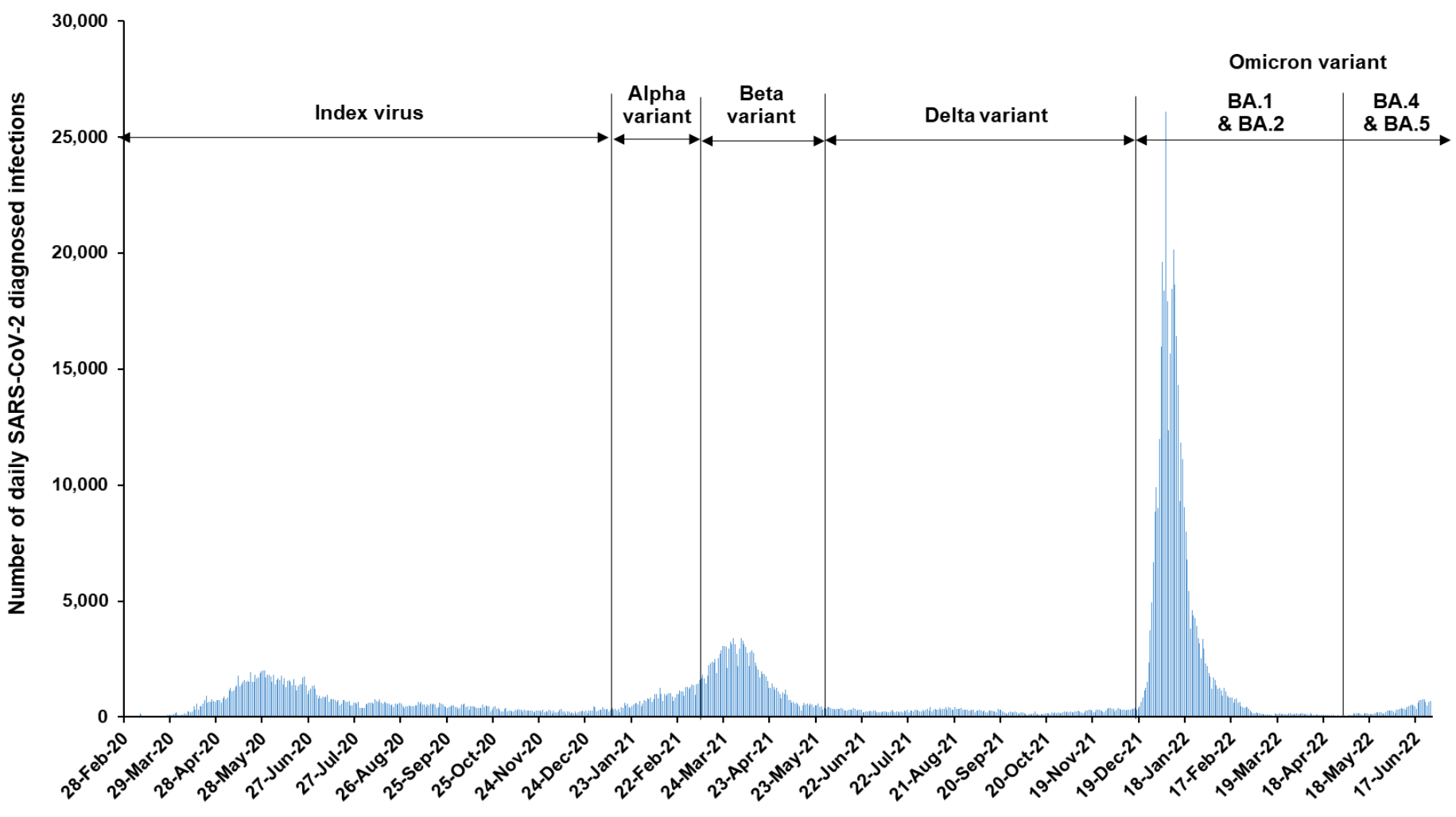
Of 2.8 million people,

89% are expatriates from

over 150 countries.



Five epidemic waves in Qatar

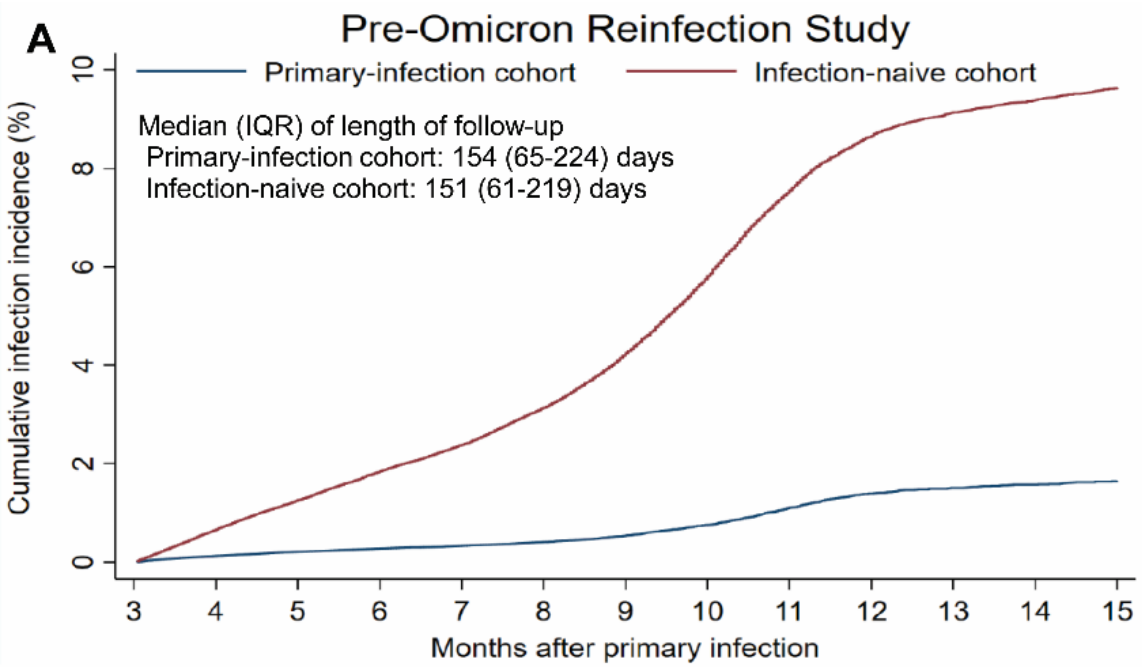


National, federated databases for COVID-19 that include all SARS-CoV-2-related such as PCR testing, rapid antigen testing, vaccinations, hospitalizations, and infection severity and mortality classifications per WHO guidelines

Natural immunity due to pre-Omicron infection

Protection of natural immunity before Omicron

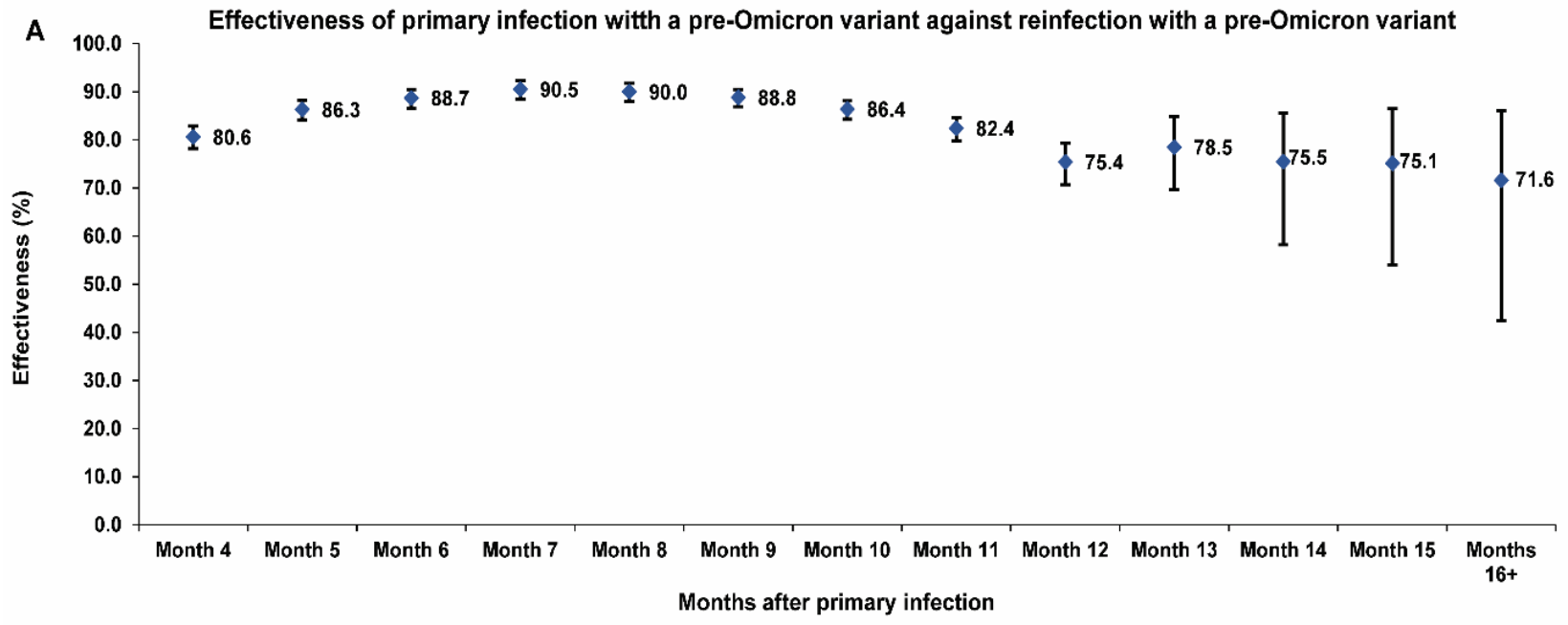
Incidence of index virus, Alpha, Beta, and Delta



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

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Waning of natural immunity before Omicron

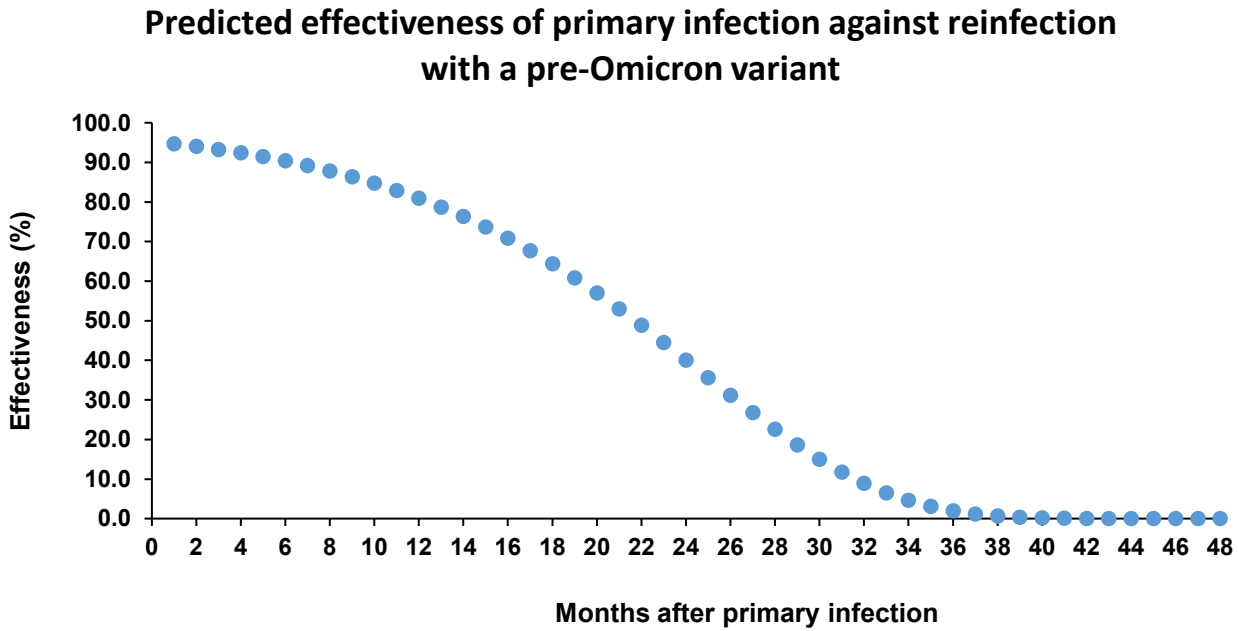


Evidence for waning of protection over time

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Modeled waning pattern

Fitting the data to Gompertz decay.

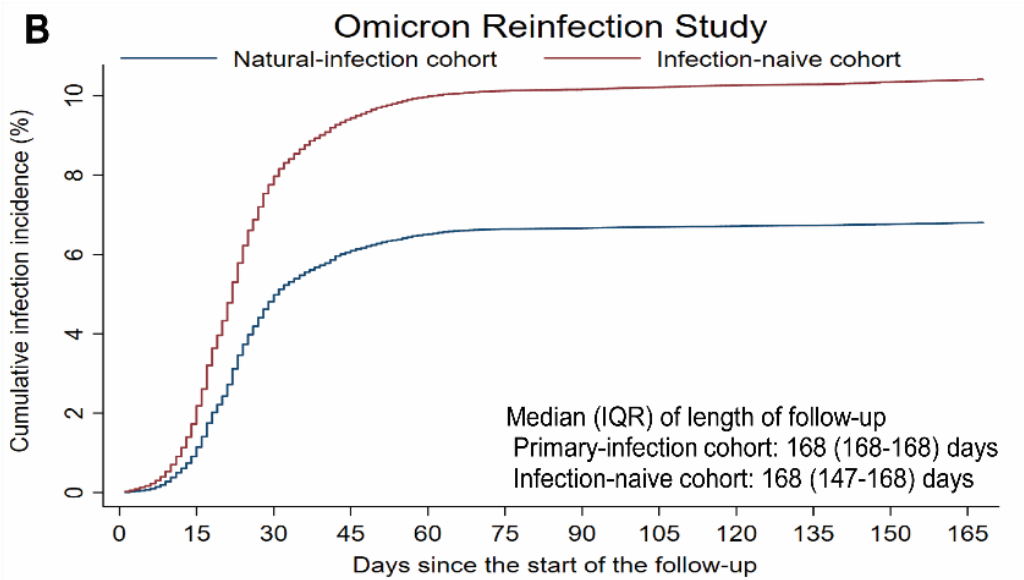


A 3-year protection

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Protection of natural immunity against Omicron infection

Incidence of BA.1, BA.2, and recently, BA.4 and BA.5

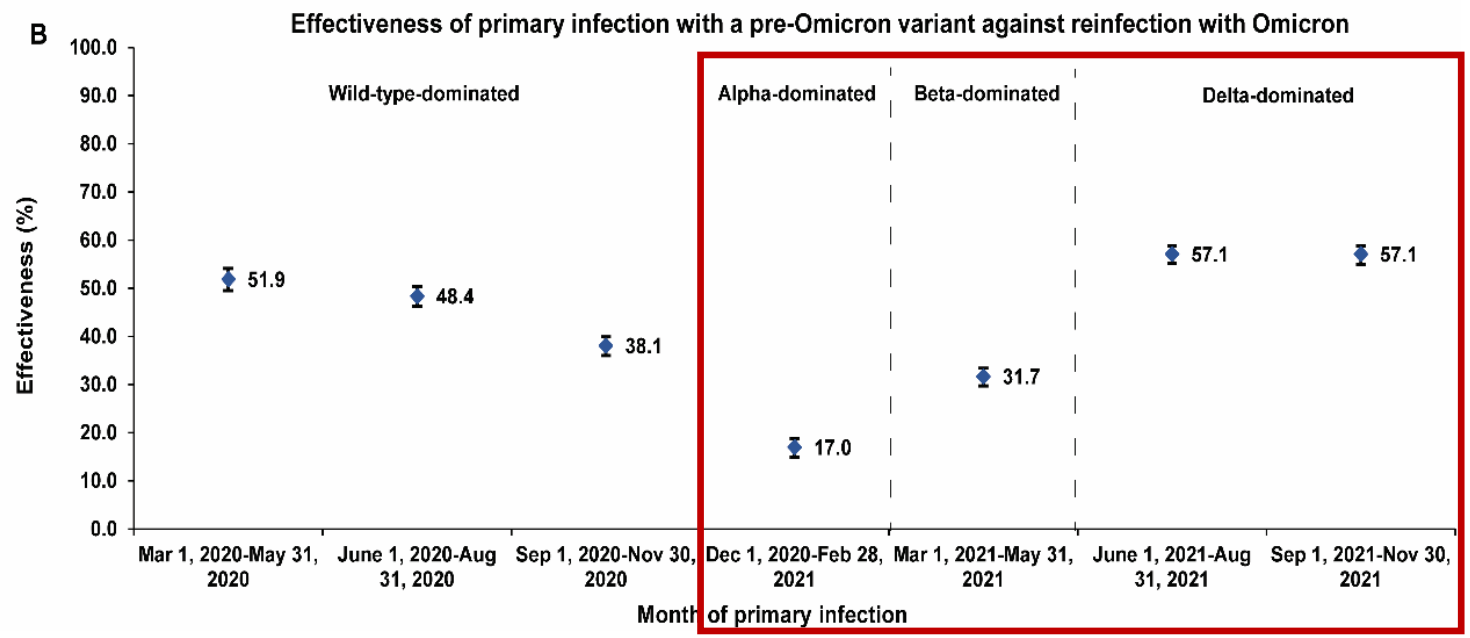


Time (days)	0	15	30	45	60	75	90	105	120	135	150	165
No. at risk												
Primary infection	120,483	117,559	111,402	108,586	106,455	104,560	103,169	100,794	98,028	95,772	93,854	91,681
Infection naive	120,483	116,596	107,947	104,716	102,497	100,617	99,235	96,892	94,135	91,926	90,046	87,940

Effectiveness of pre-Omicron primary infection against reinfection is 38.1% (36.3-39.8%)

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Waning of natural immunity against Omicron infection



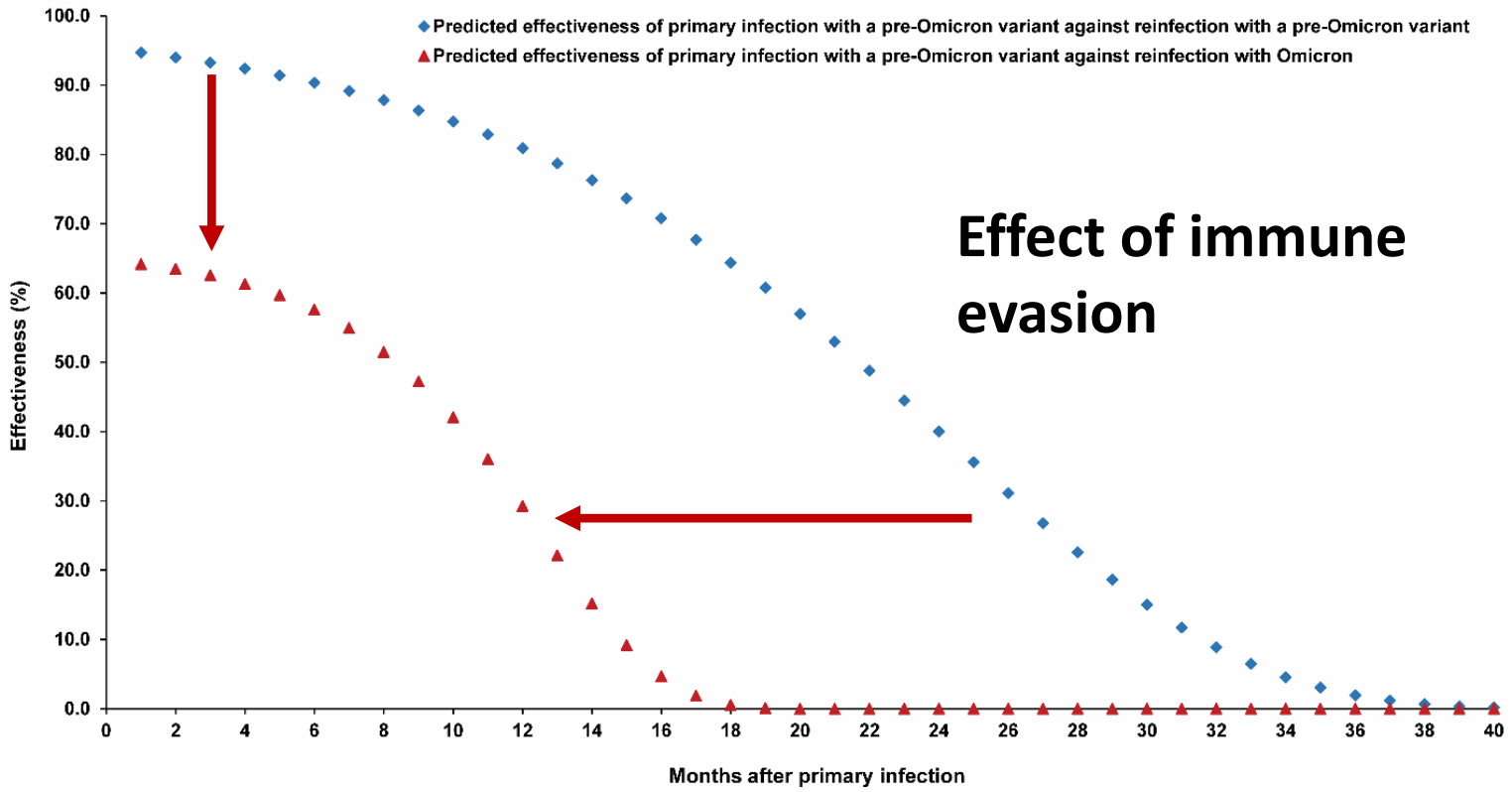
Evidence for rapid waning of protection over time

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Effect of viral immune evasion on pre-Omicron immunity

Major immune evasion:

- **Reduces the overall level of protection**
- **Accelerates the waning of the protection**



Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Natural immunity due to Omicron infection

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)

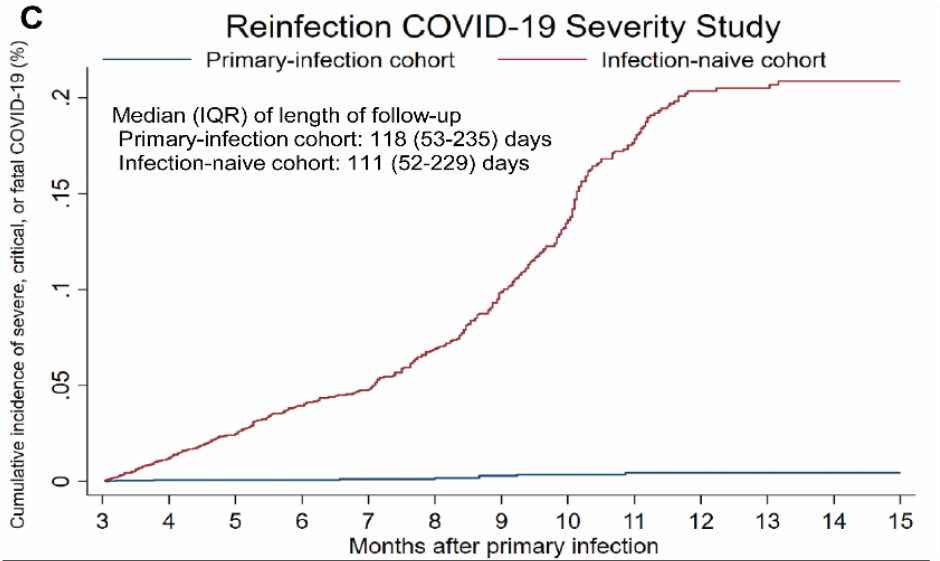
[1]*Chemaitelly et al. Protection of Omicron sub-lineage infection against reinfection with another Omicron sub-lineage. Nat Commun 2022; 13(1): 4675.*

[2]*Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Protection of SARS-CoV-2 natural infection against reinfection with the Omicron BA.4 or BA.5 subvariants. medRxiv 2022:2022.07.11.22277448.*

Protection of primary infection against COVID-19 hospitalization or death at reinfection

Protection against severe COVID-19 at reinfection

Incidence of all variants since pandemic onset



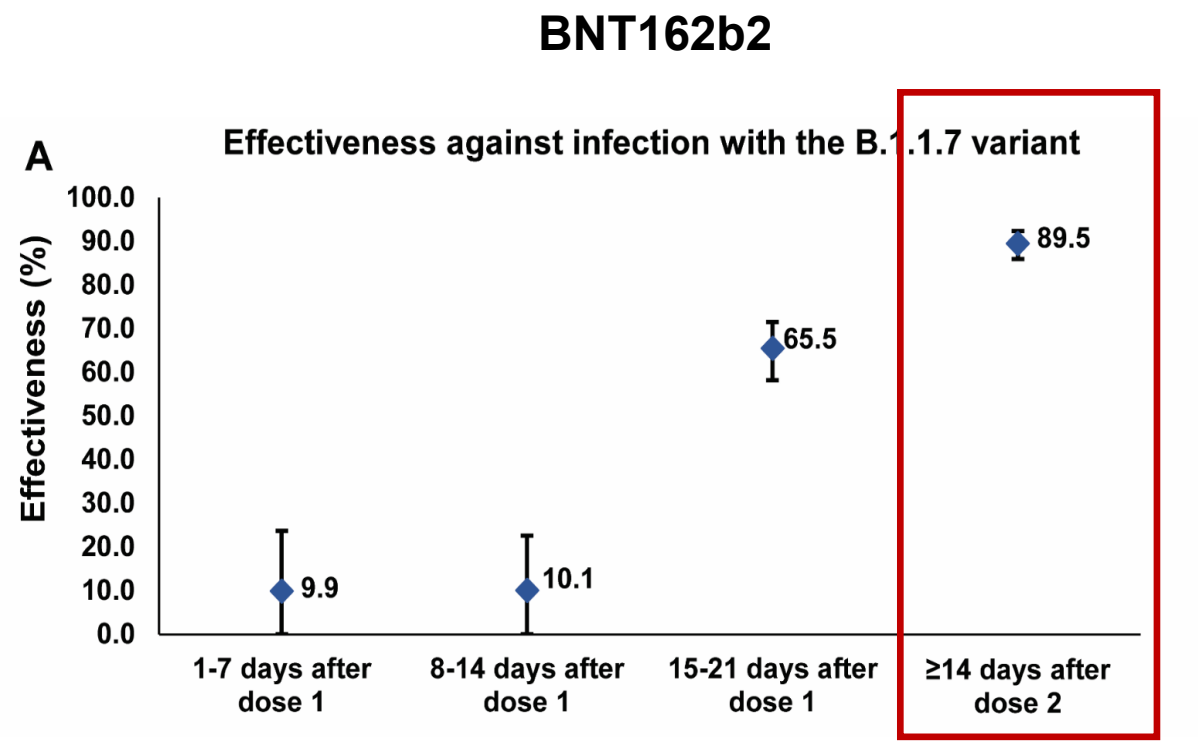
Month	0	4	5	6	7	8	9	10	11	12	13	14	15
No. at risk													
Primary infection	407,214	358,362	277,911	223,686	202,658	184,047	160,341	128,304	97,882	75,050	59,624	44,908	28,872
Infection naive	407,214	356,746	274,899	219,782	197,994	178,744	154,355	122,121	92,191	70,449	55,996	42,213	27,123

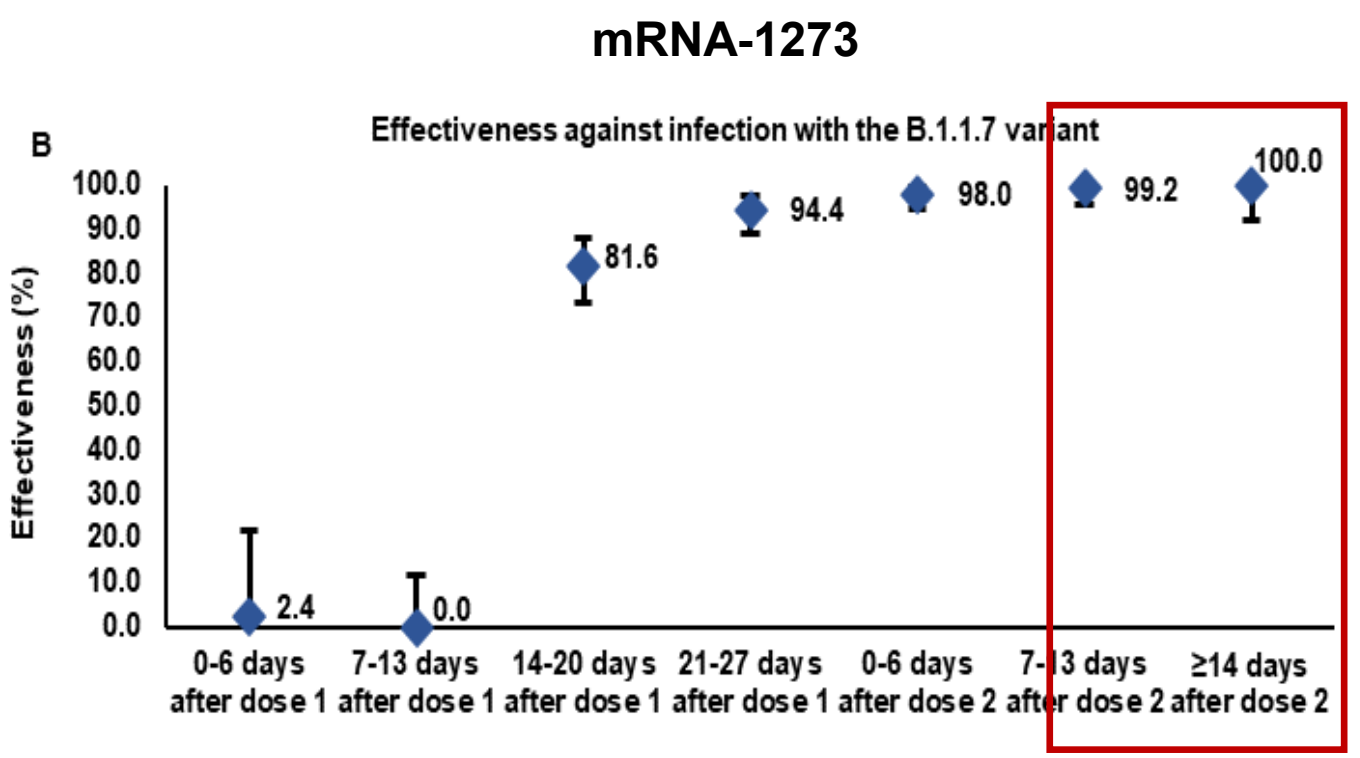
Effectiveness of primary infection against severe, critical, or fatal COVID-19 at reinfection is 97.3% (95.0-98.6%)

Chemaitelly et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar. medRxiv 2022:2022.07.06.22277306.

Vaccine immunity

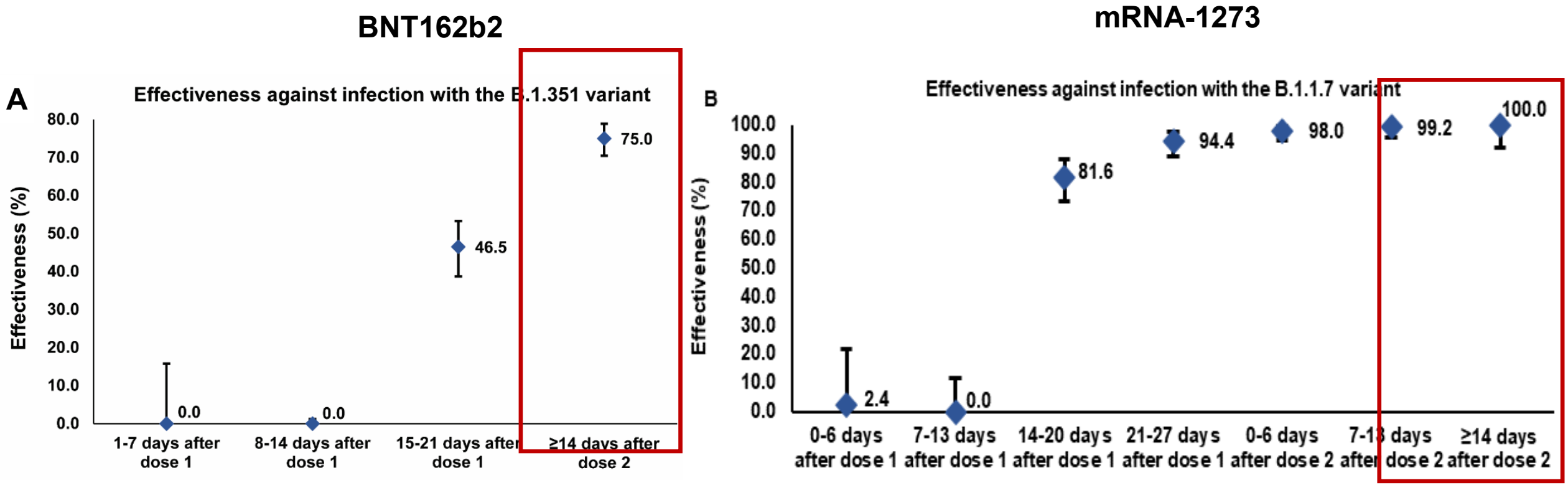
BNT162b2 vaccine protection against Alpha variant





Abu-Raddad et al. 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 et al. J Travel Med. 2021 May 28:taab083. doi: 10.1093/jtm/taab083.

BNT162b2 vaccine protection against Beta variant

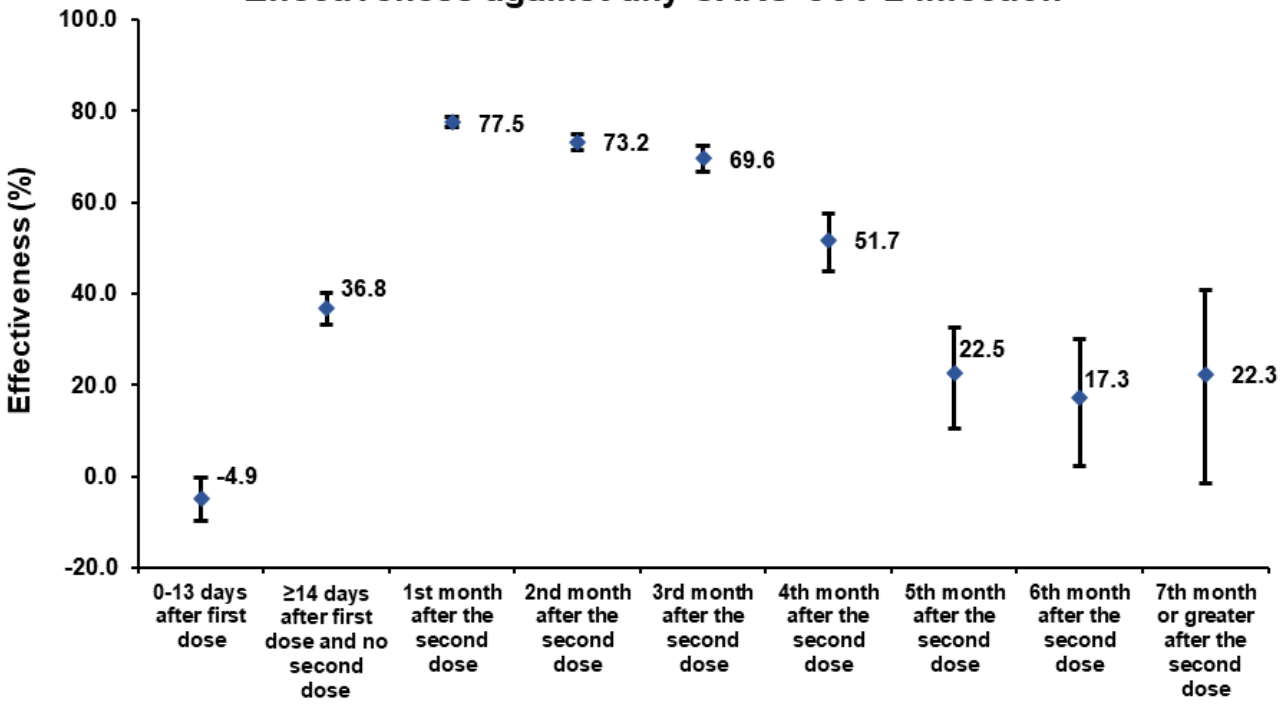


Abu-Raddad et al. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. N Engl J Med 2021;385:187-9.

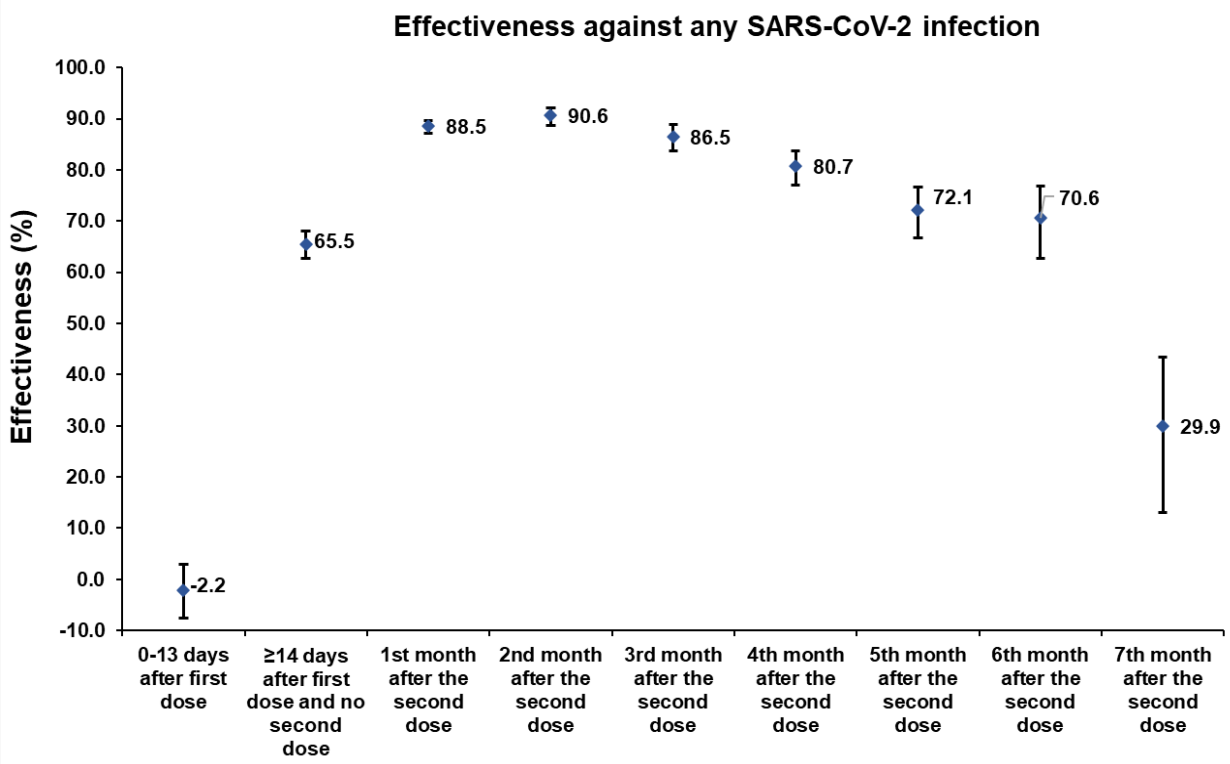
Abu-Raddad et al. J Travel Med. 2021 May 28:taab083. doi: 10.1093/jtm/taab083.

Waning of BNT162b2 and mRNA-1273 vaccine effectiveness against infection

BNT162b2



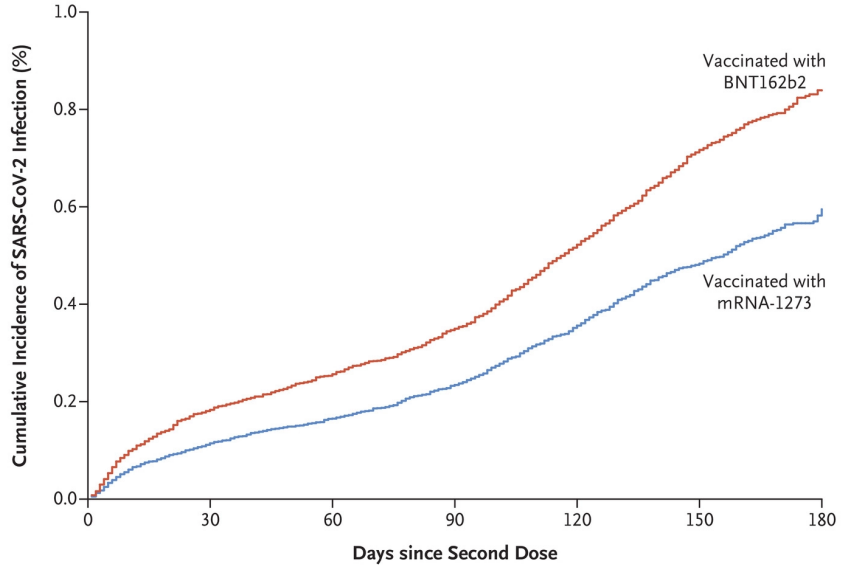
mRNA-1273



Chemaitelly et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. N Engl J Med 2021; 385(24): e83.
Abu-Raddad et al. Waning mRNA-1273 Vaccine Effectiveness against SARS-CoV-2 Infection in Qatar. N Engl J Med 2022;386:1091-3.

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

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



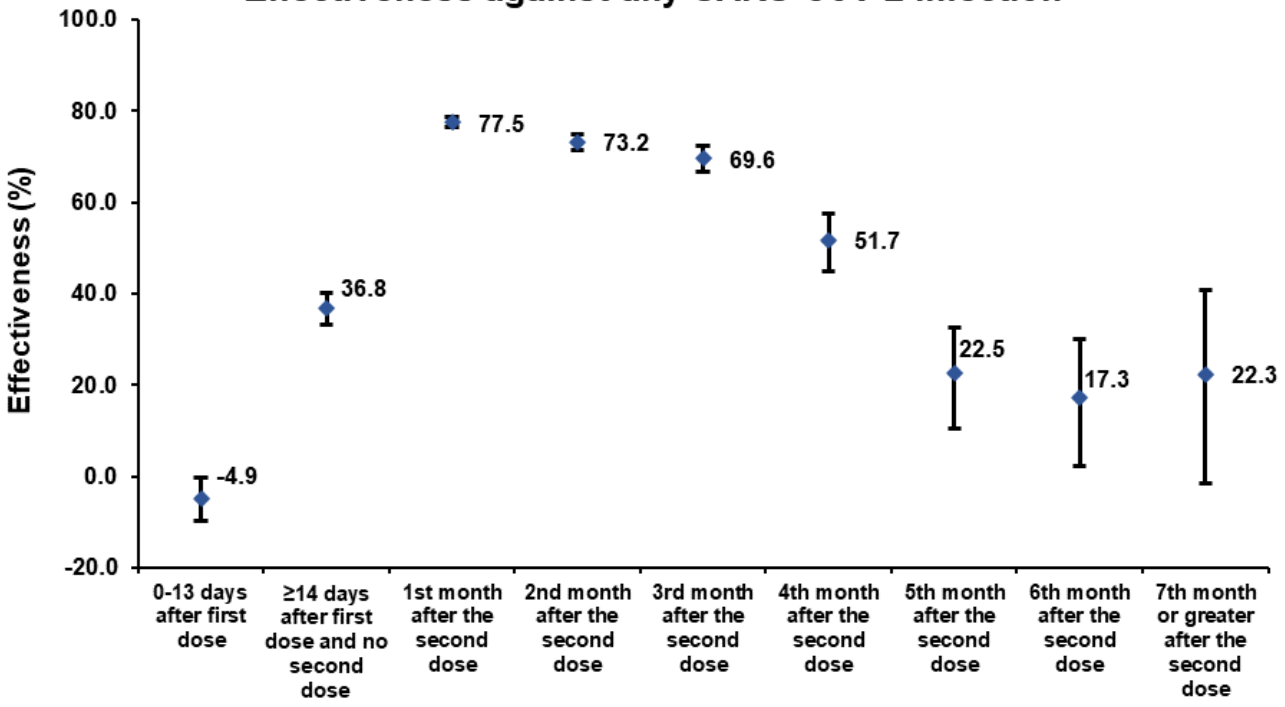
No. at Risk							
Vaccinated with BNT162b2	192,123	191,761	181,987	169,544	146,717	113,813	23,013
Vaccinated with mRNA-1273	192,123	191,890	182,265	171,164	146,223	114,672	23,400

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)

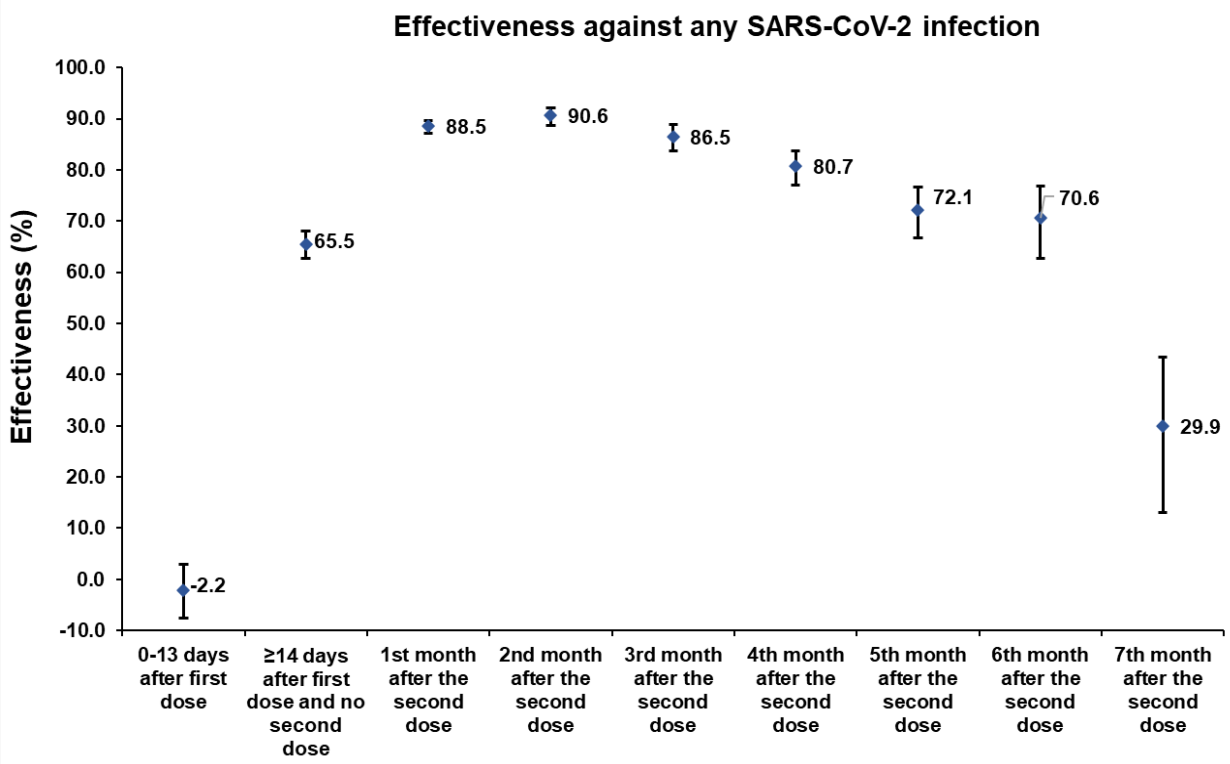
Abu-Raddad et al. Effectiveness of mRNA-1273 and BNT162b2 Vaccines in Qatar. N Engl J Med 2022;386:799-800.

Waning of BNT162b2 and mRNA-1273 vaccine effectiveness against infection

BNT162b2

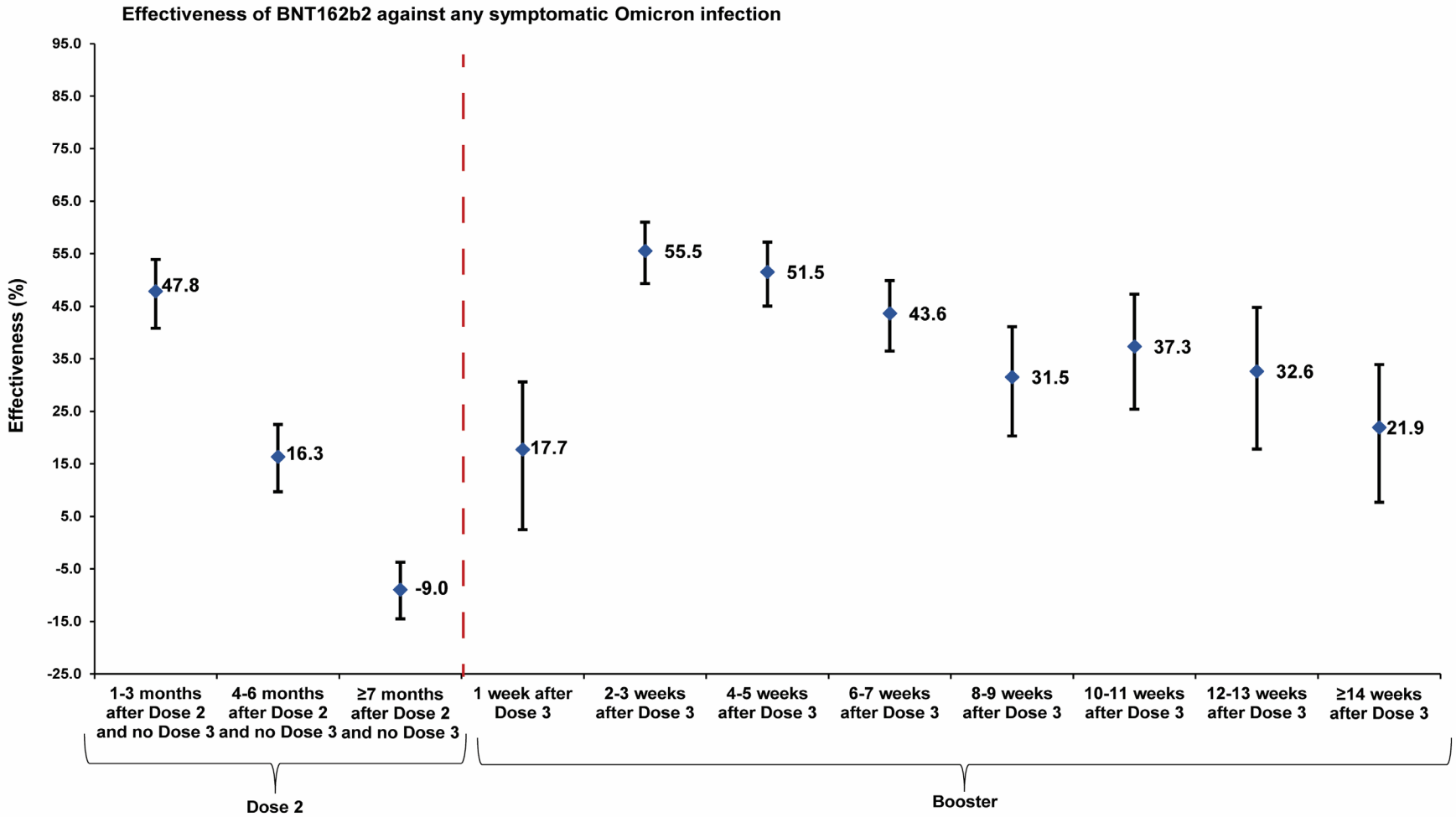


mRNA-1273



Chemaitelly et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. N Engl J Med 2021; 385(24): e83.
Abu-Raddad et al. Waning mRNA-1273 Vaccine Effectiveness against SARS-CoV-2 Infection in Qatar. N Engl J Med 2022;386:1091-3.

Effectiveness of BNT162b2 against symptomatic Omicron infection

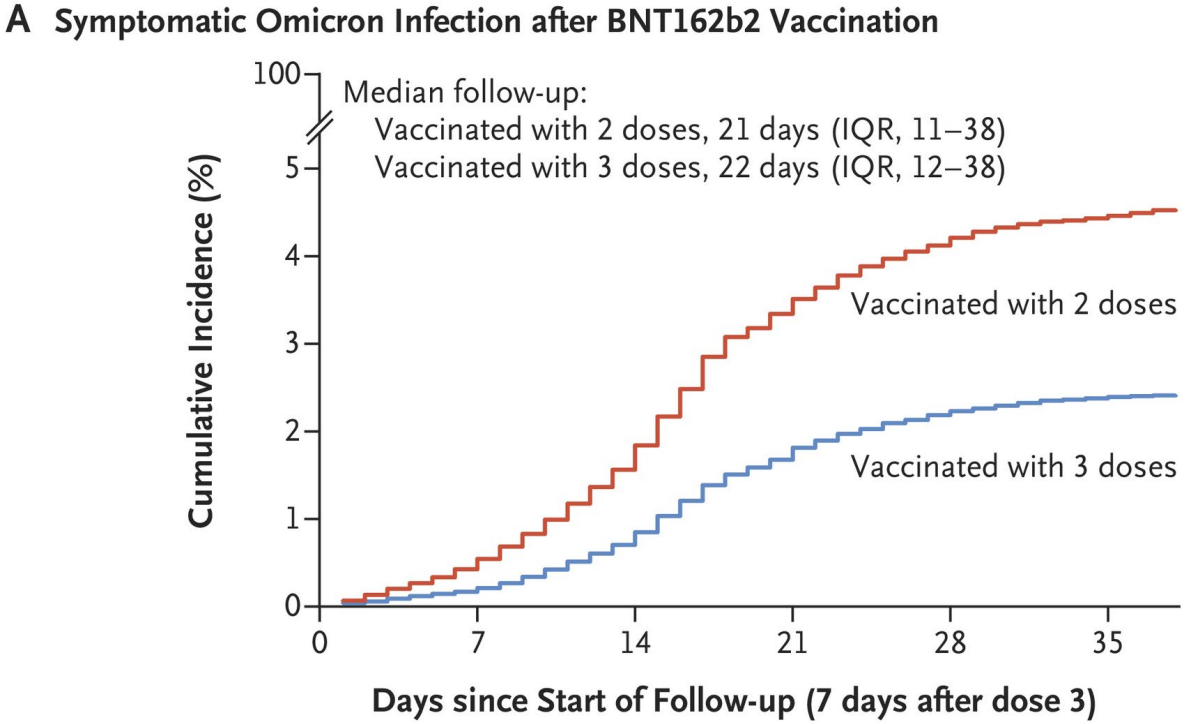


Chemaitelly et al. Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. Nature Communications 2022;13:3082.

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%)

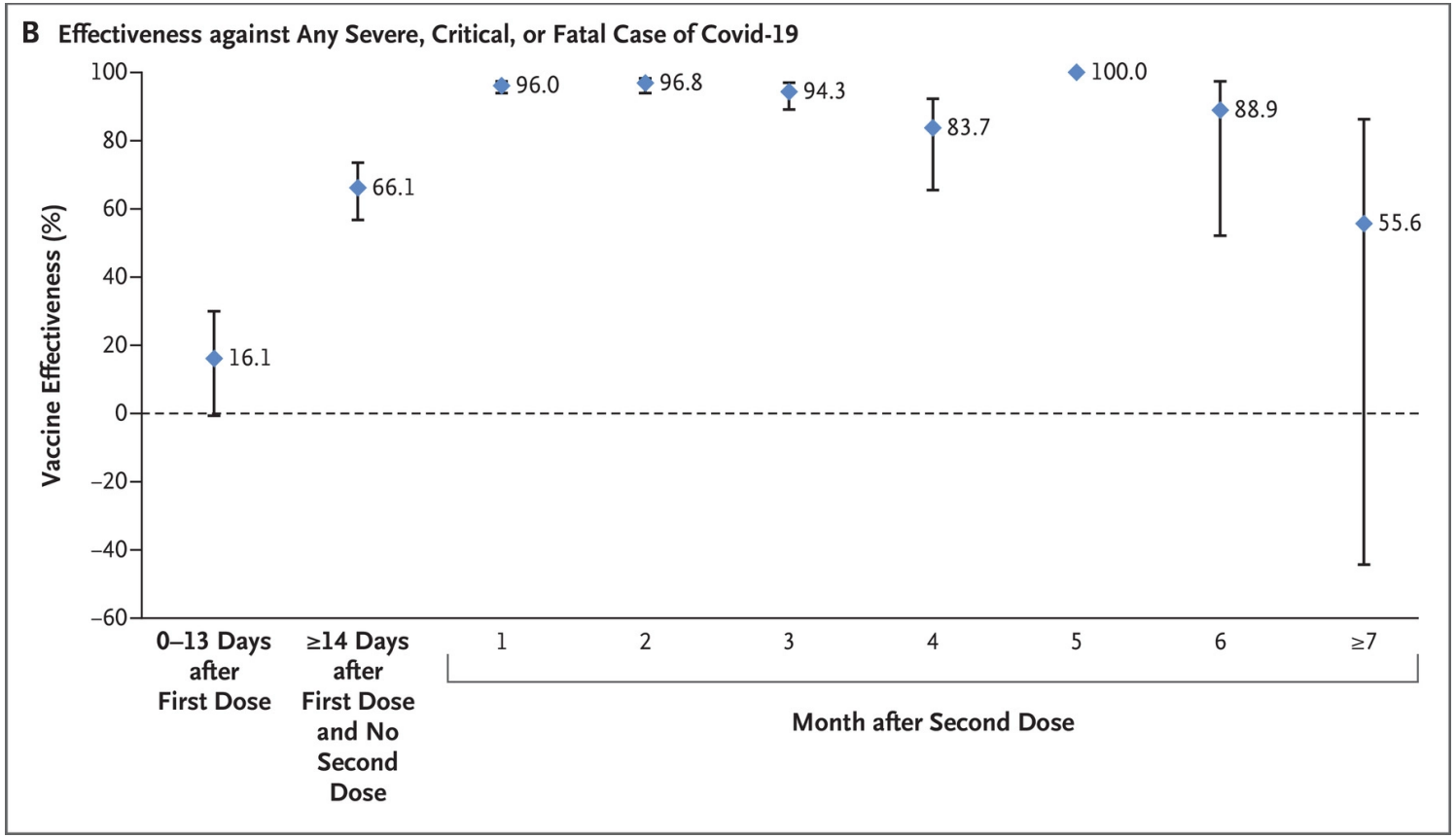
Booster effectiveness against COVID-19 hospitalization and death due to Omicron infection, relative to primary series, was
76.5% (95% CI: 55.9-87.5%)



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 et al. Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar. N Engl J Med 2022;386:1804-16.

Waning of BNT162b2 vaccine effectiveness against hospitalization and death

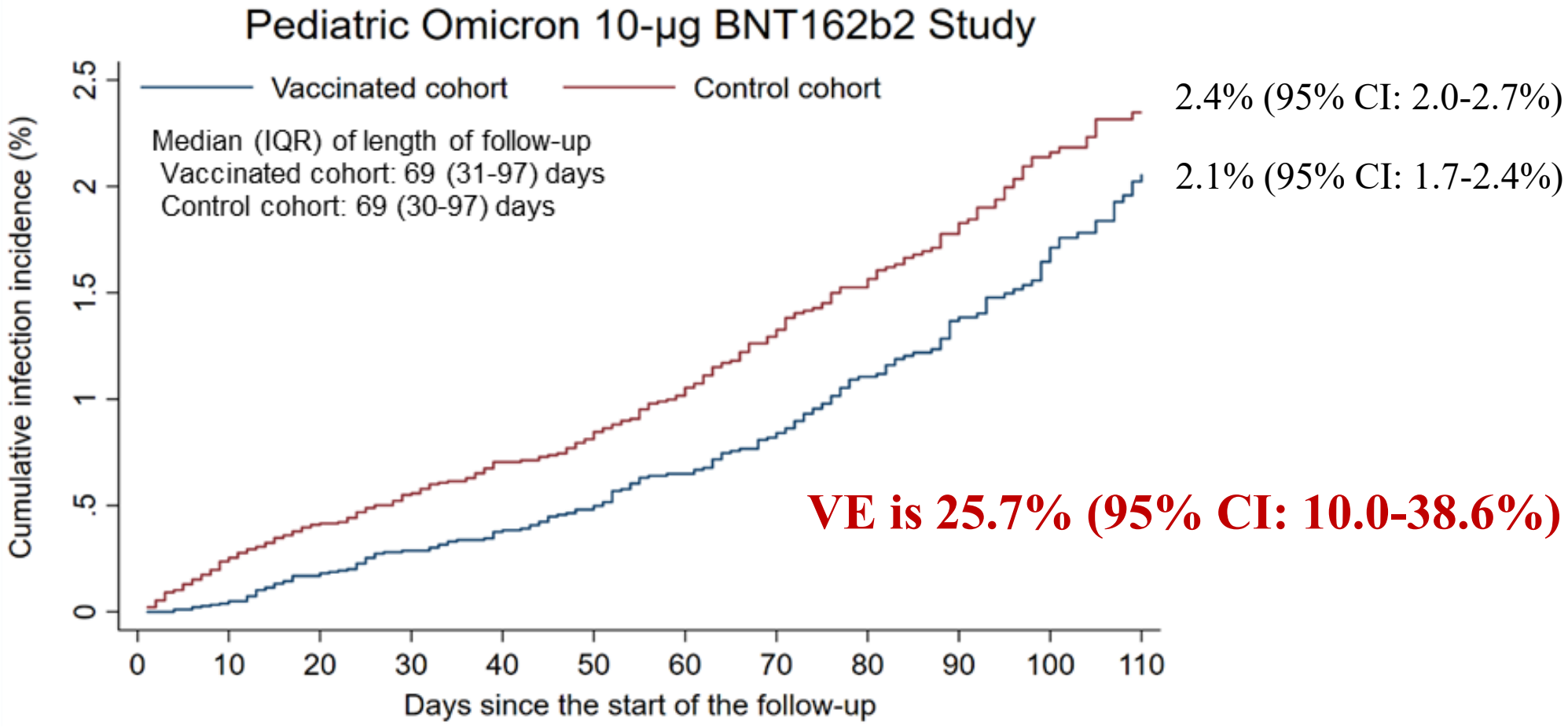


No evidence for major waning of protection against hospitalization and death

Chemaitelly et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. N Engl J Med 2021; 385(24): e83.

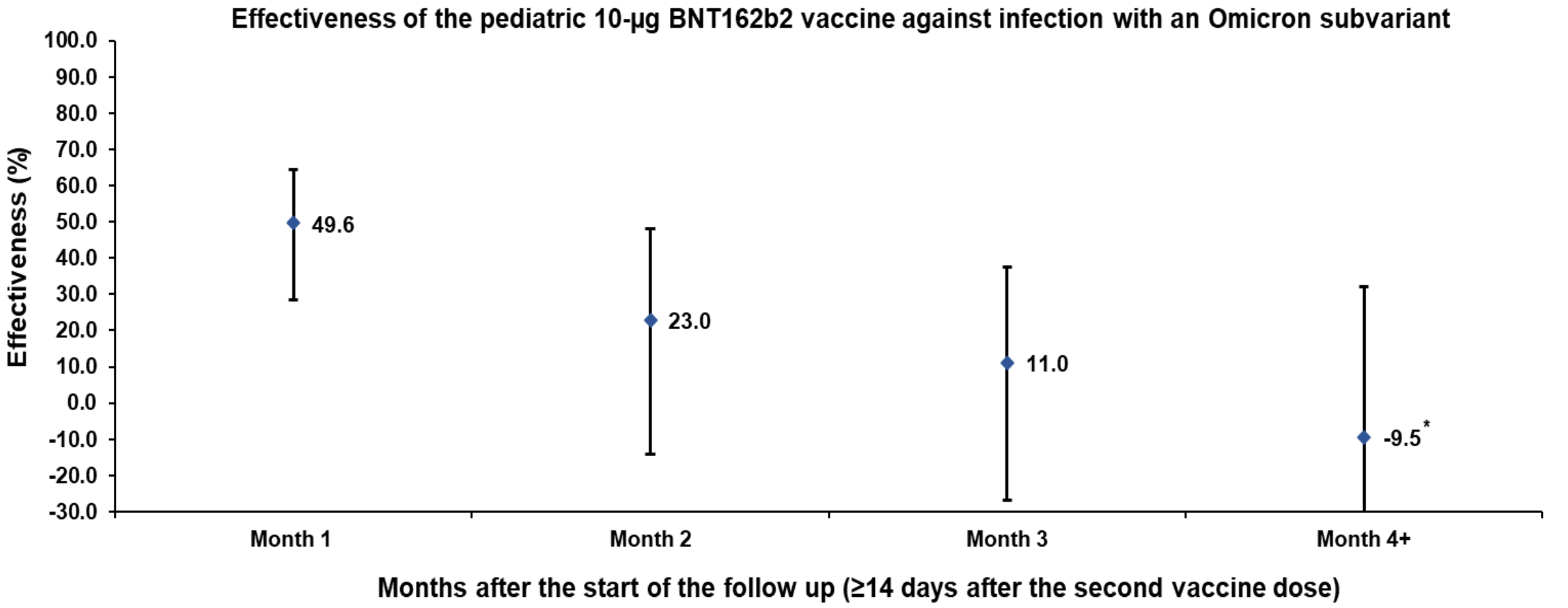
Vaccine protection among children and adolescents

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



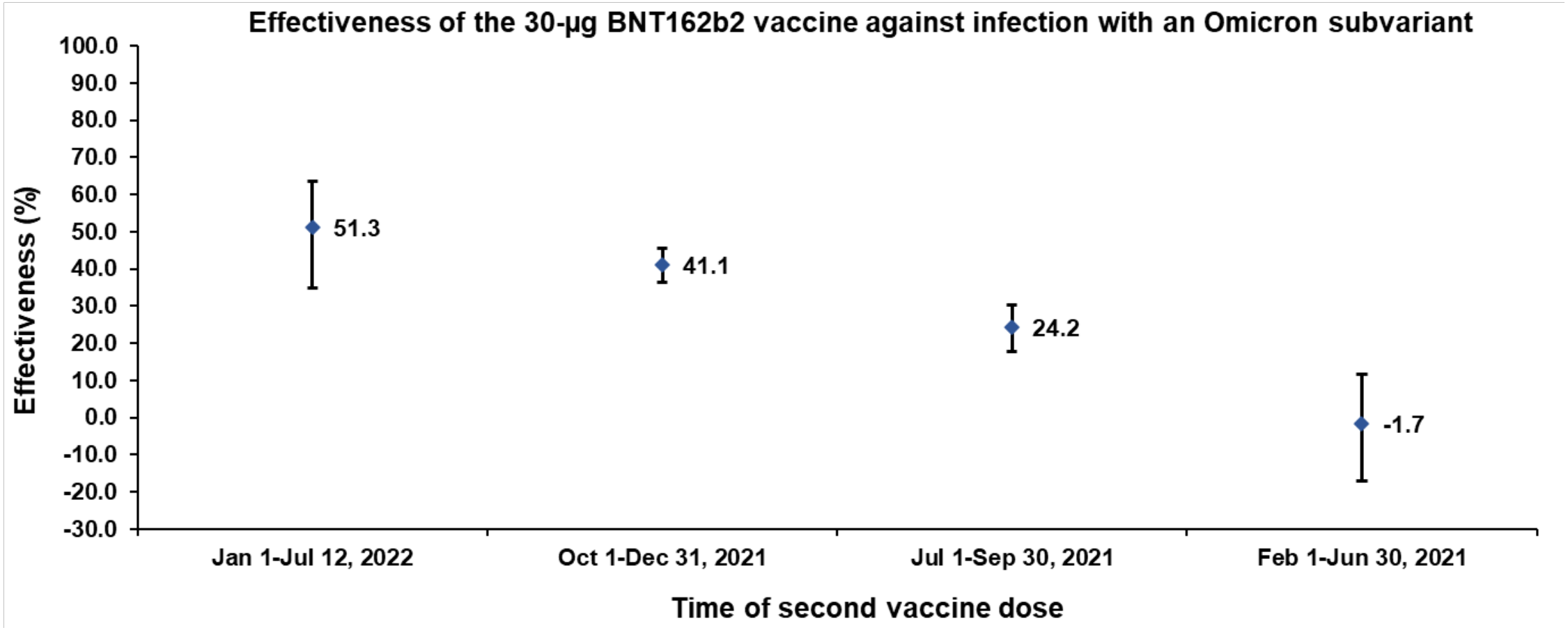
Chemaitelly et al. Effectiveness of the BNT162b2 vaccine against SARS-CoV-2 infection among children and adolescents in Qatar. medRxiv 2022: 2022.07.26.22278045.

Waning of effectiveness of the pediatric 10-µg BNT162b2 vaccine against infection with Omicron



Chemaitelly et al. Effectiveness of the BNT162b2 vaccine against SARS-CoV-2 infection among children and adolescents in Qatar. medRxiv 2022: 2022.07.26.22278045.

Waning of effectiveness of the 30-µg BNT162b2 vaccine against infection with Omicron variant



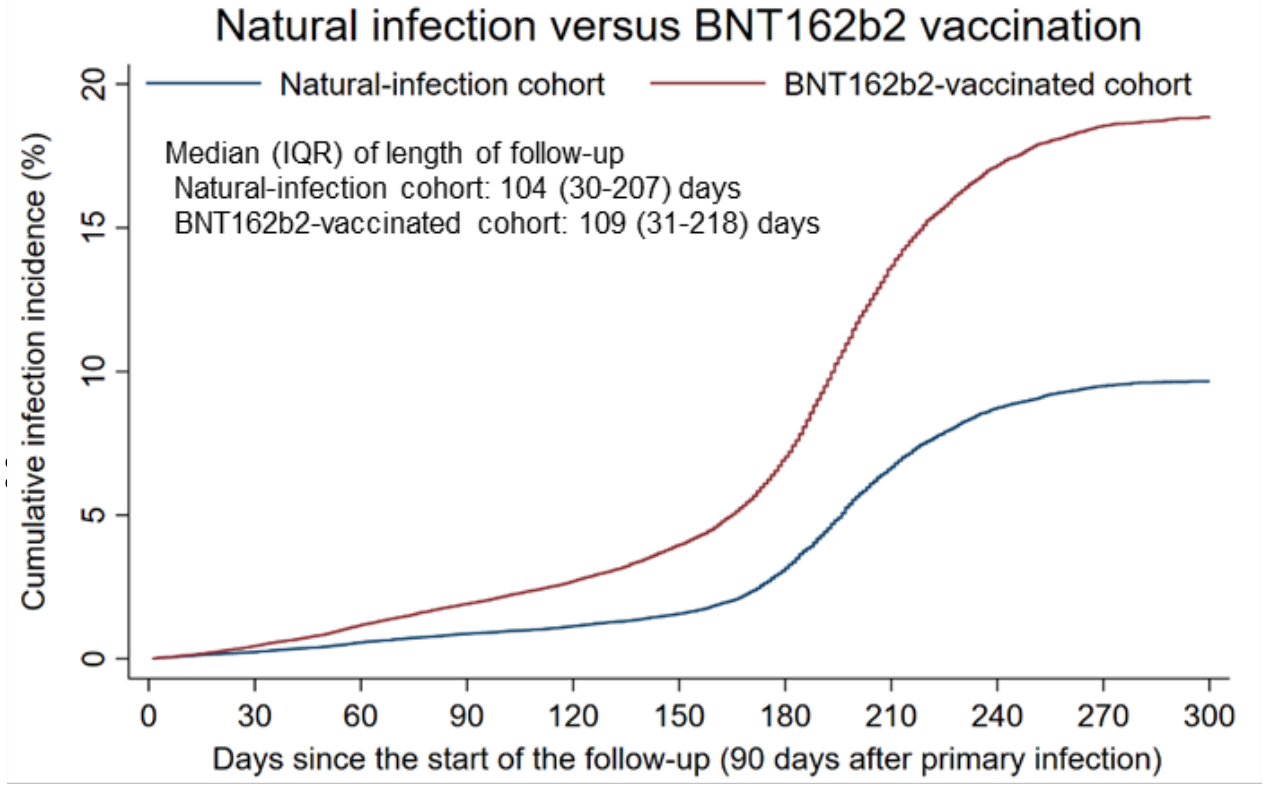
Chemaitelly et al. Effectiveness of the BNT162b2 vaccine against SARS-CoV-2 infection among children and adolescents in Qatar. medRxiv 2022: 2022.07.26.22278045.

Natural immunity
versus
Vaccine immunity

Protection of prior natural infection compared to vaccination with BNT162b2: A retrospective controlled target trial

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)

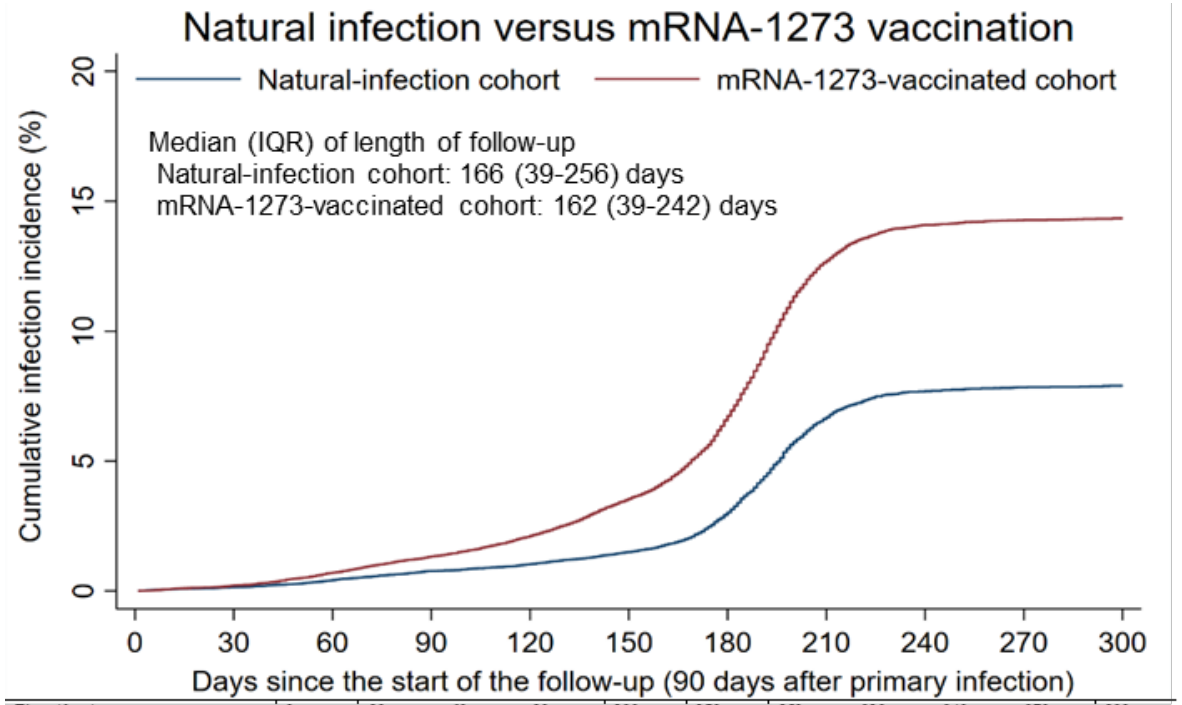


Chemaitelly et al. Protection of prior natural infection compared to mRNA vaccination against SARS-CoV-2 infection and severe COVID-19 in Qatar. medRxiv 2022:2022.03.17.22272529.

Protection of prior natural infection compared to vaccination with mRNA-1273: A retrospective controlled target trial

Adjusted hazard ratio for SARS-CoV-2 infection: 0.51 (95% CI: 0.49-0.54)

Adjusted hazard ratio for severe COVID-19: 0.24 (95% CI: 0.05-1.19)

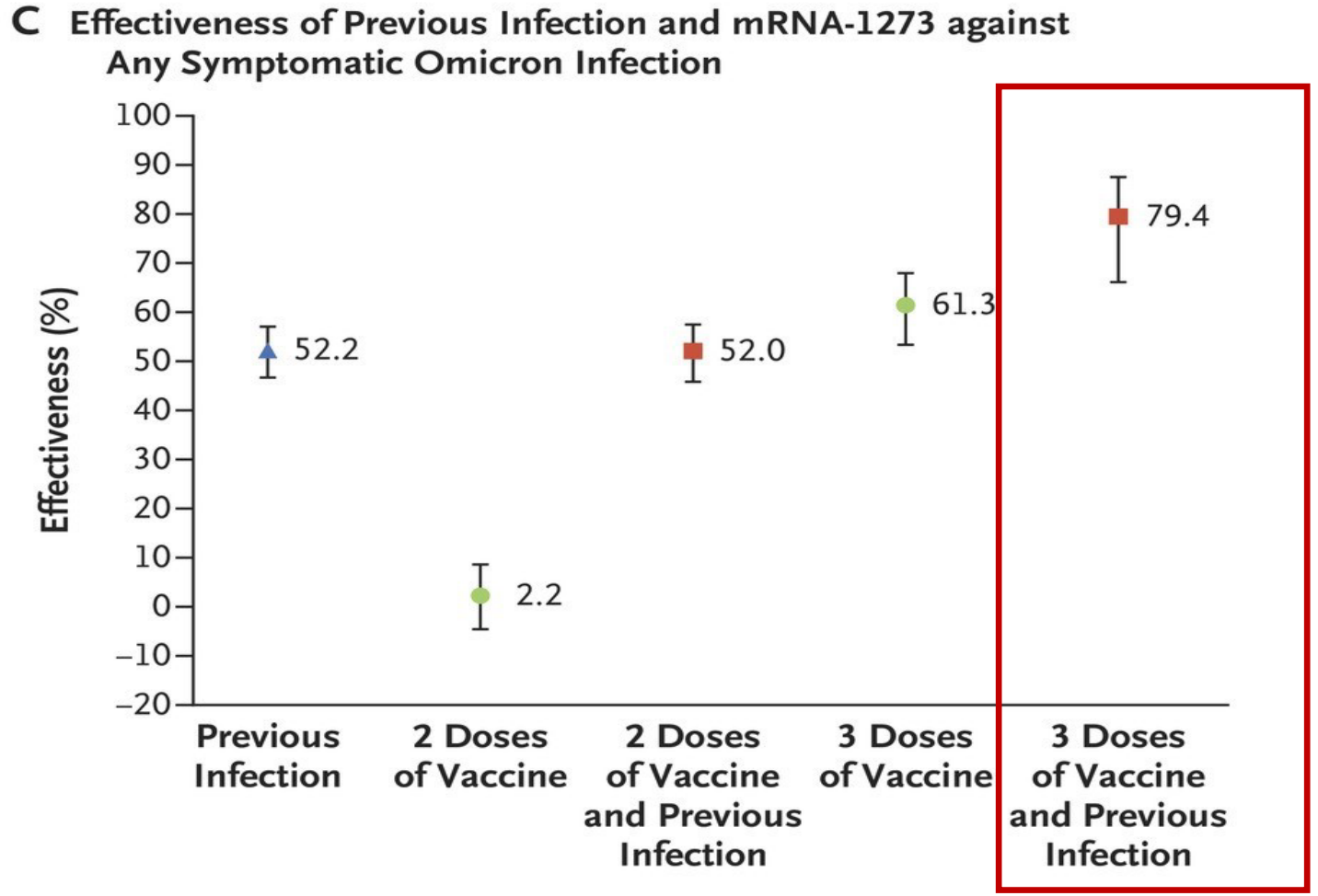


Time (days)	0	30	60	90	120	150	180	210	240	270	300
No. at risk											
Natural-infection cohort	61,955	50,026	41,721	38,972	37,030	33,544	28,054	21,701	17,436	13,610	8,651
mRNA-1273-vaccinated cohort	61,955	50,005	41,617	38,779	36,661	32,852	26,943	20,036	15,781	12,230	7,669

Chemaitelly et al. Protection of prior natural infection compared to mRNA vaccination against SARS-CoV-2 infection and severe COVID-19 in Qatar. medRxiv 2022:2022.03.17.22272529.

Hybrid immunity of natural and vaccine immunity

Effectiveness of hybrid immunity against Omicron



Altarawneh HN et al. Effects of Previous Infection and Vaccination on Symptomatic Omicron Infections. New England Journal of Medicine 2022;387:21-34.

More than two years into the COVID-19 pandemic, the global population carries heterogenous immune histories derived from various exposures to infection, viral variants, and vaccination

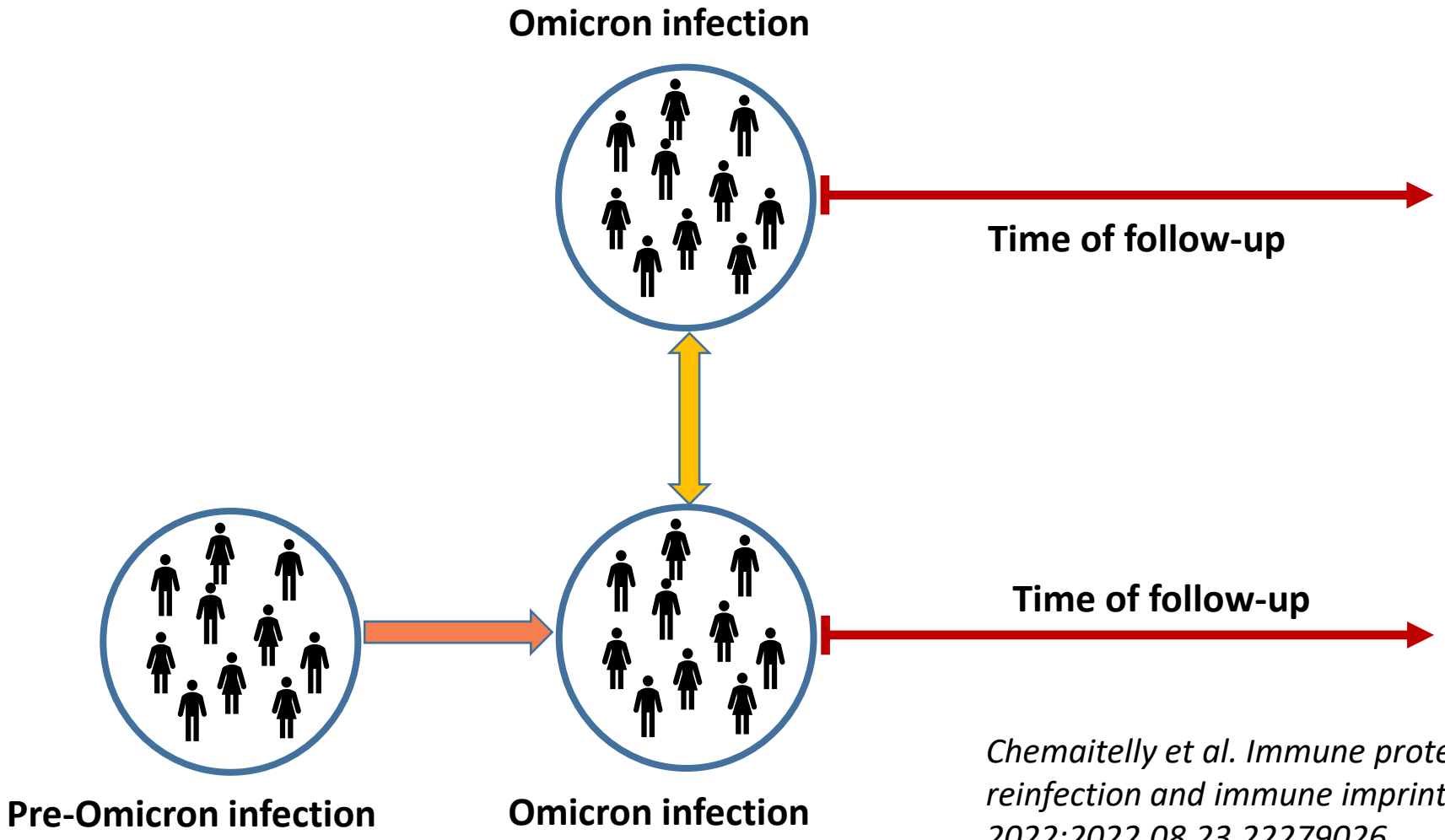
Could immune imprinting ("antigenic sin") compromise protection against infection?

Immune imprinting: Basic science laboratory 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.

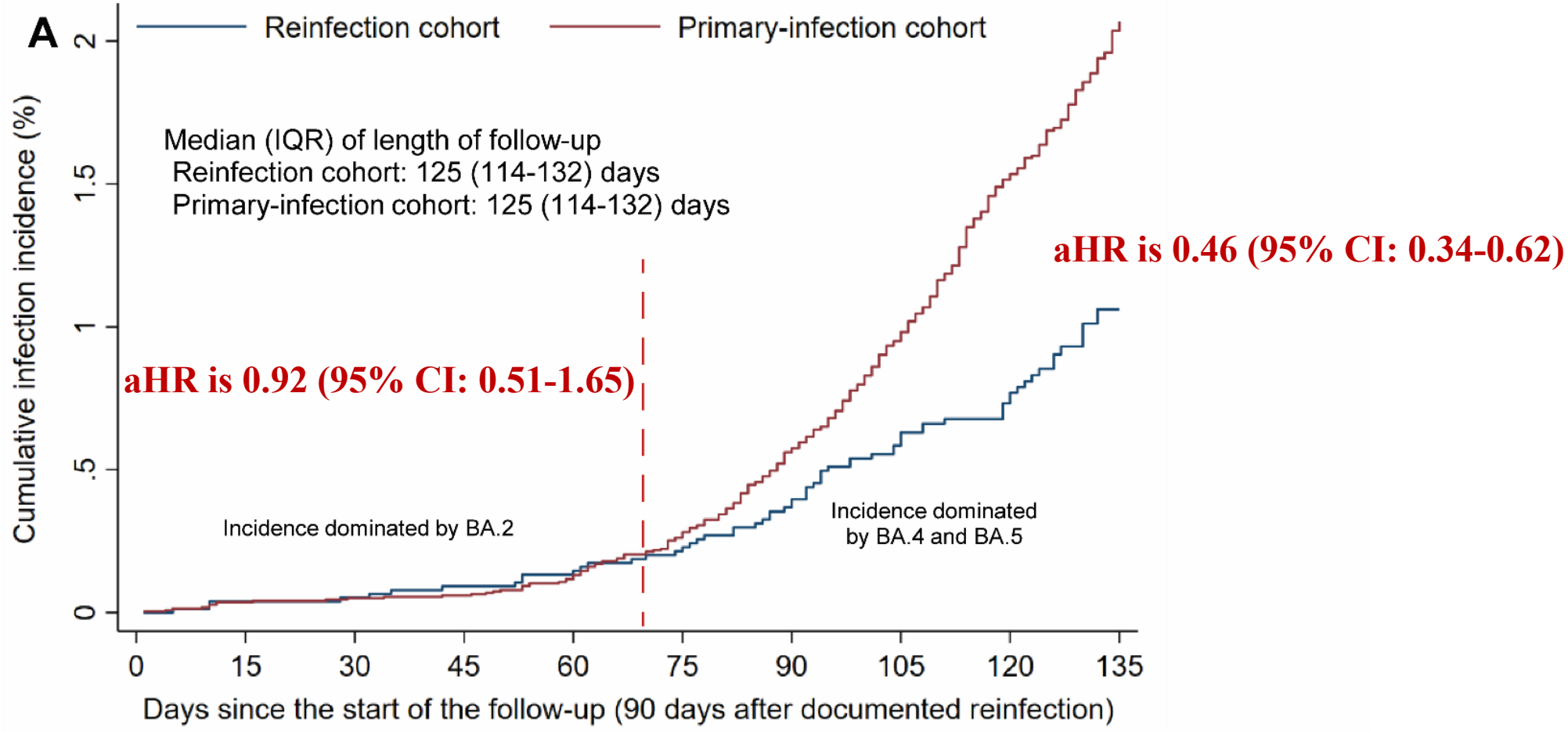
Reynolds CJ, Pade C, Gibbons JM, et al. Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure. Science 2022:eabq1841.

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



Chemaitelly et al. Immune protection against SARS-CoV-2 re-reinfection and immune imprinting. medRxiv 2022:2022.08.23.22279026.

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



Chemaitelly et al. Immune protection against SARS-CoV-2 re-reinfection and immune imprinting. medRxiv 2022:2022.08.23.22279026.

Conclusions

- Prior to Omicron, natural immunity and vaccine immunity showed strong protection against infection and stronger protection against severe COVID-19.
- However, the protection against infection, but not against severe COVID-19, waned over time.
- Against Omicron, both natural and vaccine immunity showed only moderate protection against infection that waned rapidly, but the protection against severe COVID-19 persisted.
- Natural immunity is associated with stronger protection against both infection and severe COVID-19 and wanes more slowly than vaccine immunity.
- There is no epidemiological evidence that immune imprinting compromises protection against Omicron subvariants.

THANK YOU

- *Ministry of Public Health*
- *Hamad Medical Corporation*
- *Infectious Disease Epidemiology Group & WHO Collaborating Center for Disease Epidemiology Analytics on HIV/AIDS*
- *Biomedical Research Program at Weill Cornell Medicine-Qatar*

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