



Waning of humoral immunity depending on the types of COVID-19 vaccine

Contact information

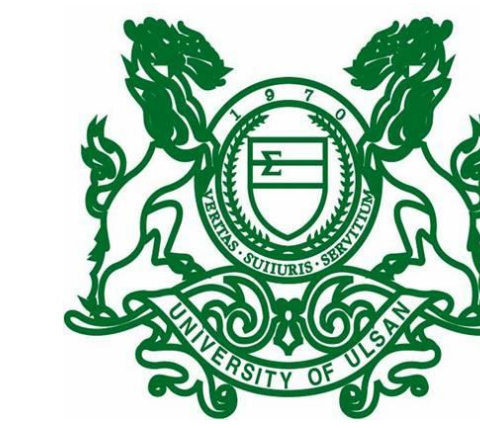
Sung-Han Kim, MD, PhD
Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
Tel: +82-2-3010-3305, E-mail: kimsunghanmd@hotmail.com

So Yun Lim, MD¹, Ji Yeun Kim, PhD¹, Jiwon Jung, MD,^{1,2} Sung-Cheol Yun, MD³, Sung-Han Kim, MD^{1,2}

¹Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

²Institut Pasteur Korea, Seongnam-si, Gyeonggi-do, Republic of Korea

³Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea



Introduction

Previous studies have demonstrated the waning of vaccine effectiveness against COVID-19 and immune responses after two-dose vaccination [1-2]. Also, vaccine effectiveness against hospitalization decreased from 91% to 78% after 4 months, even after a booster vaccination [3], and this waning vaccine effectiveness is correlated with waning antibody levels [4]. However, it is not known whether waning depends on the type of COVID-19 vaccine. We thus conducted a prospective cohort study examining waning antibody levels after two-dose and booster COVID-19 vaccination comparing homologous BNT162b2 (Pfizer–BioNTech) booster, homologous mRNA-1273 (Moderna) booster, and heterologous two-dose ChAdOx1 nCoV-19 (AstraZeneca) followed by BNT162b2 booster.

Methods

1. Study participants

Healthcare workers (HCWs) who received the COVID-19 vaccine and agreed to peripheral blood sampling were enrolled in this study from March to October 2021 in Asan Medical Center, a tertiary care hospital in Seoul, South Korea. Booster vaccination was given 6 months after the two-dose ChAdOx1 and BNT162b2 vaccines, but 4 months after mRNA-1273. All HCWs given two-dose ChAdOx1 received a subsequent booster vaccination with BNT162b2 because of the TTS issue.

2. Measurement of immune responses and statistical analysis

Blood sampling was scheduled 2 weeks and 3 months after the second dose and booster vaccinations, respectively. SARS-CoV-2 S1-specific IgG antibody titers were measured using an in-house developed enzyme-linked immunosorbent assay (ELISA) standardized with reference pooled sera from the International Vaccine Institute (Seoul, South Korea). S1-specific IgG antibody titers are presented in International Units per milliliter (IU/ml), as described in our previous study [5].

A linear mixed model was used to compare the slopes of lines drawn between peak antibody titers 2 weeks after vaccination and the lowest antibody titers 3 months after vaccination. Log transformation of the response variable was performed to confirm the normality assumption. We also performed age-based stratification.

Results

Figure 1. Estimated slopes (red lines) of waning antibody responses with BNT162b2, ChAdOx1, and mRNA-1273. A. two-dose vaccination. B. Booster vaccination.

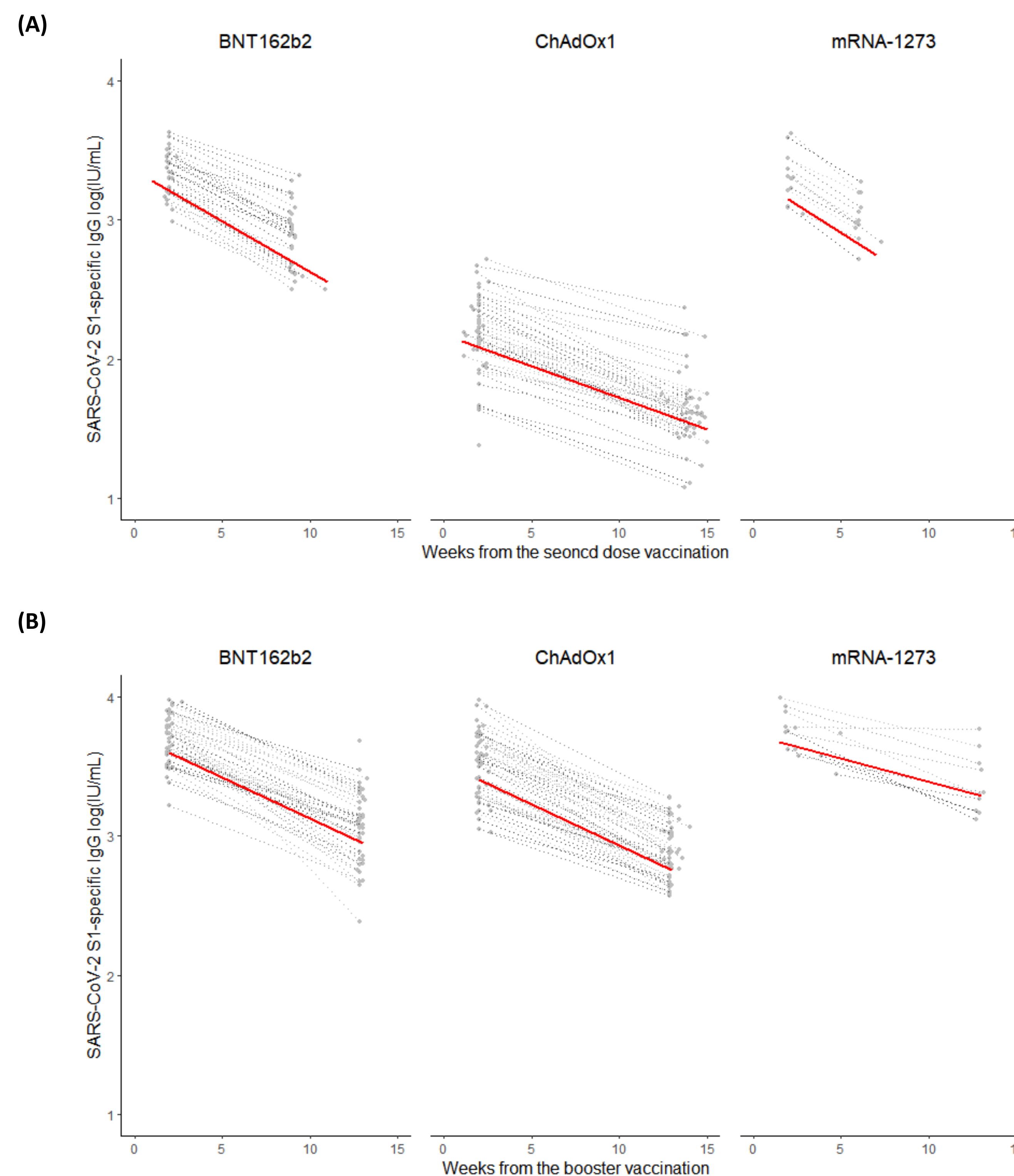


Table 1. Baseline characteristics of the study participants

	BNT162b2 (n = 48)	ChAdOx1 nCoV-19 (n = 52)	mRNA-1273 (n = 13)	p value
Sex				0.277
Female	32 (67)	41 (79)	8 (62)	
Male	16 (33)	11 (21)	5 (39)	
Age, median years (IQR)	29.0 (26, 35)	36.0 (30, 43)	26.0 (25, 28)	<0.001
Age range				<0.001
<40	42 (87.5)	32 (61.5)	12 (92.3)	
40-60	6 (12.5)	20 (38.5)	0 (0.0)	
>60	0 (0.0)	0 (0.0)	1 (7.7)	
The interval between the second and third dose	197 (196, 201)	175 (169, 182)	134 (127, 135)	<0.001

Conclusion

Two-dose homologous ChAdOx1 vaccination or homologous three-dose mRNA-1273 vaccination appears to induce more-durable antibody responses than two-dose homologous mRNA vaccination, homologous three-dose BNT162b2 vaccination, or 2-dose ChAdOx1 followed by BNT162b2 boosting.

References

- 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(24): e83.
- Levin EG, Lustig Y, Cohen C, et al. Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months. *N Engl J Med* 2021; 385(24): e84.
- Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance - VISION Network, 10 States, August 2021-January 2022. *MMWR Morb Mortal Wkly Rep* 2022; 71(7): 255-63.
- Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; 27(7): 1205-11.
- Kim JY, Lim SY, Park S, et al. Immune Responses to the ChAdOx1 nCoV-19 and BNT162b2 Vaccines and to Natural Coronavirus Disease 2019 Infections Over a 3-Month Period. *J Infect Dis* 2022; 225(5): 777-84.