

COVID-19 Aşıları:

Primer Şema ve Tekrar Dozları

Dr. Alpay AZAP
Ankara Üniversitesi Tıp Fakültesi

3. Doz, 4. Doz gerekli mi?



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Posted February 15, 2022.

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Strength and durability of antibody responses to BNT162b2 and CoronaVac

Benjamin J. Cowling, Irene O. L. Wong, Eunice Y. C. Shiu, Amber Y. T. Lai, Samuel M. S. Cheng, Sara Chaothai, [View Full Text](#)

Hong-Kong,

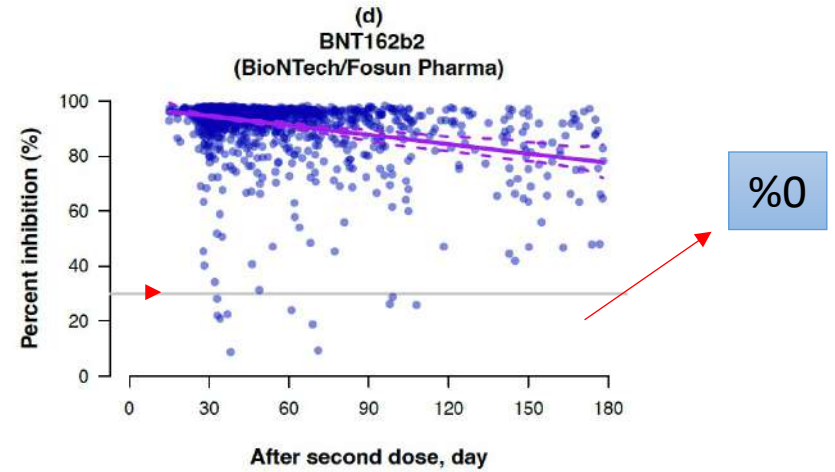
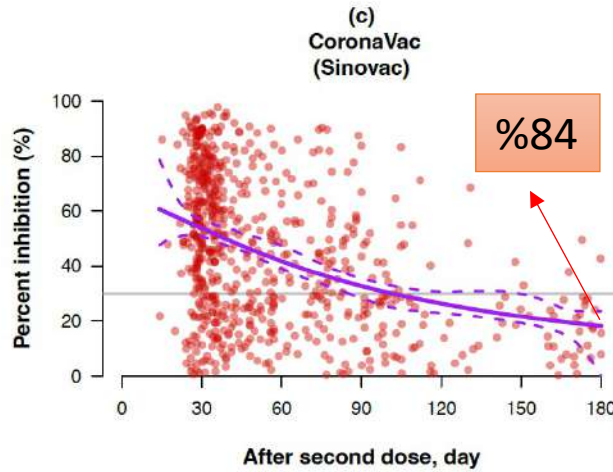
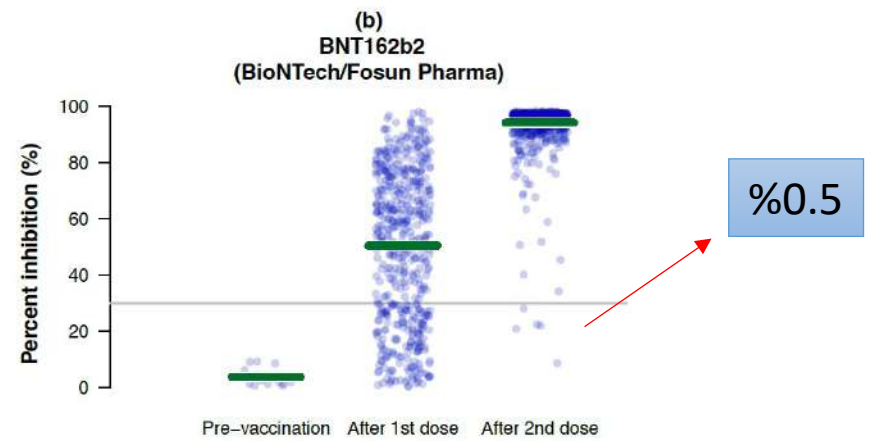
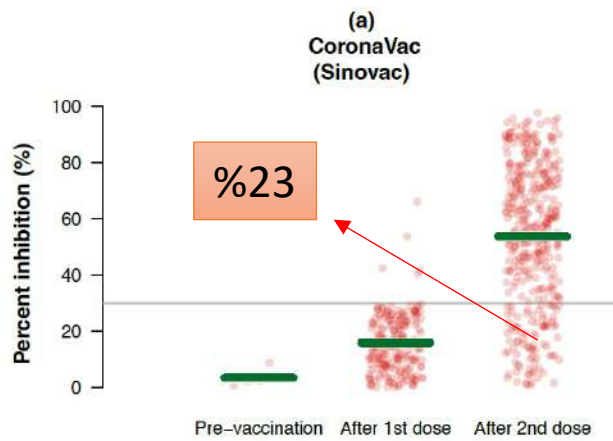
11.7 milyon doz aşı (7.2 milyon BioNTech, 4.5 milyon CoronaVac) 11 Şubat 2022

2 doz aşı uygulanmış kişilerde antikor düzeylerinin 6 aylık seyri

Aşılananlardan belli aralıklarla serum örnekleri alınıp ELISA ve sVNT ile çalışılmış

CoronaVac uygulanan 799 kişiden (59.4 yaş, %46 erkek) 1528 örnek

BioNTech uygulanan 1981 kişiden (49.3 yaş, %44./ erkek) 3939 örnek çalışılmış.



Gençlerde ve kadınlarda antikor yanıtı daha iyi (her iki aşı için)

CoronaVac uygulanan >60 y kişilerin %51'inde antikorlar sınırın altında

Risk of infection, hospitalisation, and death up to 9 months after a second dose of COVID-19 vaccine: a retrospective, total population cohort study in Sweden

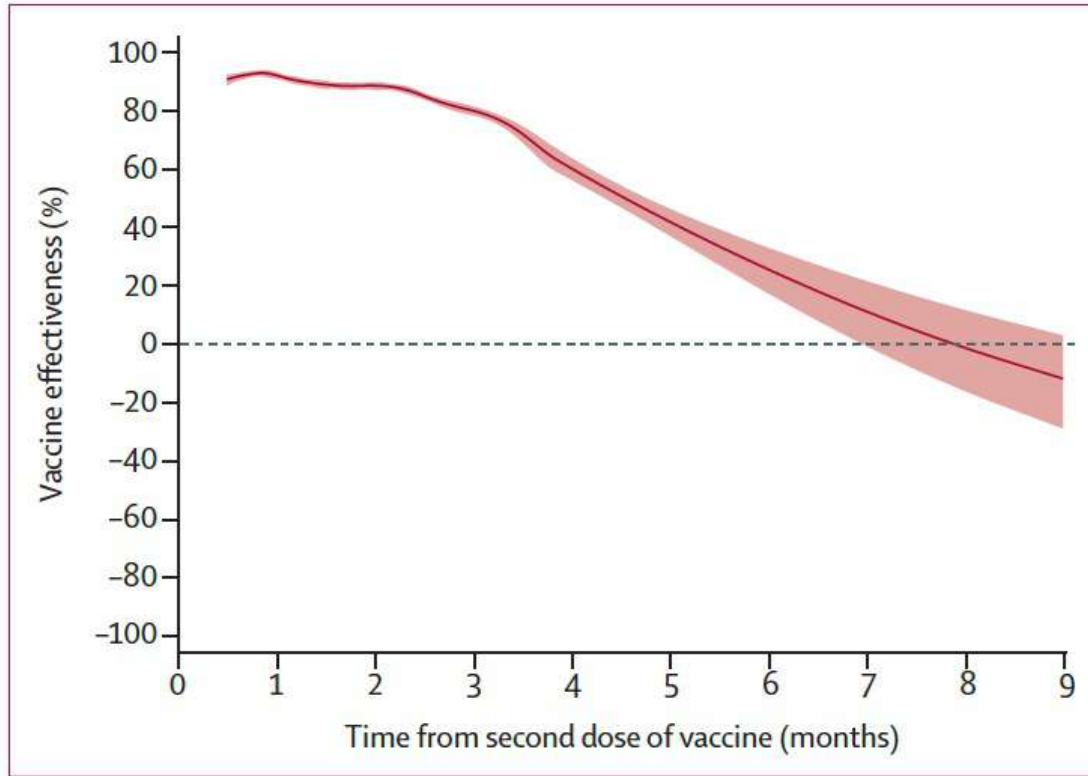
Peter Nordström, Marcel Ballin, Anna Nordström

Summary

Background Vaccine effectiveness against COVID-19 beyond 6 months remains incompletely understood. We aimed

Lancet 2022; 399: 814–23

İsveç, iki doz mRNA aşısı uygulanmış 842 974 kişi (yaş-cinsiyet eşleştirilmiş 842 974 aşısız)



Erkeklerde ve ileri yaşta azalma daha hızlı

Figure 2: Vaccine effectiveness (any vaccine) against SARS-CoV-2 infection of any severity in 842 974 vaccinated individuals matched to an equal number of unvaccinated individuals for up to 9 months of follow-up

ORIGINAL ARTICLE

Waning Immunity after the BNT162b2 Vaccine in Israel

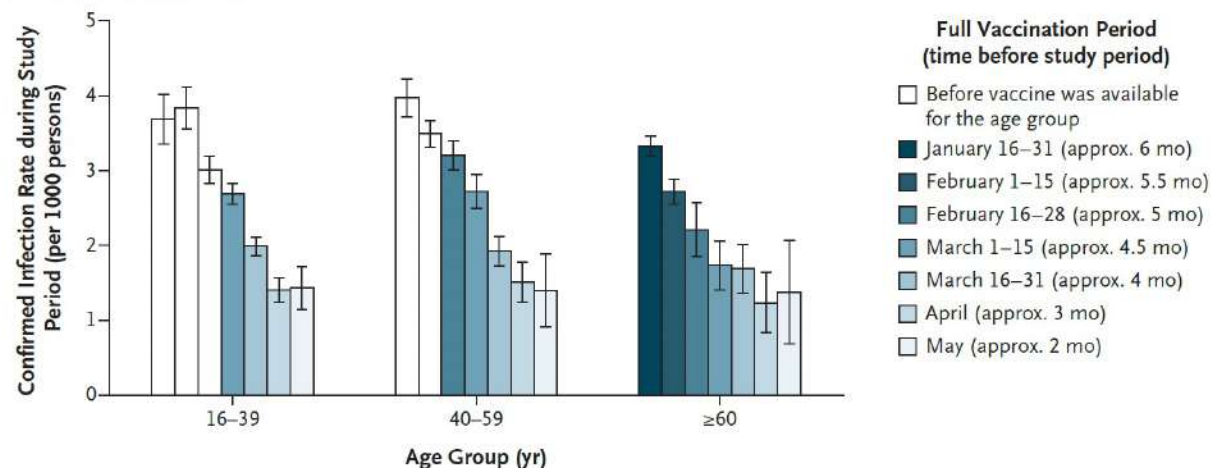
Yair Goldberg, Ph.D., Micha Mandel, Ph.D., Yinon M. Bar-On, M.Sc.,

This article was published on October 27, 2021, at NEJM.org.

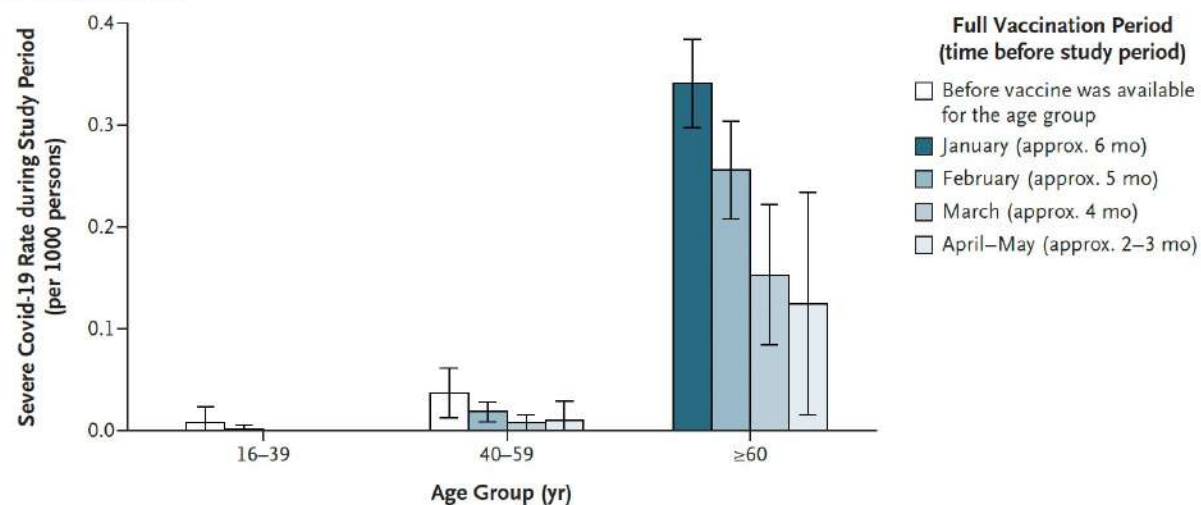
DOI: 10.1056/NEJMoa2114228

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A SARS-CoV-2 Infection



B Severe Covid-19



When cases rose in Israel months after its vaccination campaign, rates climbed almost as quickly among people with **two doses** as among the **unvaccinated**

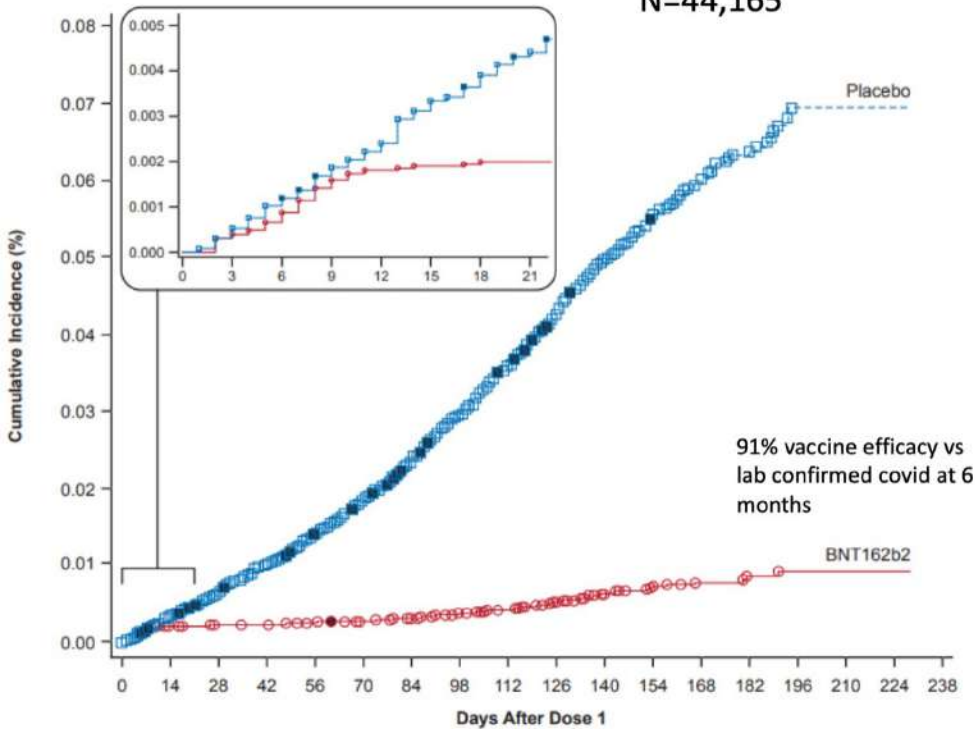
Cases per 100,000 people aged 60+, by vaccination status



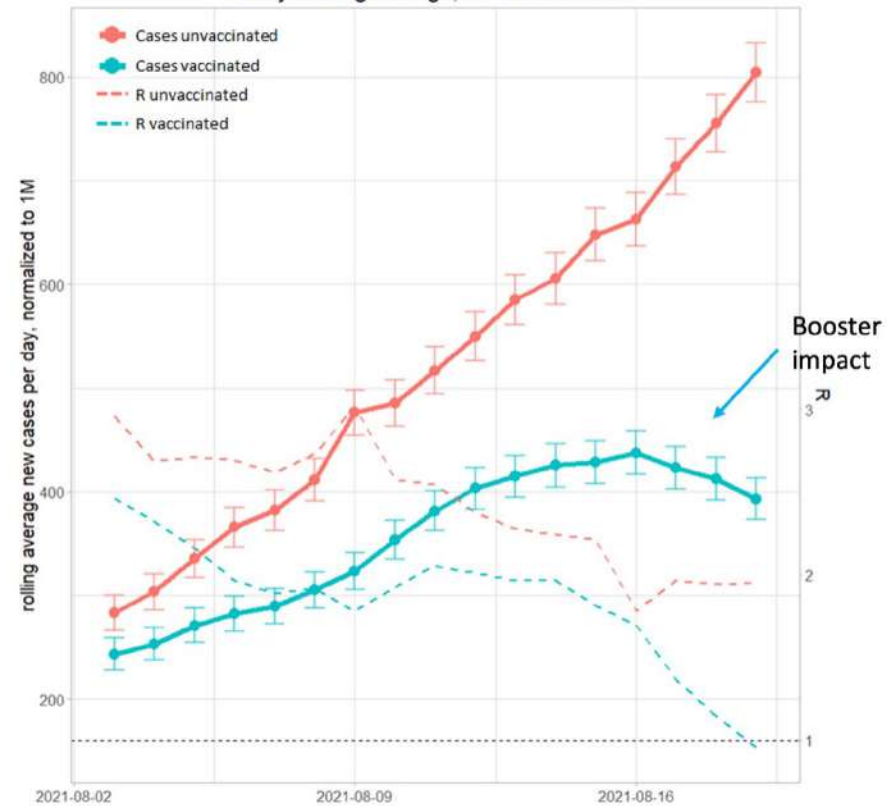
Source: Israeli Ministry of Health
© FT

6 month follow-up of Pfizer trial

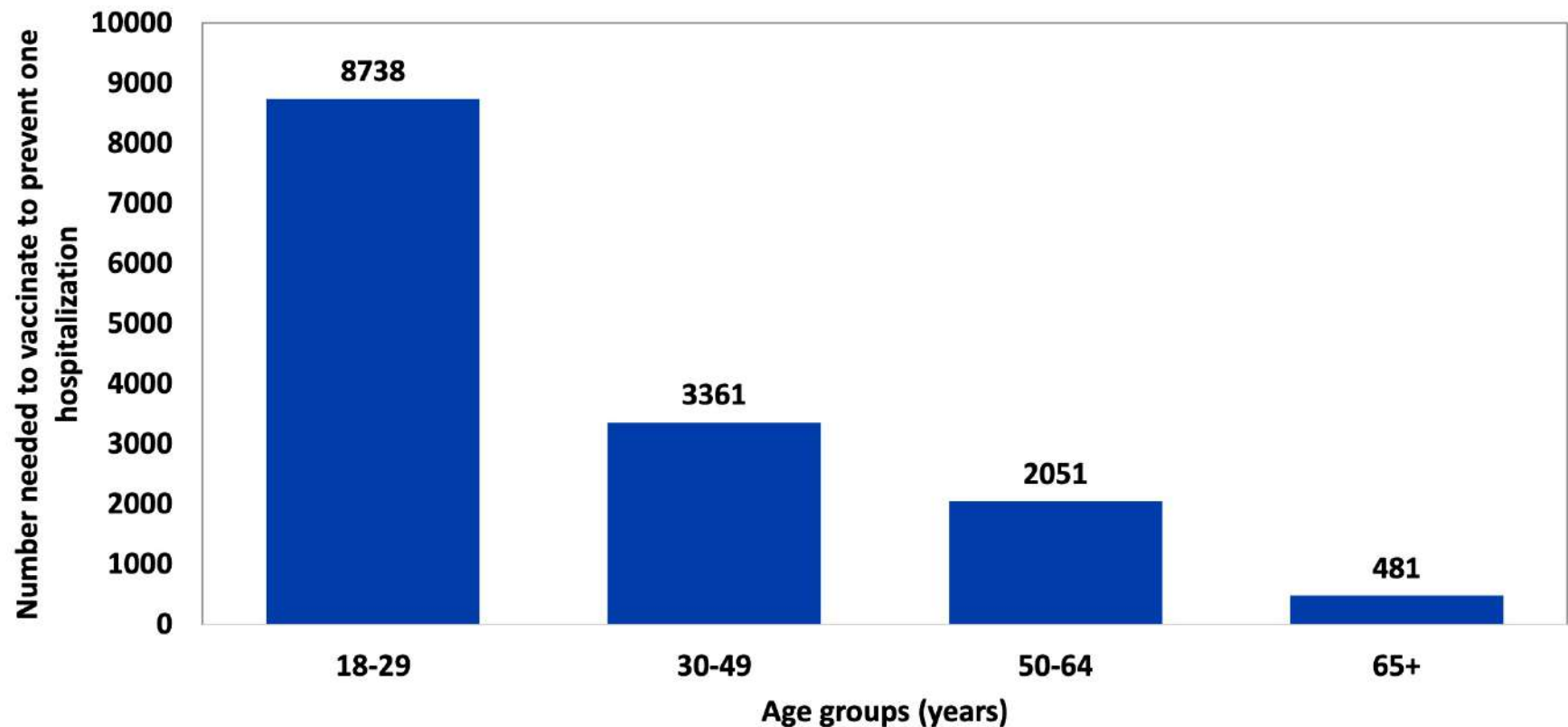
N=44,165



New cases in Israel during the last two weeks, over 60y/o 7 days rolling average, normalized to 1M



Number needed to vaccinate with booster dose to prevent one hospitalization over 6 months



3. Doz 4. Doz uygulanmalı mı????

Bireysel vs Toplumsal Fayda

Her yaş/risk grubu için gerekli mi?

Yayılmayı mı önleyeceğiz? İnsanların Ölmesini mi?
(İnsidans! Aşılanma oranı!)

BNT162b2 vaccine booster dose protection: A nationwide study from Israel

Yinon M. Bar-On^{†1}, Yair Goldberg^{†2*}, Micha Mandel^{†3}, Omri Bodenheimer⁴, Laurence Freedman⁵, Nir Kalkstein⁶, Barak Mizrahi⁶, Sharon Alroy-Preis⁴, Nachman Ash⁴, Ron Milo^{8†}, Amit Huppert^{8,7}

27/8/2021

Cohort	Person-days at risk	Confirmed infections	Severe COVID-19	Estimated booster protection (95% CI)	
				Against confirmed infection	Against severe illness
2 doses only (“no-booster” cohort)	4,018,929	3,473	330	1	1
12+ days from 3 rd dose (“booster” cohort)	3,351,598	313	32	11.4 [10, 12.9]	15.5 [10.5, 22.8]

ORIGINAL ARTICLE

Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant

N. Andrews, J. Stowe, F. Kirsebom, S. Toffa, T. Rickeard, E. Gallagher, C. Gower, M. Kall, N. Groves, A.-M. O'Connell, D. Simons, P.B. Blomquist, A. Zaidi, S. Nash, N. Iwani Binti Abdul Aziz, S. Thelwall, G. Dabrera, R. Myers, G. Amirthalingam, S. Gharbia, J.C. Barrett, R. Elson, S.N. Ladhani, N. Ferguson, M. Zambon, C.N.J. Campbell, K. Brown, S. Hopkins, M. Chand, M. Ramsay, and J. Lopez Bernal

Test negatif vaka kontrol çalışması
1 572 623 test negatif,
204 154 Delta
886 774 Omikron olgusu

This article was published on March 2, 2022, at NEJM.org.

DOI: 10.1056/NEJM-2022-03-02

B Two Doses of BNT162b2 with a Booster Dose of BNT162b2 or mRNA-1273

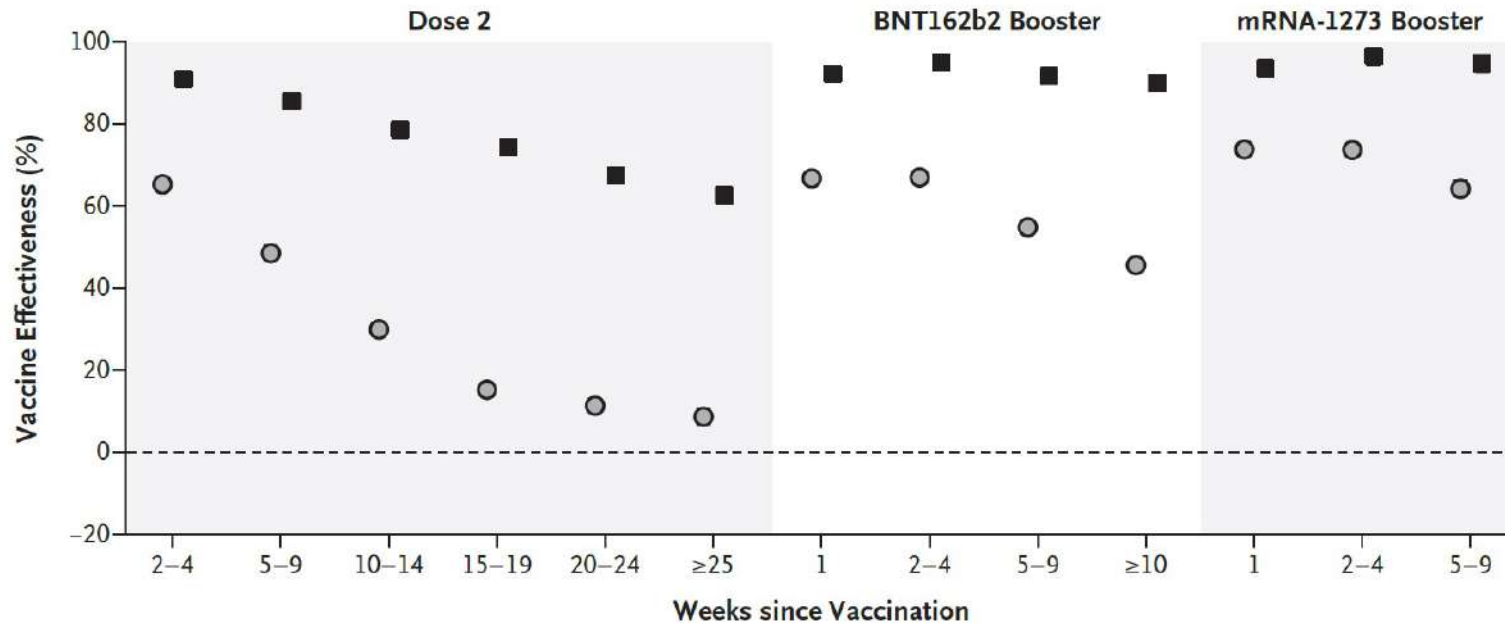
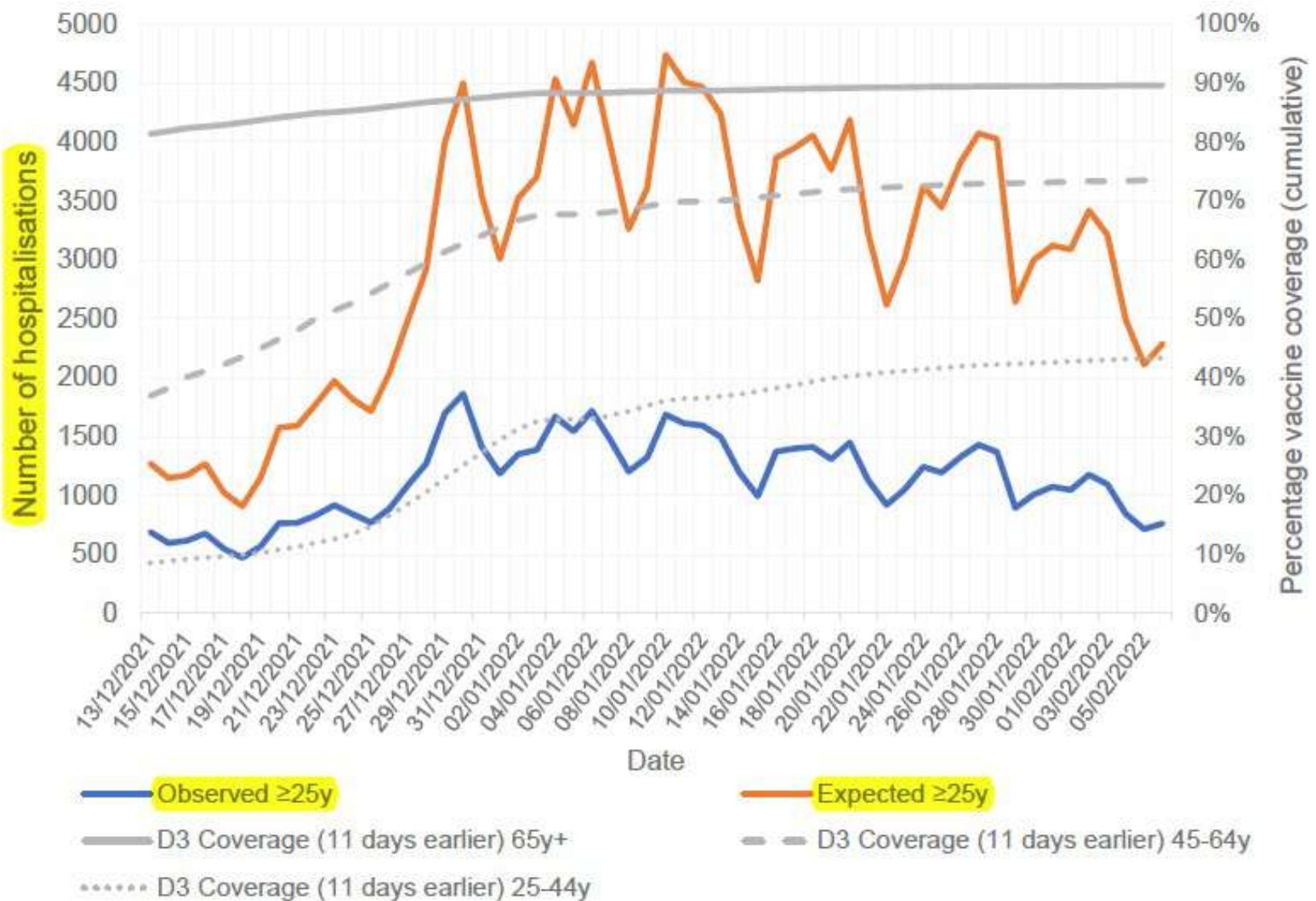
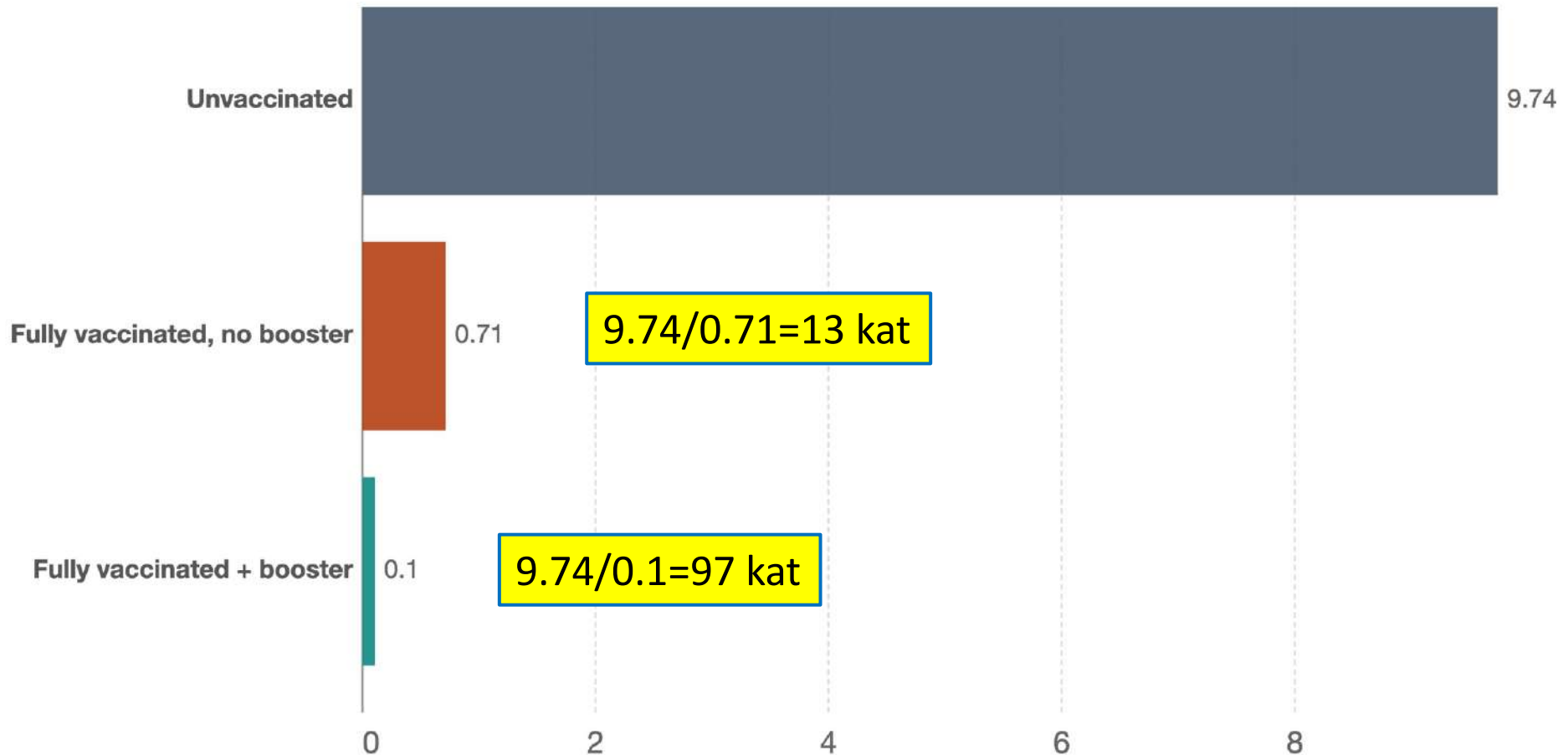


Figure 16. Estimated number of hospitalisations averted by booster vaccinations since 13 December 2021



United States: COVID-19 weekly death rate by vaccination status, All ages, Dec 4, 2021

Death rates are calculated as the number of deaths in each group, divided by the total number of people in this group. This is given per 100,000 people.



Source: CDC COVID-19 Response, Epidemiology Task Force

OurWorldInData.org/coronavirus • CC BY

Note: Unvaccinated people have not received any dose. Partially-vaccinated people are excluded. Fully-vaccinated people have received all doses prescribed by the initial vaccination protocol. The mortality rate for the 'All ages' group is age-standardized to account for the different vaccination rates of older and younger people.

ORIGINAL ARTICLE

Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar

L.J. Abu-Raddad, H. Chemaitelly, H.H. Ayoub, S. AlMukdad, H.M. Yassine,

This article was published on March 9, 2022, at NEJM.org.

DOI: 10.1056/NEJMoa2200797

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19 Aralık 2021-26 Ocak 2022

İki doz mRNA (1 299 010 kişi) vs hatırlatma dozu uygulananlar (281 093 kişi)

İki doz arası medyan 21 gün, hatırlatma dozu medyan 249 gün sonra yapılmış

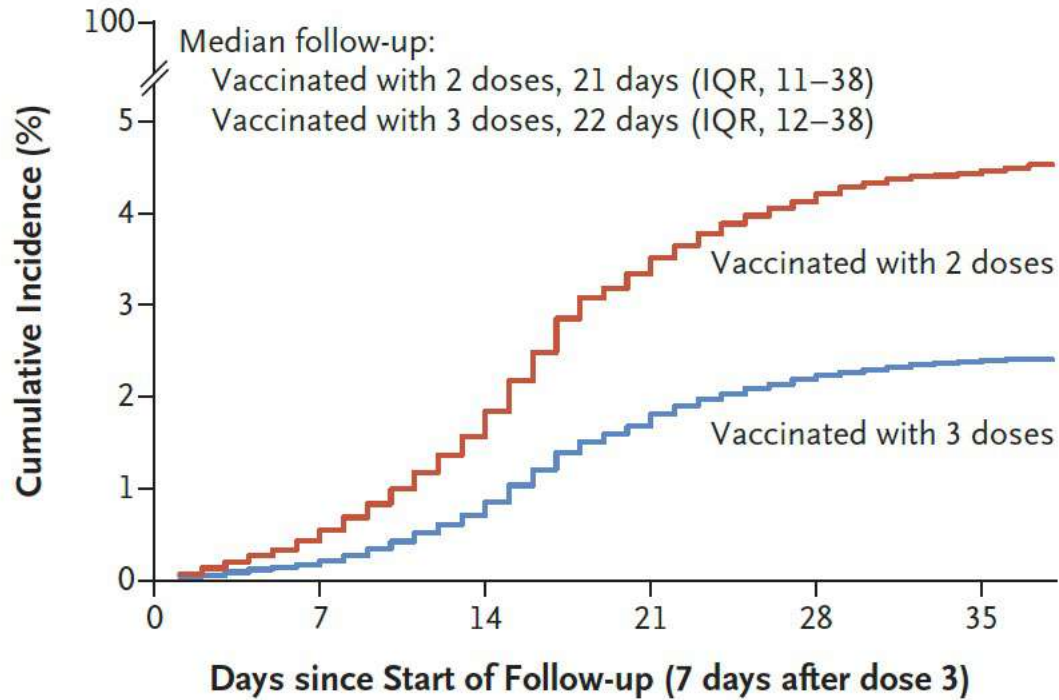
Yaş, cinsiyet, milliyet ikinci dozun uygulandığı hafta konusunda 1:1 eşleştirilmiş

Medyan takip süresi 21 gün (10-38 gün)

İki doz uygulananlarda: 25 266 enfeksiyon: 45 ağır, 4 kritik, ölüm yok

Hatırlatma dozu uygulananlarda: 17 745 enfeksiyon: 12 ağır, kritik yok, ölüm yok.

A Symptomatic Omicron Infection after BNT162b2 Vaccination



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

Kümülatif insidans:

%4.5 (4.3-4.6)

%2.4 (2.3-2.5)



HR: 0.51 (0.48-0.53)

Covid-19'a bağlı hastane yatışı ve ölüm için HR: 0.23 (0.12-0.44)

ARTICLE



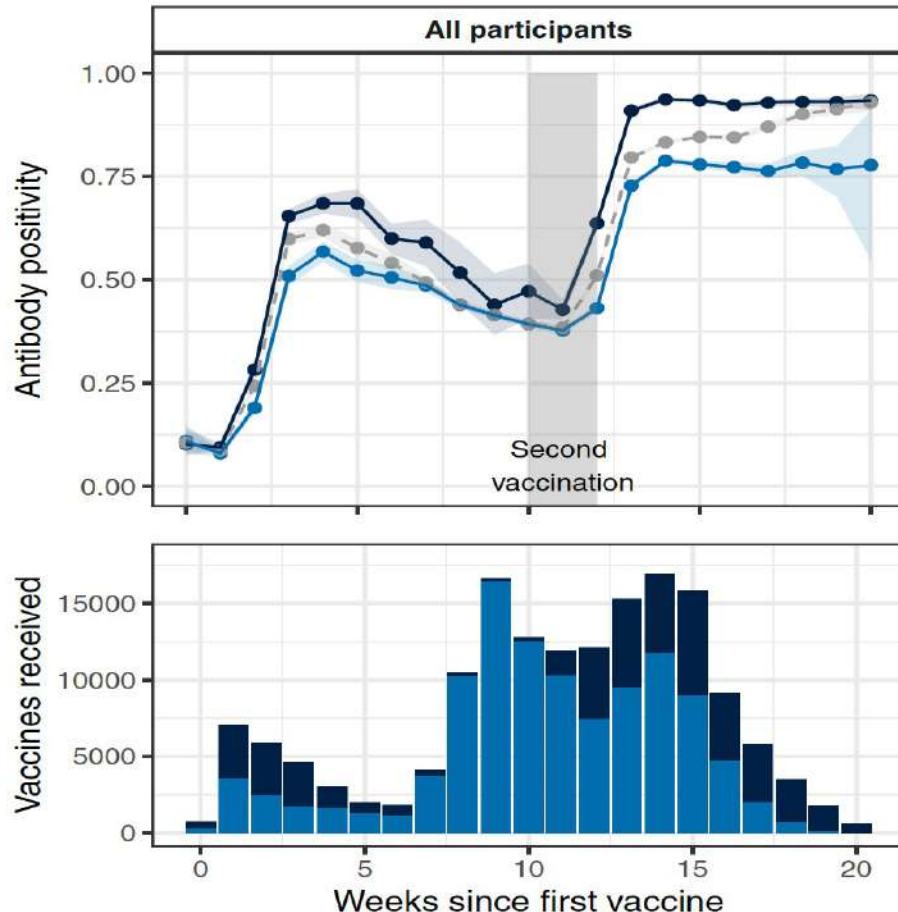
<https://doi.org/10.1038/s41467-022-28527-x>

OPEN

Population antibody responses following COVID-19 vaccination in 212,102 individuals

Helen Ward^{1,2,3,4}, Matthew Whitaker¹, Barnaby Flower^{3,5}, Sonja N. Tang¹, Christina Atchison¹

NATURE COMMUNICATIONS | (2022) 13:907



İngiltere,
REal-Time Assessment for Community
Transmission (REACT-2)
çalışmasına katılan 212 102 kişinin verileri
Lateral Flow IA ile antikor bakılmış
Rutin uygulama 10-12. haftada 2. doz

Antikor pozitiflik oranı:

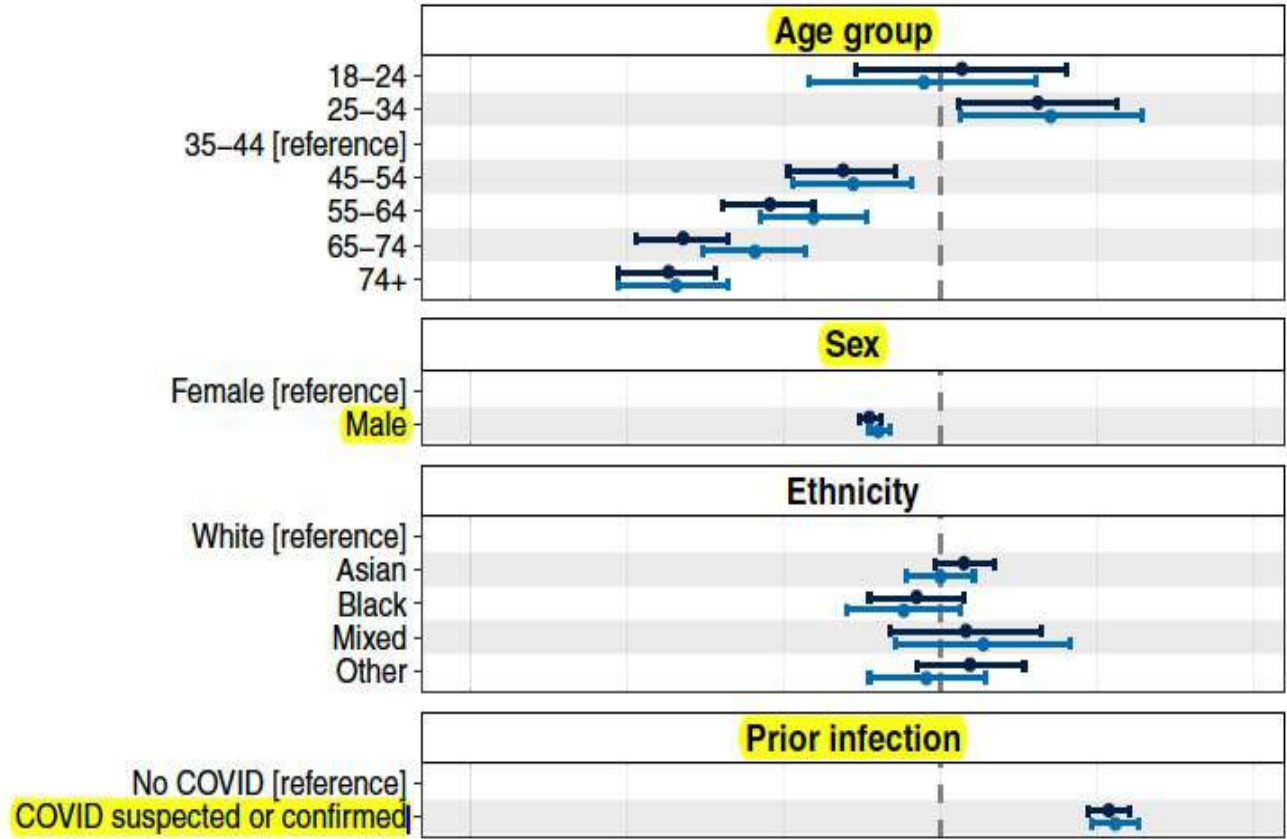
Doz1 4hf: %70

Doz1 10hf: %62.4

Doz2 4hf: >%90

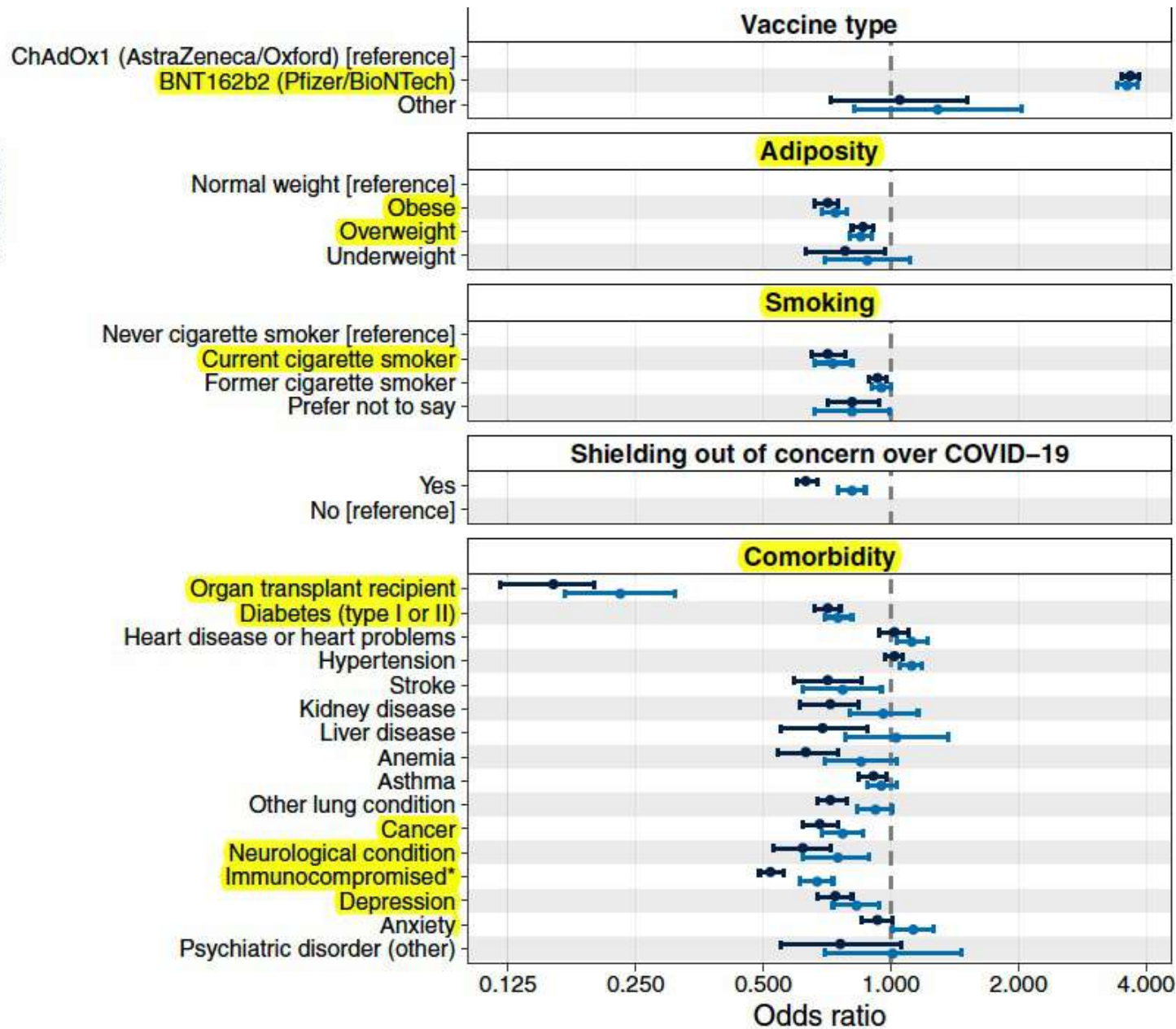
Doz2 10hf: >%90

All vaccines,
2 doses + 21 days (n=68060)



Seropozitiflik yaştan çok etkileniyor: >74y grubunda 35-44 yaşa kıyasla %70 daha düşük
Tüm yaş gruplarında kadınlarda seropozitiflik daha yüksek

Predictor



Model —●— Age and sex adjusted —●— Fully mutually adjusted

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Protection by 4th dose of BNT162b2 against Omicron in Israel

Yinon M. Bar-On, Yair Goldberg, Micha Mandel, Omri Bodenheimer, Ofra Amir, Laurence Freedman, Sharon Alroy-Preis, Nachman Ash, Amit Huppert, Ron Milo

doi: <https://doi.org/10.1101/2022.02.01.22270232>

Posted February 01, 2022.

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İsrail 3 Ocak 2022'de ≥ 60 yaş kişiler ve Sağlık Çalışanlarına 4. dozu uygulamaya başladı

Çalışma 1 Ocak itibariyle ≥ 60 yaş kişilerin 15 Ocak 27 Ocak takiplerini içeriyor

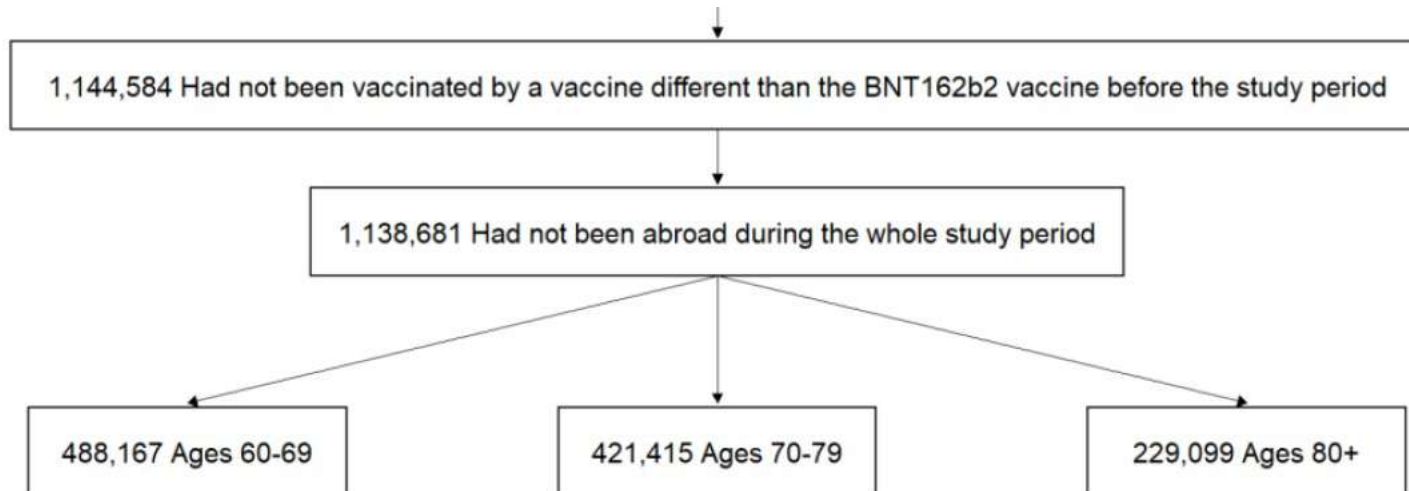


Table 2. Results of the Poisson regression analysis for confirmed infection and severe illness between the different study groups.

	Cases (person-days at risk)			Rate Ratio (95% CI)		Adjusted rate difference per 100,000 person-days at risk (95% CI)	
	3rd dose only	3-7 days after 4th dose	12+ days after 4th dose	3rd dose only vs. 12+ days after 4th dose	3-7 vs. 12+ days after 4th dose	3rd dose only vs. 12+ after 4th dose	3-7 vs. 12+ days after 4th dose
Confirmed Infections	42,693 (7,603,132)	5,945 (1,264,767)	9,071 (3,421,826)	2.0 [2.0, 2.1]	1.9 [1.8, 2.0]	279 [271, 287]	234 [219, 247]
Severe illness	195 (4,277,639)	55 (1,023,355)	13 (980,984)	4.3 [2.4, 7.6]	4.0 [2.2, 7.5]	3.8 [2.8, 4.8]	3.5 [2.1, 5.1]

Four doses of the inactivated SARS-CoV-2 vaccine redistribute humoral immune responses away from the Receptor Binding Domain

Ji Wang, Caiguanxi Deng, Ming Liu, Yihao Liu, Liubing Li, Zhangping Huang, Liru Shang, Juan Jiang, Yongyong Li,

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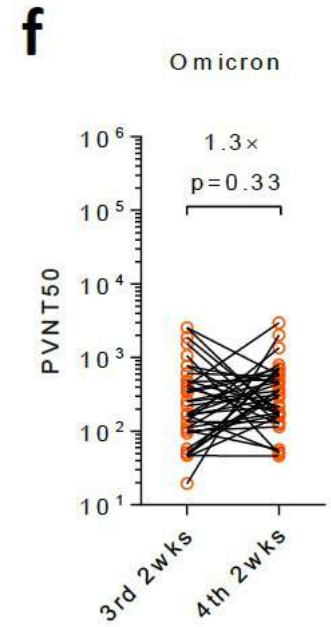
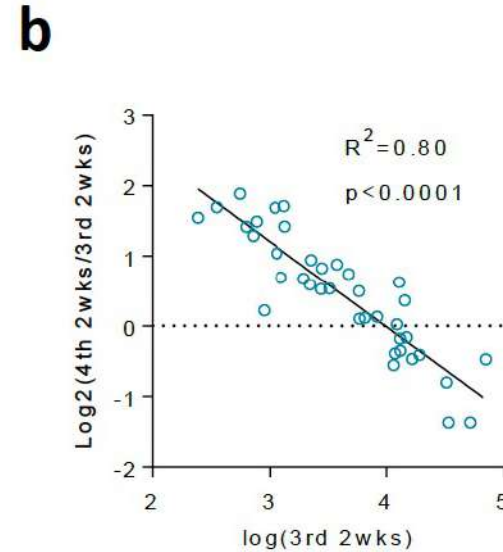
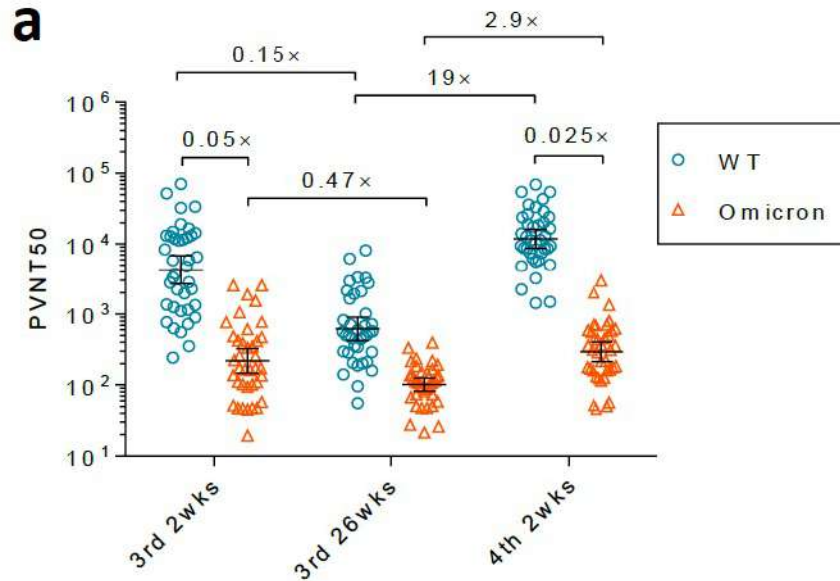
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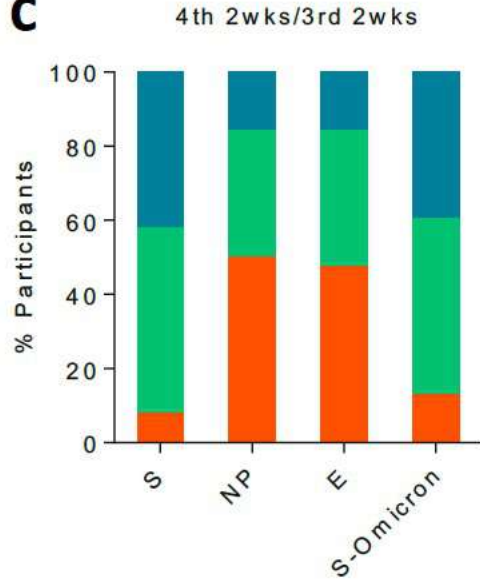
3. doz çalışmasına dahil edilen 38 sağlık çalışanına 6 ay sonra 4. doz (sinopharm) uygulanmış



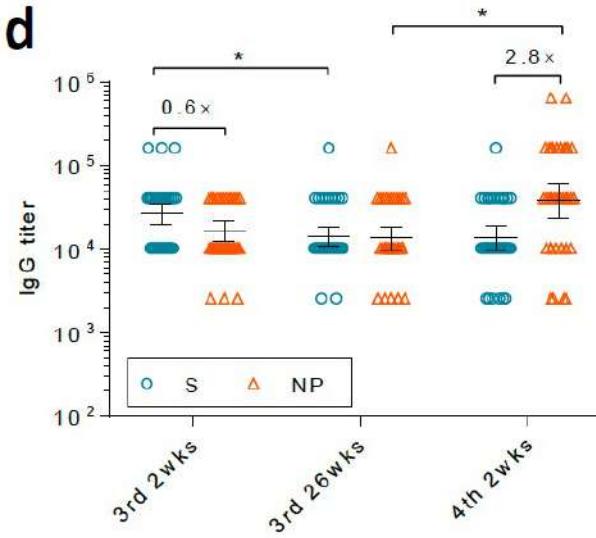
Anti Omikron RBD Ab'lar artmamış, 3. doza iyi yanıt verenlerde 4. doza yanıt düşük (b, f)

Anti-S Antikorlar artmıyor, Anti-NP antikorlar artıyor

c



d

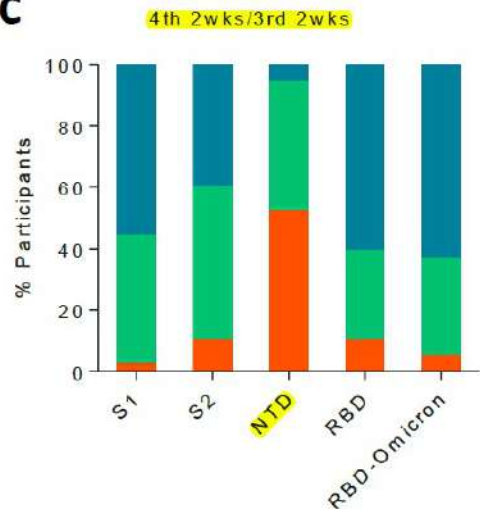


Anti-S antikordaki sınırlı artış RBD'den NTD'ye yönleniyor

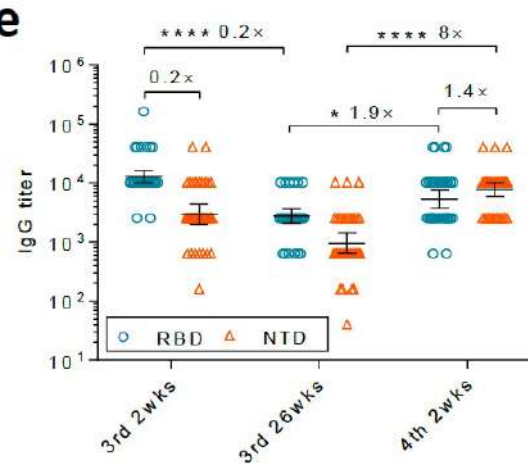


Omikron NTD değişmiş olduğundan etki ↓

c



e



neutralizing potency against the evolving virus. Our data reveal that immune responses could not be endlessly elevated, while suppression of heightened immune responses focusing on one subunit together with a shift of immune responses to other subunits would occur after repeated vaccination. Thus, an updated vaccine with more diverse epitopes capable of inducing NABs against VOCs would be a future direction for boosters.

İki doz arası süre ne kadar olmalı?

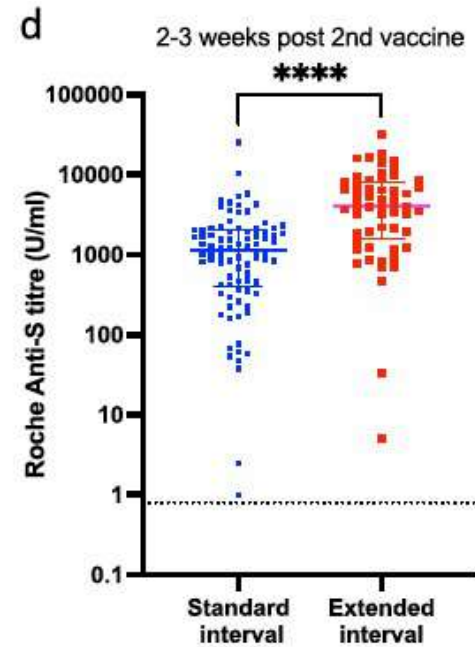


ARTICLE OPEN

Extended interval BNT162b2 vaccination enhances peak antibody generation

Helen Parry¹, Rachel Bruton¹, Christine Stephens¹, Christopher Bentley¹, Kevin Brown¹, Gayatri Amirthalangam¹, Bassam Hallis³, Ashley Otter³, Jianmin Zuo¹ and Paul Moss¹✉

Süreyi 3 hafta yerine 11 haftaya uzatmak antikor titresini 3.5 kat artırıyor





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Spring
Harbor
Laboratory

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bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

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Determining the optimal SARS-CoV-2 mRNA vaccine dosing interval for maximum immunogenicity

Michael Asamoah-Boaheng, David M. Goldfarb, Martin A. Prusinkiewicz, Liam Golding,

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Posted March 04, 2022.

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Kanada, paramedikler (564 kişi) ilk doz aşıdan sonra 160-190 gün sonunda AntiRBD Ab

İki doz arası süreye göre 4 kategori:

≤ 30 gün:kısa, 31-38 gün:orta, 39-73 gün: uzun, ≥ 74 çok uzun

Süre uzadıkça antikor yanıtı artıyor! Belli bir noktada sabitlenmiyor.

İki dozun arasını açmak hatırlatma dozlarını geciktirerek ihtiyaç sahibi ülkelere yönlendirilmesini sağlayabilir

Heterolog Aşılama

The Lancet Regional Health - Europe 11 (2021) 100249



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The Lancet Regional Health - Europe

journal homepage: www.elsevier.com/lanep



Research paper

Effectiveness of heterologous ChAdOx1 nCoV-19 and mRNA prime-boost vaccination against symptomatic Covid-19 infection in Sweden: A nationwide cohort study

Peter Nordström^{1,*}, Marcel Ballin^{1,2}, Anna Nordström^{2,3}

Eylül 2021

Table 2
Vaccine effectiveness of different vaccine schedules against symptomatic

Vaccine schedule	Incident symptomatic Covid-19 infection (N)		Fully adjusted vaccine effectiveness (95% CI)*
	Vaccinated	Unvaccinated	
ChAdOx1 nCoV-19 / BNT162b2	170	259	67% (59-73)
ChAdOx1 nCoV-19 / mRNA-1273	17	47	79% (62-88)
ChAdOx1 nCoV-19 / ChAdOx1 nCoV-19	446	323	50% (41-58)
BNT162b2 / BNT162b2	5,113	10,188	78% (78-79)
mRNA-1273 / mRNA-1273	312	889	87% (84-88)

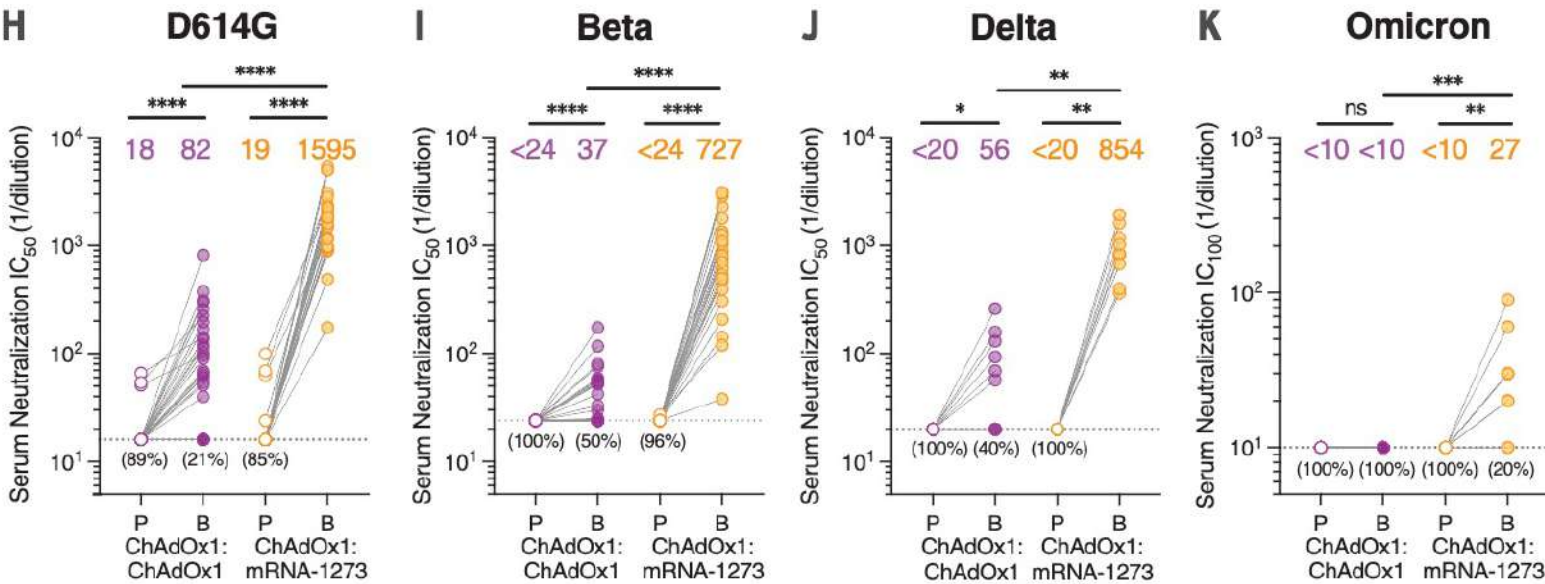
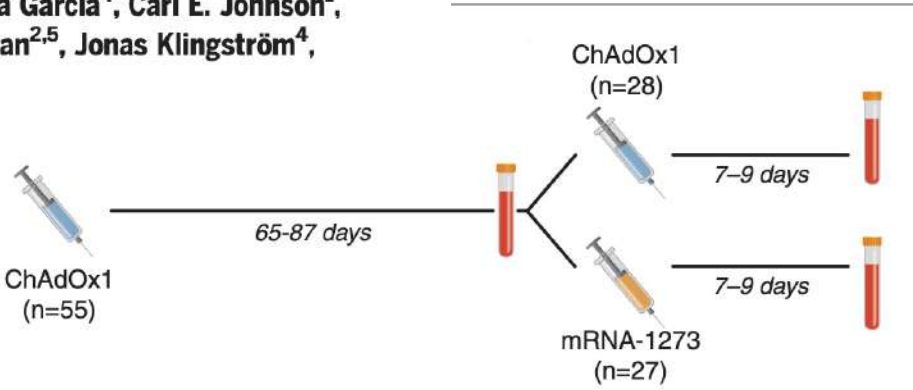
* Adjusted for age, sex, baseline date for vaccination, home maker serv

Etkililikte %50 artış

CORONAVIRUS

Broad anti-SARS-CoV-2 antibody immunity induced by heterologous ChAdOx1/mRNA-1273 vaccination

Chengzi I. Kaku^{1,2}, Elizabeth R. Champney¹, Johan Normark³, Marina Garcia⁴, Carl E. Johnson¹, Clas Ahlm³, Wanda Christ⁴, Mrunal Sakharkar¹, Margaret E. Ackerman^{2,5}, Jonas Klingström⁴, Mattias N. E. Forsell³, Laura M. Walker^{1,6*}



Homologous and Heterologous Vaccine Boost Strategies for Humoral and Cellular Immunologic Coverage of the SARS-CoV-2 Omicron Variant

C. Sabrina Tan, Ai-ris Y. Collier, Jinyan Liu, Jingyou Yu, Abishek Chandrashekar, Katherine McMahan, Huahua Wan, Xuan He, Catherine Jacob-Dolan, Daniel Sellers, John D. Ventura, Yannic Bartsch, Blake M. Hauser, Jennifer E. Munt, Melissa Mattocks,  Kathryn E. Stephenson, Samuel J. Vidal, Kate Jaegle, Marjorie Rowe, Rachel Hemond, Lorraine Bermudez Rivera, Tochi Anioke, Julia Barrett, Benjamin Chung, Sarah Gardner, Makda S. Gebre, Nicole Hachmann, Michelle Lifton, Jessica Miller, Felix Nampanya, Olivia Powers, Michaela Sciacca, Mazuba Siamatu, Nehalee Surve, Lisa H. Tostanoski, Haley VanWyk, Cindy Wu, Ralph S. Baric, Aaron G. Schmidt, Galit Alter, Dan

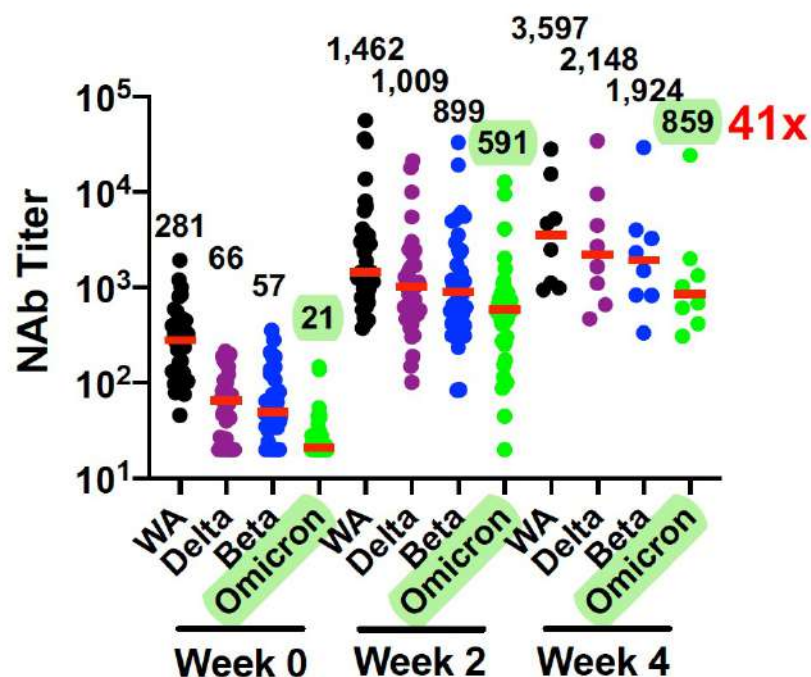
doi: <https://doi.org/10.1101/2021.12.02.21267198>

Table S1. Characteristics of the study population

	BNT162b2 (2 dose) Ad26.COV2.S (booster) N=41	BNT162b2 (2 dose) BNT162b2 (booster) N=24
Age (years), median (range)	36 (23-84)	34 (23-69)
Sex at birth, female	32 (78)	21 (88)
Race		
White	30 (73)	20 (83)
Asian	5 (12)	2 (8)
Black	3 (7)	1 (4)
More than one race	2 (5)	1 (4)
Unknown/Other*	1 (2)	0
Ethnicity		
Hispanic or Latino	2 (5)	2 (8)
Non-Hispanic	39 (95)	22 (88)
Other	0	1 (4)
Medical condition		
Obese (BMI ≥ 30 kg/m ²)	9 (22)	1 (4)
Hypertension	4 (10)	2 (8)
Diabetes	1 (2)	2 (8)
Stroke	1 (2)	0
Pregnant	1 (2)	1 (4)
Days from second vaccine to boost, median (IQR)	235 (191-245)	254 (248-258)

- 65 kişi
- 2 doz BioNTech ‘ten en az 6 ay sonra; J&J (41 kişi) BioNTech (24 kişi)

Ad26.COVS.S



BNT162b2

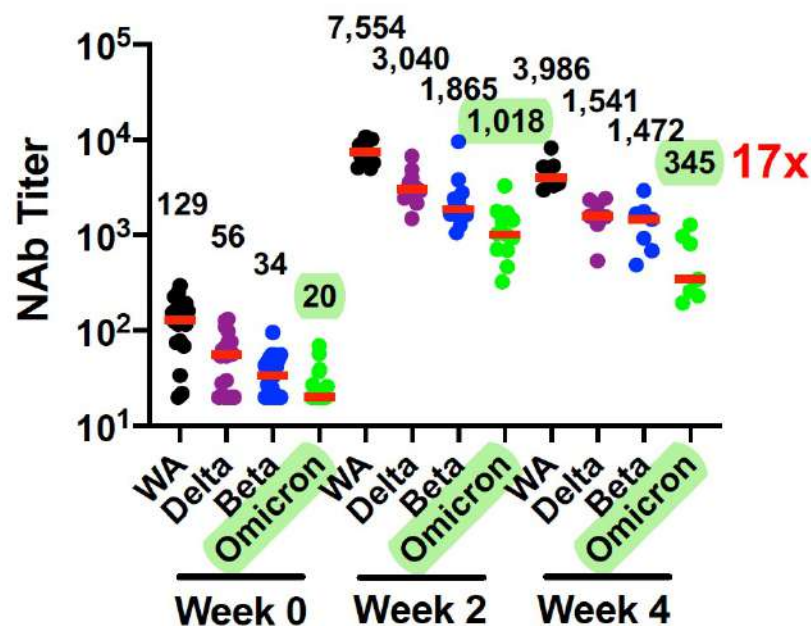


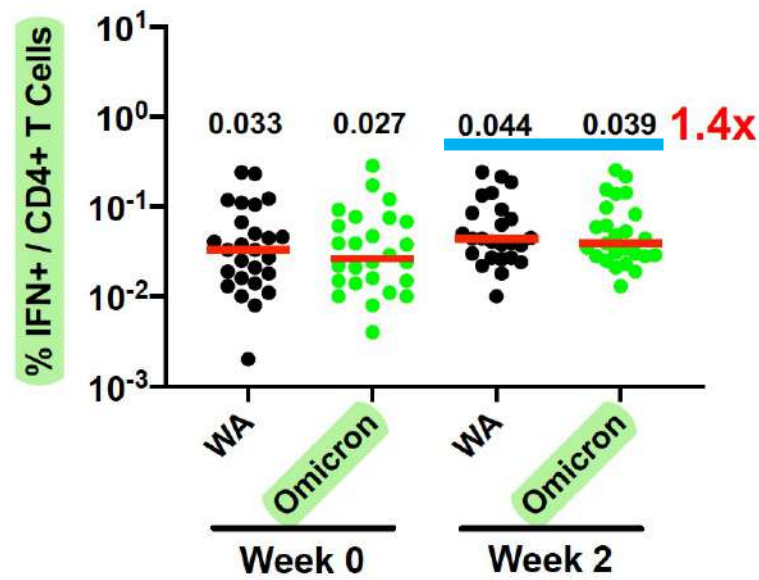
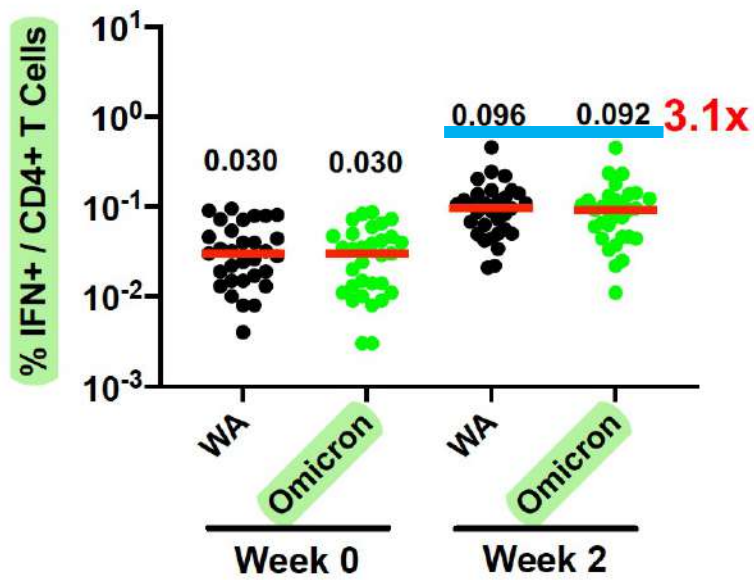
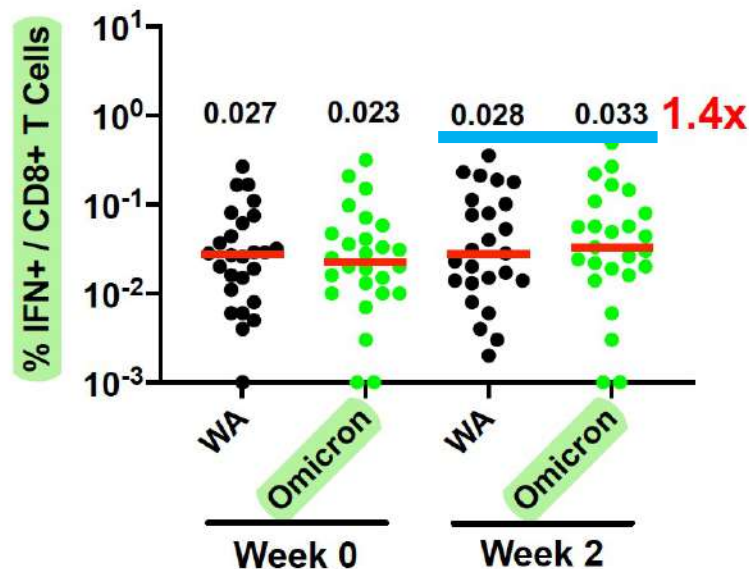
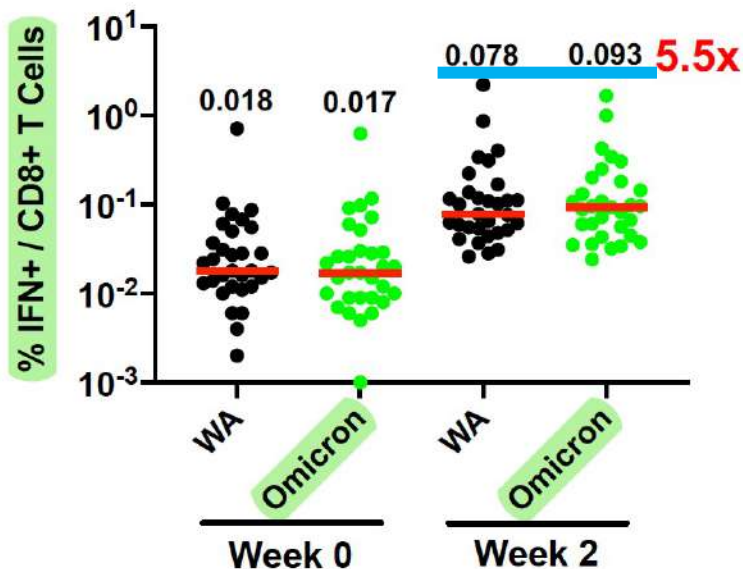
Table S2. Ratio of NAb titers (week 4 / week 2)

	Ad26.COVS.S Boost			BNT162b2 Boost		
	Week 2	Week 4	Ratio	Week 2	Week 4	Ratio
WA1/2020	1,462	3,597	2.46	7,554	3,986	0.53
Delta	1,009	2,148	2.13	3,040	1,541	0.51
Beta	899	1,924	2.14	1,865	1,472	0.79
Omicron	591	859	1.45	1,018	345	0.34

Ad26.COV2.S

BNT162b2

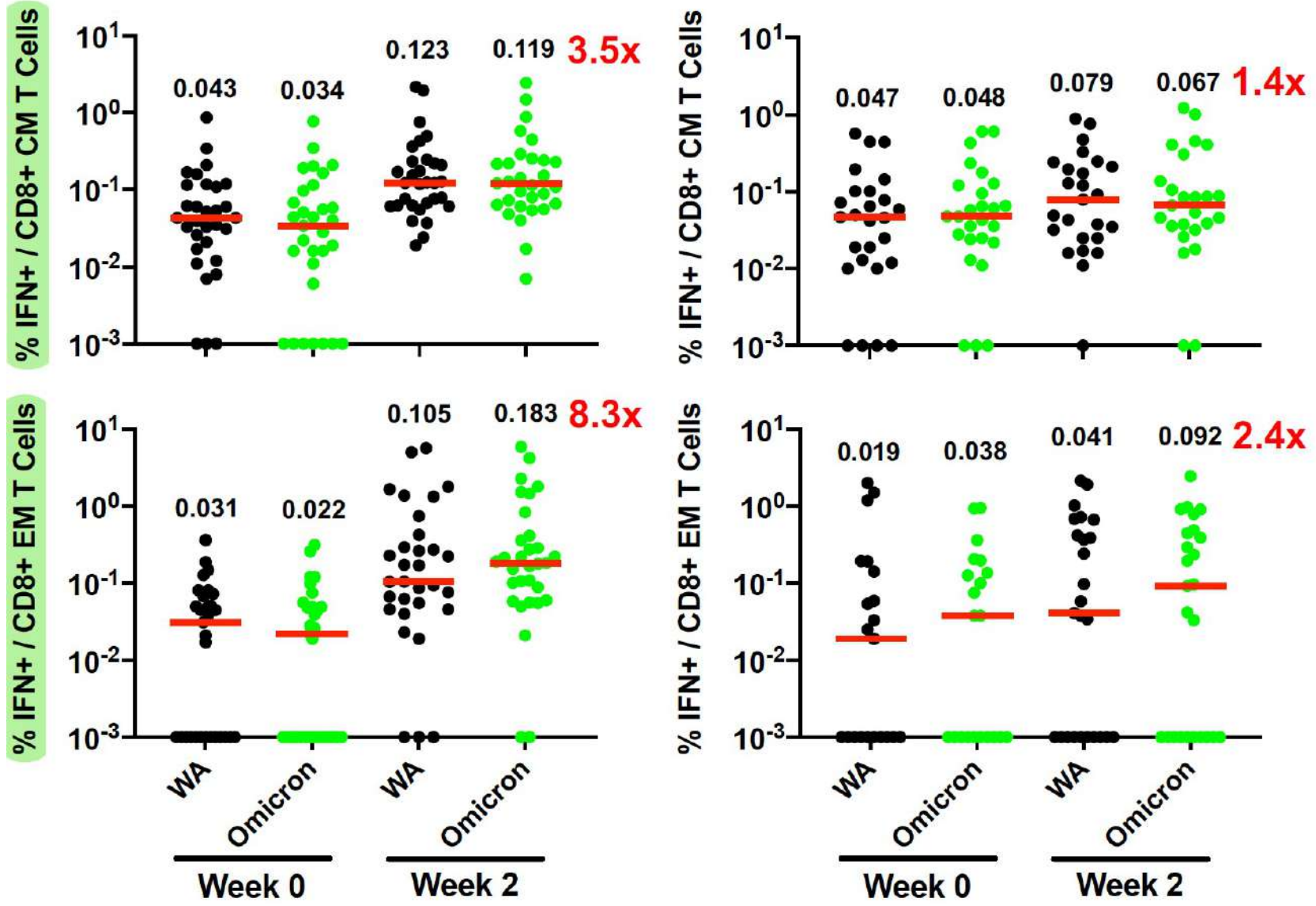
pooled peptide-stimulated intracellular cytokine staining (ICS) assay



IFN-g CD4+ central memory (CM) & effector memory (EM) T cell

Ad26.COV2.S

BNT162b2



Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): a phase 4, non-inferiority, single blind, randomised study

Sue Ann Costa Clemens, Lily Weckx, Ralf Clemens, Ana Verena Almeida Mendes, Alessandra Ramos Souza, Mariana B V Silveira,

Published Online
January 21, 2022
[https://doi.org/10.1016/
S0140-6736\(22\)00094-0](https://doi.org/10.1016/S0140-6736(22)00094-0)

Faz IV, randomize, tek kör çalışma

21-98 yaş (medyan 60y), her grupta deneklerin yarısı $\leq 60y$, yarısı $>60y$

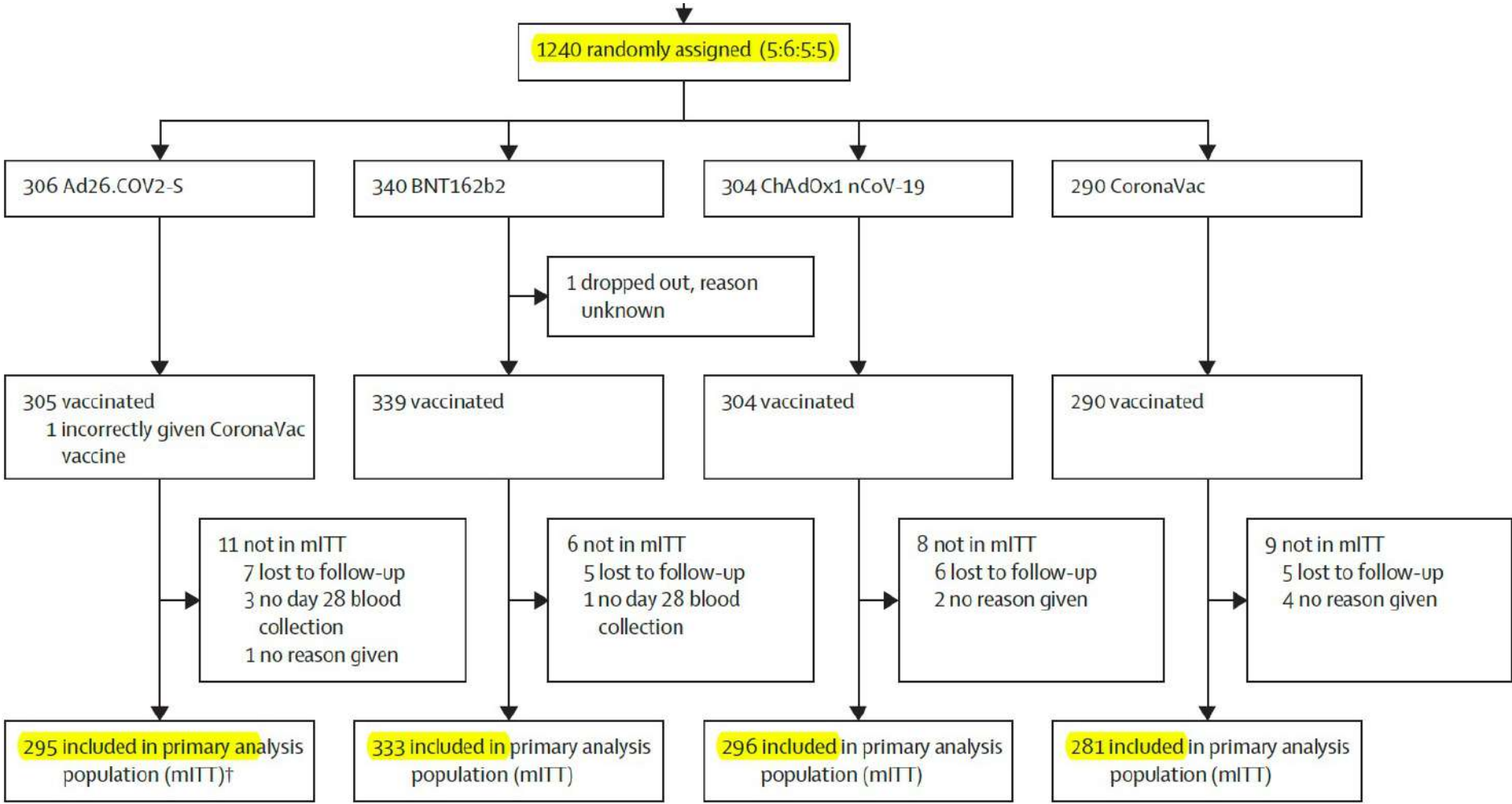
2. doz CoronoVac 182 ± 30 gün önce

Hastalık geçirmiş olanlar, gebeler, IVIg, kan ürünü alanlar dışlanmış

4 grup belirlenmiş: J&J, BioNTech, Az-Ox, CoronaVac

İmmünojenite: Anti-RBD IgG

Nötralizasyon: Psödovirüs NT, 20'şer denekte canlı virüs (Delta ve omikron) FRNT₅₀

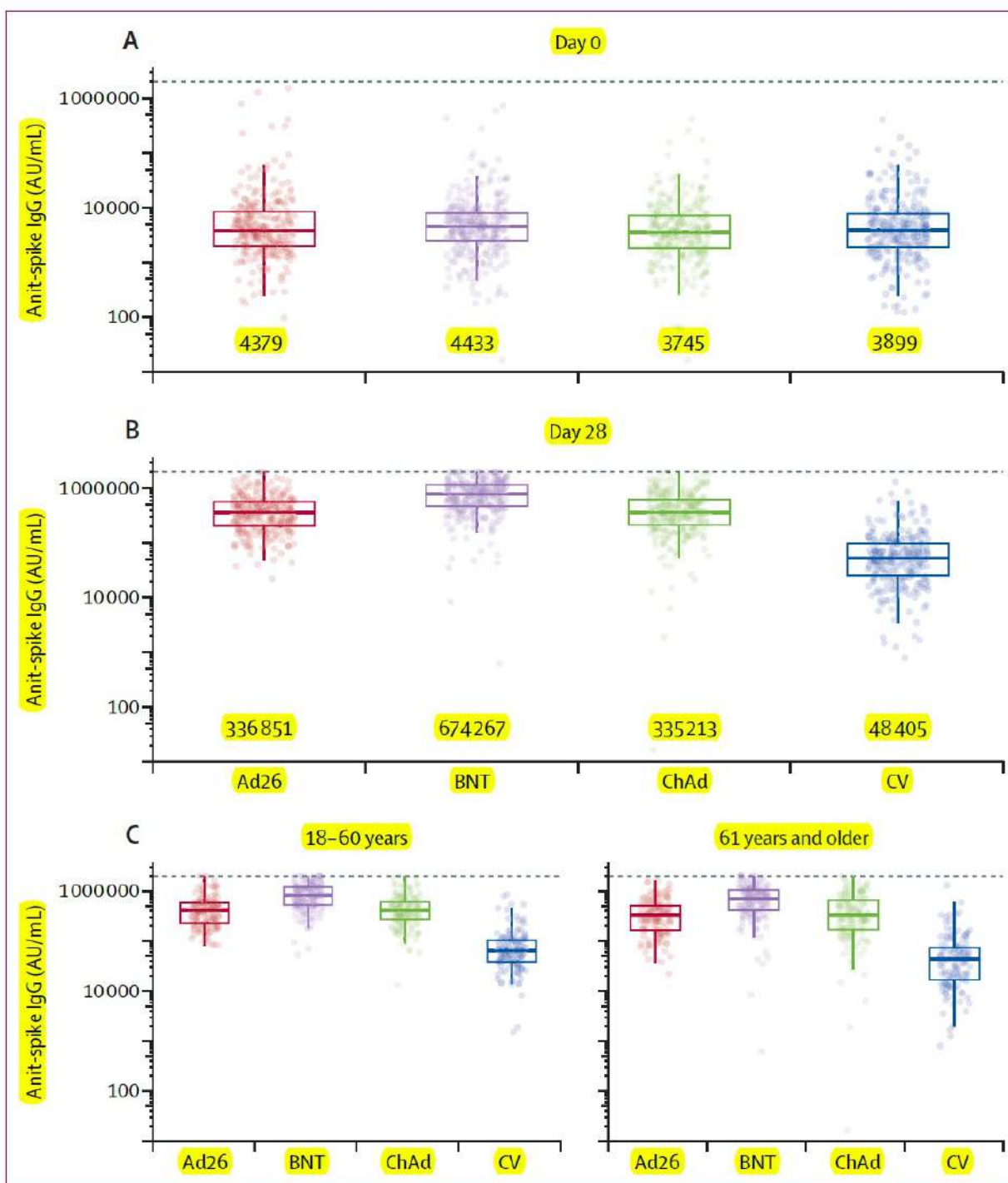


J&J

BioNTech

Az-Ox

CoronaVac

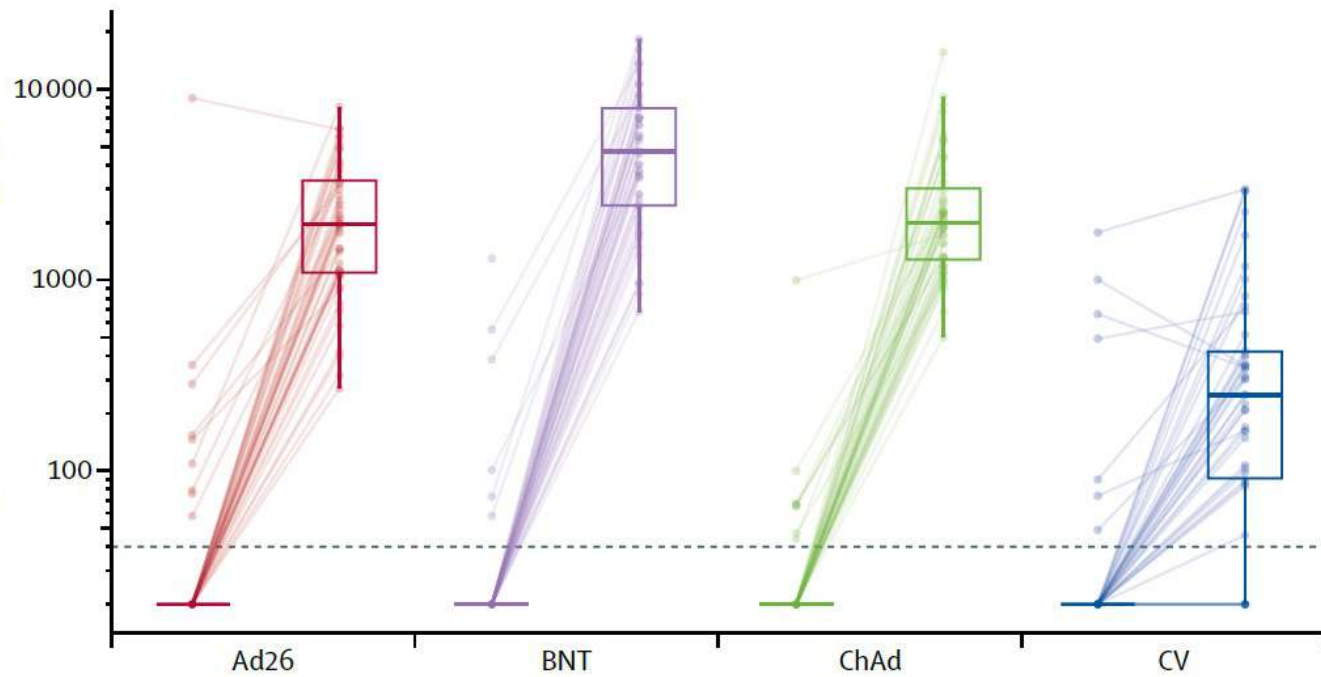


	Ad26.COV2-S	BNT162b2	ChAdOx1 nCoV-19	CoronaVac	p value*
Anti-spike IgG by multiplex immunoassay					
All participants					
Number of participants	294	333	296	281	..
Geometric mean ratio	6.7 (5.8-7.7)†	13.4 (11.6-15.3)†	7.0 (6.1-8.1)†	ref	<0.0001
18-60 years					
Number of participants	152	165	150	148	..
Geometric mean ratio	6.1 (5.1-7.2)	12.1 (10.3-14.2)	6.4 (5.5-7.6)	ref	..
61 years and over					
Number of participants	142	168	146	133	..
Geometric mean ratio	7.3 (5.8-9.2)	15.0 (12.0-18.6)	7.6 (6.1-9.5)	ref	..

Hatırlatma dozuna yanıtlar

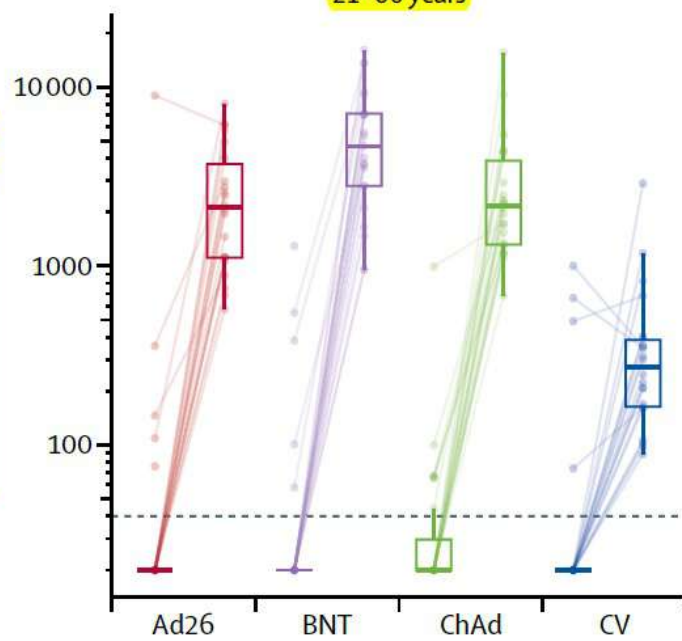
>60y deneklerde %19 daha düşük (GMR:0.81, %95 CI:0.73-0.89)

Pseudovirus neutralisation (IC_{50})

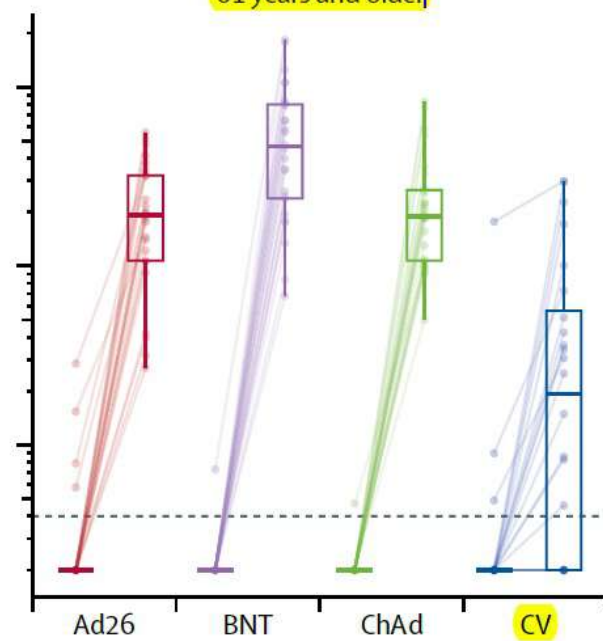


21-60 years

Pseudovirus neutralisation (IC_{50})



61 years and older



Immunogenicity and reactogenicity against the SARS-CoV-2 variants following heterologous primary series involving CoronaVac and ChAdOx1 and BNT162b2 plus heterologous BNT162b2 booster vaccination: An open-label randomized study in healthy Thai adults

Suvimol Niyomnaitham, Zheng Quan Toh, Patimaporn Wongprompitak, Laddawan Jansarikit, Kanjana Srisutthisamphan, Sompong Sapsutthipas, Yuparat Jantraphakorn, Natthakarn Mingngamsup,  Paul V Licciardi,  Kulkanya Chokephaibulkit

doi: <https://doi.org/10.1101/2022.03.03.22271601>

 Previous

Posted March 06, 2022.

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210 katılımcı, 19-60 yaş, %51 kadın

The groups by vaccine used as the first and second dose

CoronaVac -ChAdOx1	CoronaVac -BNT162b2	ChAdOx1 - CoronaVac	ChAdOx1- BNT162b2	BNT162b2 - CoronaVac	BNT162b2 - ChAdOx1	BNT162b2 - BNT162b2
-----------------------	------------------------	------------------------	----------------------	-------------------------	-----------------------	------------------------

Numbers of
enrolled
participants

n=30

n=30

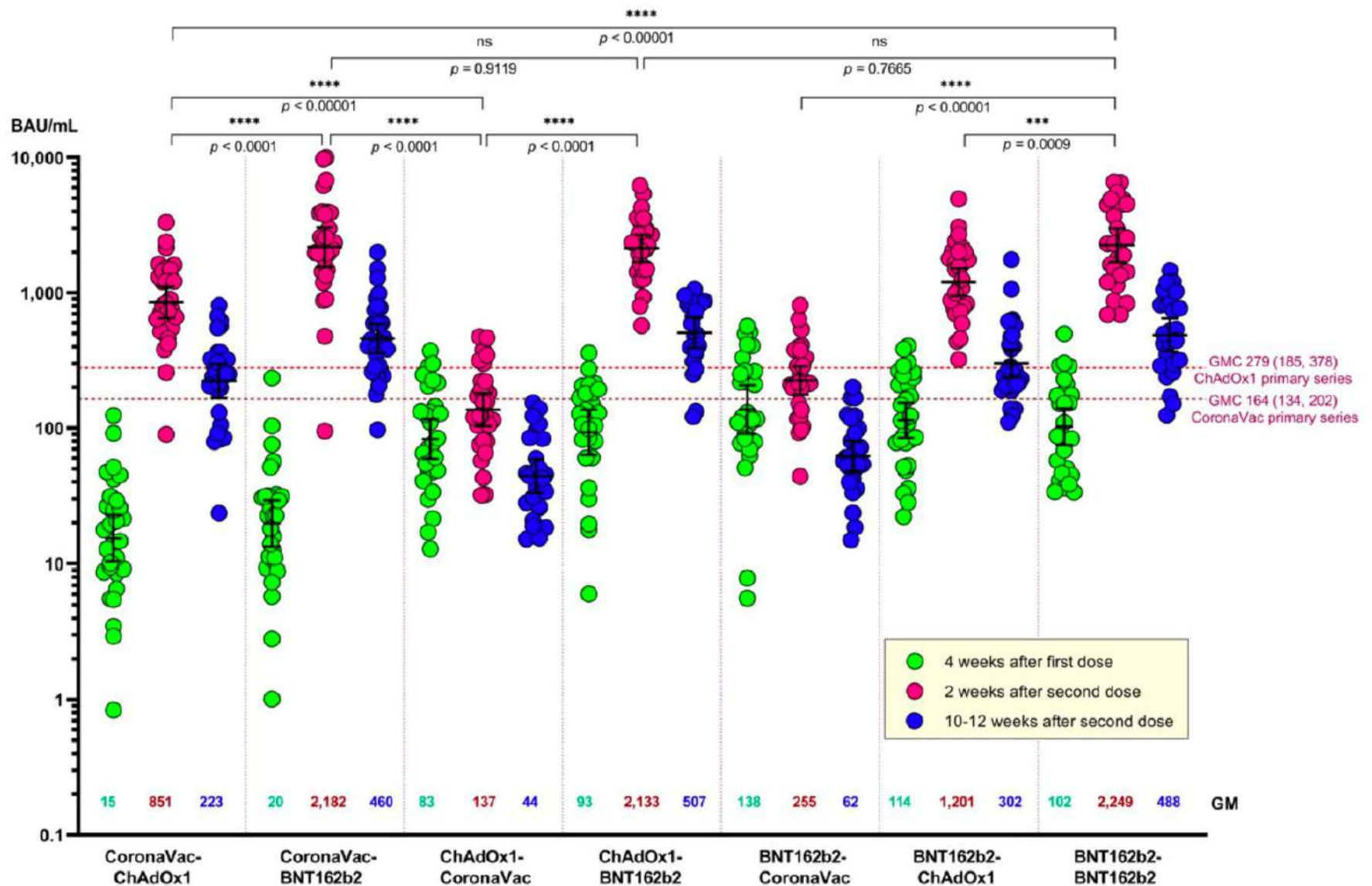
n=30

n=30

n=30

n=30

n=30



Article

Safety and Immunogenicity of the Third Booster Dose with Inactivated, Viral Vector, and mRNA COVID-19 Vaccines in Fully Immunized Healthy Adults with Inactivated Vaccine

Sitthichai Kanokudom ^{1,2}, Suvichada Assawakosri ^{1,2}, Nungruthai Suntronwong ¹, Chompoonut Auphimai ¹,

Tayland, Şubat 2021’de CoronaVac ile başlamış,

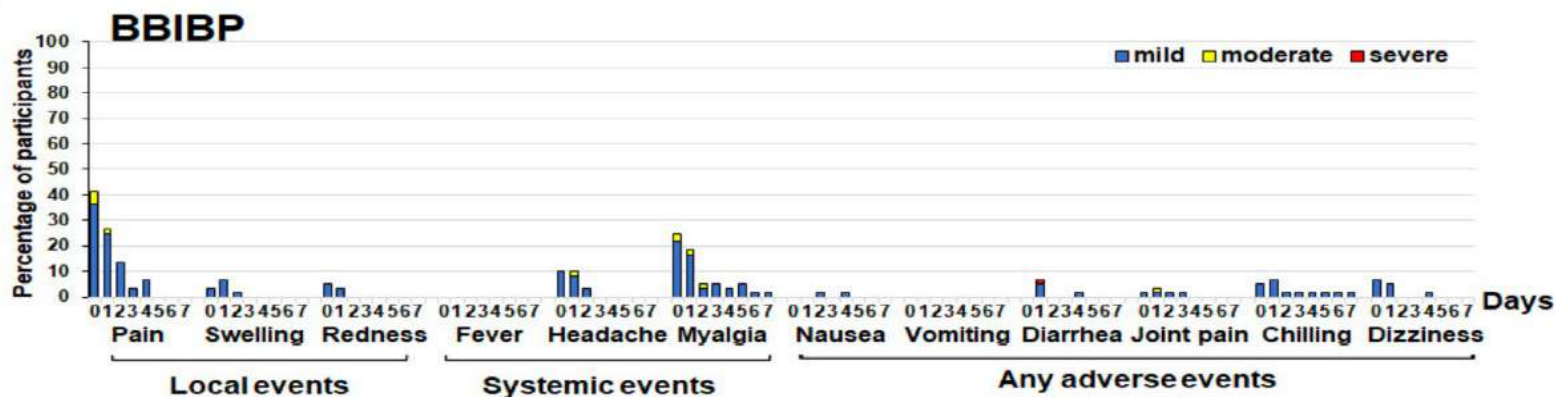
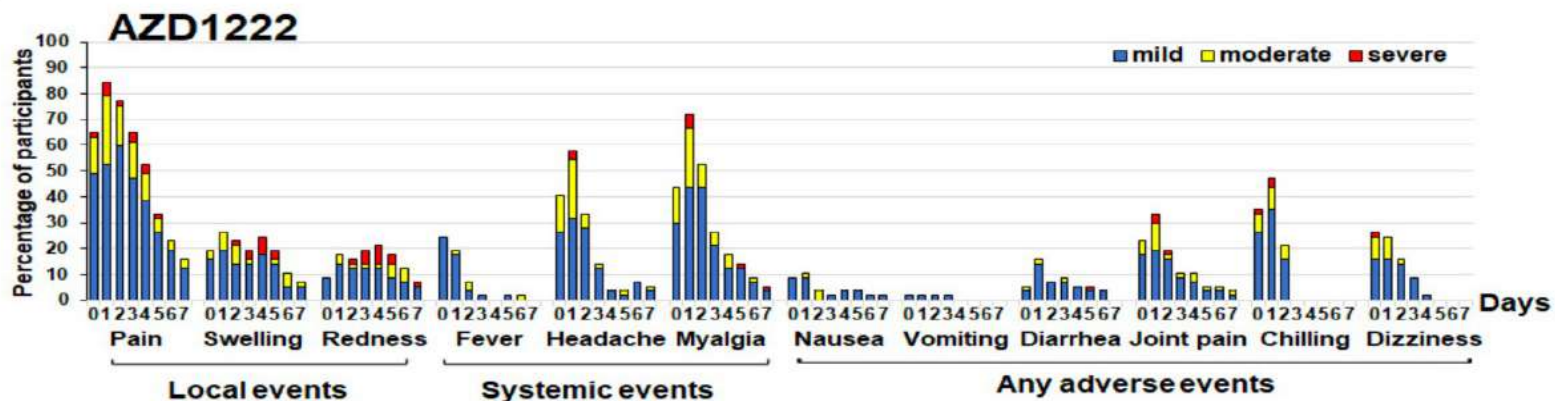
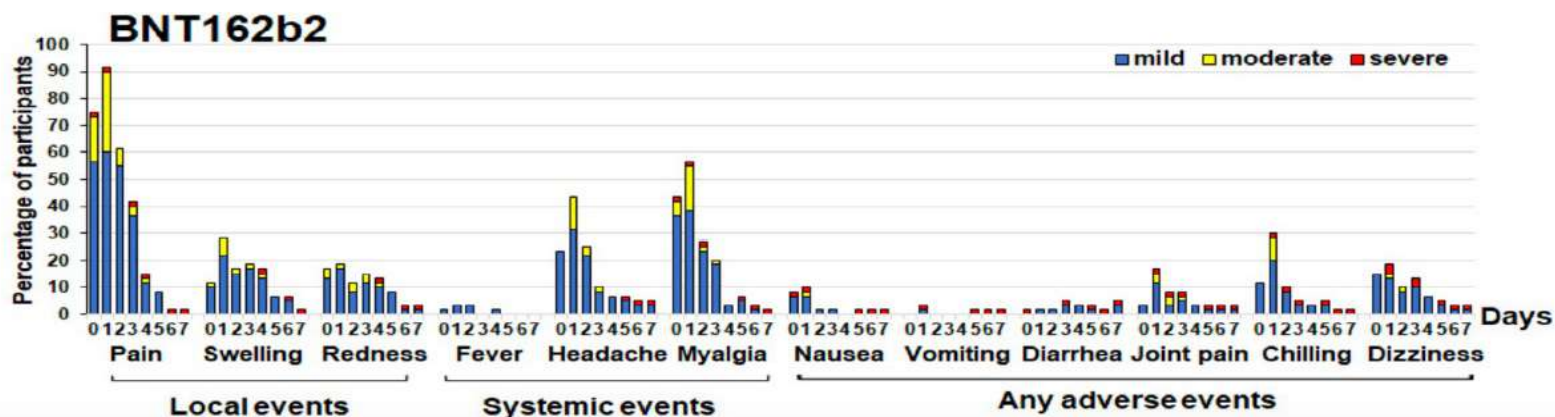
Haziran 2021’den itibaren Az-Ox, SinoPharm, BioNTech ve Moderna uygulanmış

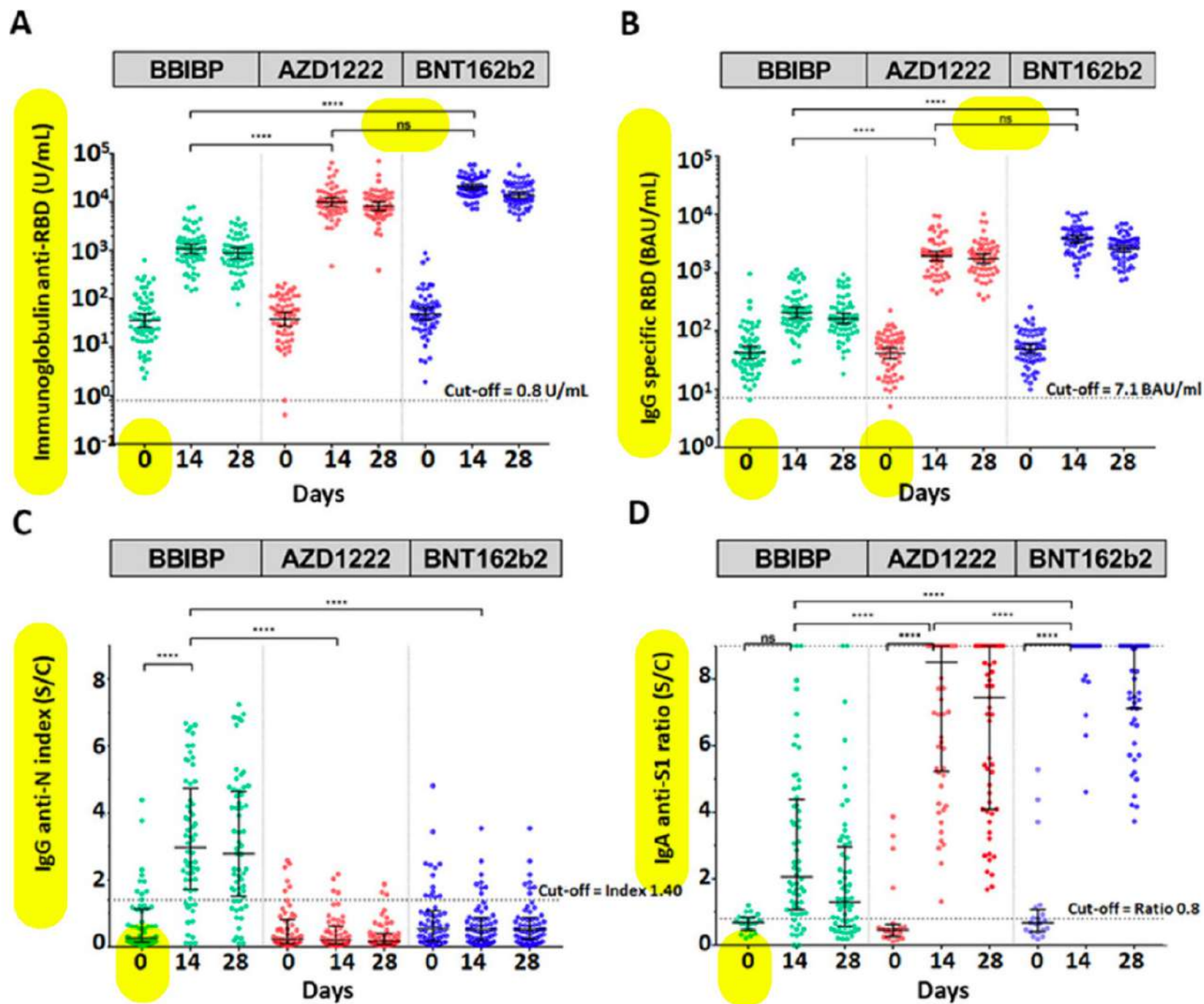
İki doz CoronaVac ile aşılanmış >18 yaş, sağlıklı 177 gönüllü,

1. doz CoronaVac’tan 3-4 ay sonra SinoPharm (60), Az-Ox (57), BioNtech (60)

İmmünojenite: Anti RBD IgG, Anti-N IgG, Anti S1 IgA, IFNgamma salınım testi,

Nötralizasyon: Beta, Gamma ve Delta suşları, sVNT (ELISA temelli)

A**B****C**

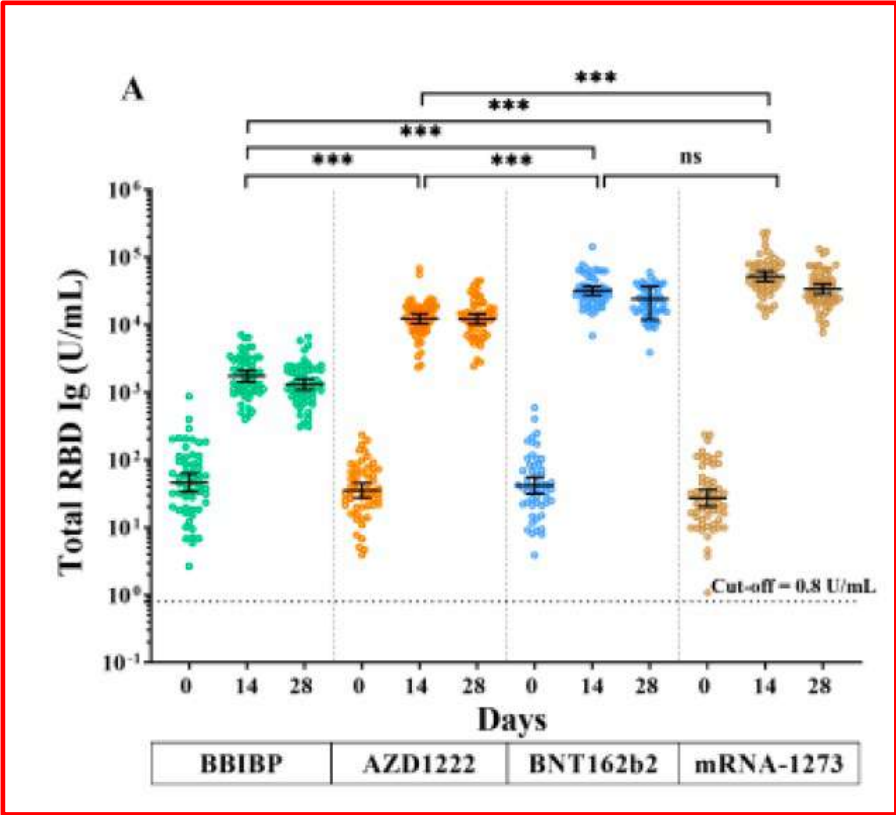


Neutralizing Activities against the Omicron Variant after a Heterologous Booster in Healthy Adults Receiving Two Doses of CoronaVac Vaccination

Suvichada Assawakosri, Sitthichai Kanokudom, Nungruthai Suntronwong, Chompoonut Auphimai, Pornjarim Nilyanimit, Preeyaporn Vichaiwattana, Thanunrat Thongmee, Thaneeya Duangchinda, Warangkana Chantima, Pattarakul Pakchotanon ... Show more

The Journal of Infectious Diseases, jiac092, <https://doi.org/10.1093/infdis/jiac092>

Published: 10 March 2022 Article history ▼



6 ay önce iki doz CoronaVac ile aşılanmış 224 kişi

Characteristic	Total	BBIBP	AZD1222	BNT162b2	mRNA-1273
Total number(n)	224	57	55	54	58

Rapel:

Primer seride uygulanandan bağımsız olarak FDA onaylı herhangi bir aşıyla

		Group	Sample Size	EUA Vaccine	Interval (weeks)	Delayed Booster Vaccination	Strategy Tested
Booster Vaccination	Moderna (100 mcg)	1	50	Previously dosed Janssen – Ad26.COV2-S	≥12	Moderna- mRNA-1273	Same Strain Heterologous platform
		2	50	Previously dosed Moderna – mRNA-1273	≥12	Moderna- mRNA-1273	Control - Same Strain & platform
		3	50	Previously dosed Pfizer/BioNTech –BNT162b2	≥12	Moderna- mRNA-1273	Same Strain Similar platform
	Janssen (5x10 ¹⁰ vp)	4	50	Previously dosed Janssen – Ad26.COV2-S	≥12	Janssen – Ad26.COV2.S	Control - Same Strain & platform
		5	50	Previously dosed Moderna – mRNA-1273	≥12	Janssen – Ad26.COV2.S	Same Strain Heterologous platform
		6	50	Previously dosed Pfizer/BioNTech –BNT162b2	≥12	Janssen – Ad26.COV2.S	Same Strain Heterologous platform
	Pfizer (30 mcg)	7	50	Previously dosed Janssen – Ad26.COV2-S	≥12	Pfizer/BioNTech – BNT162b2	Same Strain Heterologous platform
		8	50	Previously dosed Moderna – mRNA-1273	≥12	Pfizer/BioNTech- BNT162b2	Same Strain Similar platform
		9	50	Previously dosed Pfizer/BioNTech –BNT162b2	≥12	Pfizer/BioNTech – BNT162b2	Control - Same Strain & platform

Study Visits: Days 1, 8 (safety call), 15, 29, Months 3, 6, 12
Blood for immunogenicity studies

3

Atmar et al. ACIP Oct 21, 2021

Robert L. Atmar, MD representing Mix and Match Study Team Baylor College of Medicine

Conclusions -

1. Use of mRNA-1273, Ad26.COV2.S and BNT162b2 as booster vaccines led to anamnestic serologic responses in all 3 EUA-dose vaccine groups
2. For a given primary EUA Covid-19 vaccine, heterologous boosts elicited similar or higher serologic responses as compared to their respective homologous booster responses
3. mRNA vaccines resulted in higher antibody titers in the first 28 days after the boost
4. No safety concerns identified

Preprint: <https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2>

15

Atmar et al. ACIP Oct 21, 2021

participants. Booster vaccines increased the neutralizing activity against a D614G pseudovirus (4.2-76-fold) and binding antibody titers (4.6-56-fold) for all combinations; homologous boost increased neutralizing antibody titers 4.2-20-fold whereas heterologous boost increased titers 6.2-76-fold. Day 15 neutralizing and binding antibody titers varied by 28.7-fold and 20.9-fold, respectively, across the nine prime-boost combinations.

30.11.2021



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

<https://www.ema.europa.eu/en/news/ema-ecdc-recommendations-heterologous-vaccination-courses-against-covid-19-mix-match-approach-can-be>

13 December 2021
EMA/349565/2021
Biological Health Threats and Vaccine Strategy Office
EMA Pandemic Task Force for COVID-19 (COVID-ETF)

Heterologous primary and booster COVID-19 vaccination

Evidence based regulatory considerations

Primer Bağışıklama:

- Vektör aşı/mRNA aşı kombinasyonu iyi tolere ediliyor ve VA/VA'ya kıyasla artmış immün yanıt sağlıyor
- Bazı çalışmalarda aşı reaksiyonunda artış (%20-25) görülse de kesin kanı belirtmek için yeterli veri yok
- VA/mRNA hafıza B lenfosit yanıtı dahil olmak üzere immün yanıtta belirgin artış sağlıyor. Humoral yanıt bazı çalışmalarda mRNA/mRNA şemasına kıyasla daha yüksek tespit edilse bile çoğunda benzer
- Aşı etkililiğini değerlendiren gözlemsel çalışmalarda semptomatik infeksiyondan koruma etkililiği heterolog aşılama VA/VA'ya kıyasla daha yüksek (~%20), mRNA/mRNA ile benzer
- Öncül ancak tutarlı çalışmalar heterolog aşılama ile humoral ve hücresel yanıtın dahil olduğu daha geniş bir bağışıklık yanıtı sağlandığını gösteriyor

- Elimizdeki mevcut veri VA/mRNA aşılmasının kullanılmasını destekliyor.
- mRNA/mRNA heterolog aşılmasıyla ilgili yeterli veri olmamakla birlikte mevcut veriler toplumdaki aşılama sürecinin hızlandırılması için esneklik sağlanmasına izin veriyor. Bu uygulamanın miyokardit gibi yan etkiler açısından ne kadar riskli olduğuna dair araştırmalar devam ediyor.
- mRNA/VA şemasının immünolojik açıdan VA/mRNA şemasına kıyasla daha dezavantajlı olduğu gözlense de aşıya erişim sorunu olduğunda mRNA'dan sonra VA aşısı yapılabilir.
- Heterolog aşılama ile elde edilen bağışıklığın 6 aydan sonra azaldığını gösteren çalışmalar bulunmakla birlikte en hızlı bağışıklık azalması VA/VA şemasında olmaktadır. Yaşlı ve düşükün kişilerde azalma hızı her iki şemada daha fazladır.
- Bağışıklık yetmezliği olanlarda heterolog aşılama ile ilgili yeterli veri yoktur.

Hatırlatma Dozları

Daha fazla sayıda ve çeşitlilikte aşı tipleriyle çalışmalar var
(TR'den immünojenite çalışması var: Keskin ve ark.)

- Hangi aşı tipiyle olursa olsun heterolog hatırlatma dozu homolog uygulamaya kıyasla immünojenite yönünden ya benzer ya da daha başarılı.
- VA/VA → mRNA mRNA/mRNA → VA şemasına kıyasla daha etkili
- Güvenlik açısından sorun yok
- Heterolog aşı ile hatırlatma uygulaması bazı aşılarda koruyuculuğunu artırmak, aşı temini ve aşı reddi sorunlarının aşılması için uygun bir yaklaşım olarak değerlendirilebilir.
- Primer şemadan 3 ay sonrasında itibaren güvenli ve etkili bir şekilde uygulanabilir. (3 ay halk sağlığı açısından 6 aya kıyasla daha tercih edilir bir süre olabilir)
- Güvenlik verisi sınırlı olup aşı reaksiyonları için daha fazla veriye ihtiyaç vardır
- İmmünojenitedeki artışın aşı etkililiğine ne ölçüde yansıdığı net olmamakla birlikte Delta'nın yoğun olduğu ülkelerden hatırlatma dozları ile ilgili gelen veriler olumludur.
- Bağışıklık yetmezliği olanlarda heterolog aşılama ile ilgili yeterli veri yoktur.

Hastalığı geçirenler ne zaman? nasıl aşılanmalı?

ORIGINAL ARTICLE

Effectiveness of the BNT162b2 Vaccine after Recovery from Covid-19

Ariel Hammerman, Ph.D., Ruslan Sergienko, M.A., Michael Friger, Ph.D.,

This article was published on February 16, 2022, at NEJM.org.

DOI: 10.1056/NEJMoa2119497

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İsrail, retrospektif kohort çalışması,
1 Mart-26 Kasım 2021 döneminde COVID-19 tanısı almış 149 032 kişi
83 356 (%56) hastalık sonrasında BioNTech ile aşılanmış

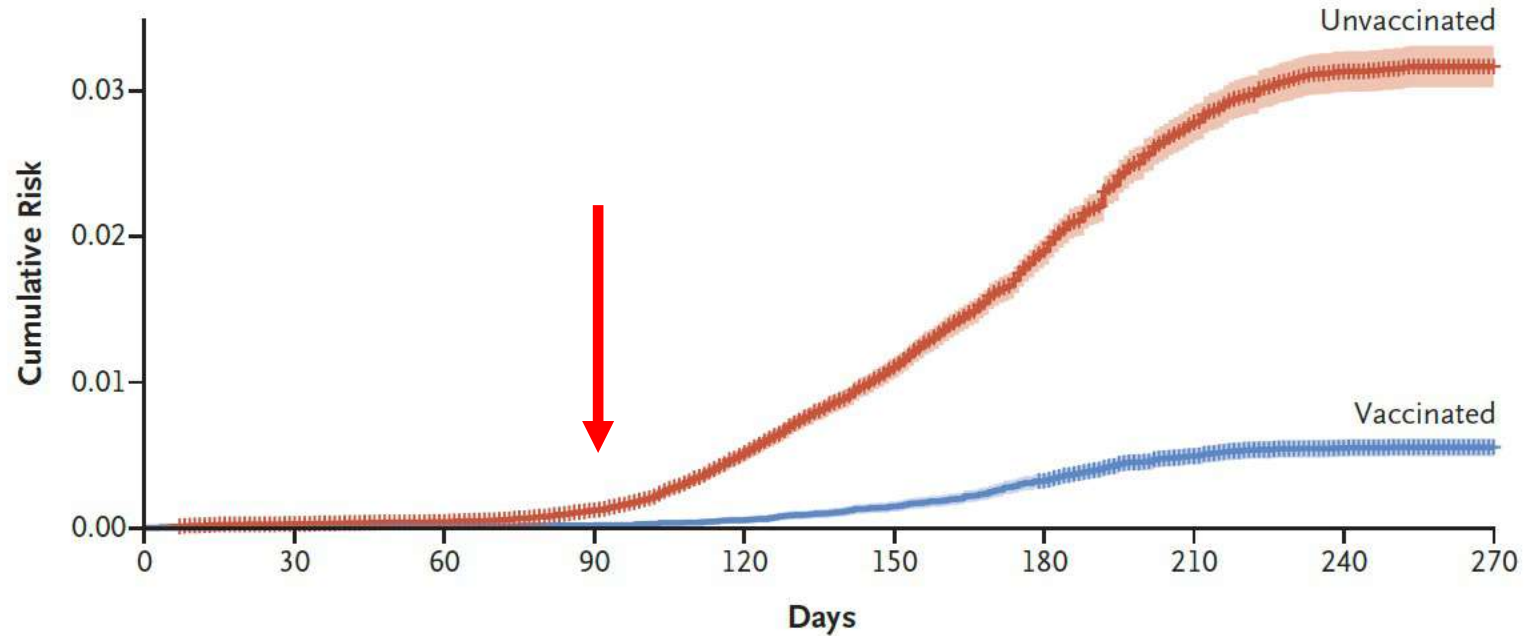
Table 3. Association between SARS-CoV-2 Reinfection and Demographic and Clinical Variables, According to Age Group.*

Variable	Hazard Ratio for Reinfection (95% CI)	
	16–64 Yr of Age (N=134,849)	≥65 Yr of Age (N=14,183)
Vaccination	0.18 (0.16–0.20)	0.40 (0.24–0.64)

years of age or older. No substantial difference was found in reinfection risk for two doses of vaccine as compared with one dose. The evidence that was gathered in this study during a

Bir doz vs İki doz: FARK YOK

A 16–64 Yr of Age



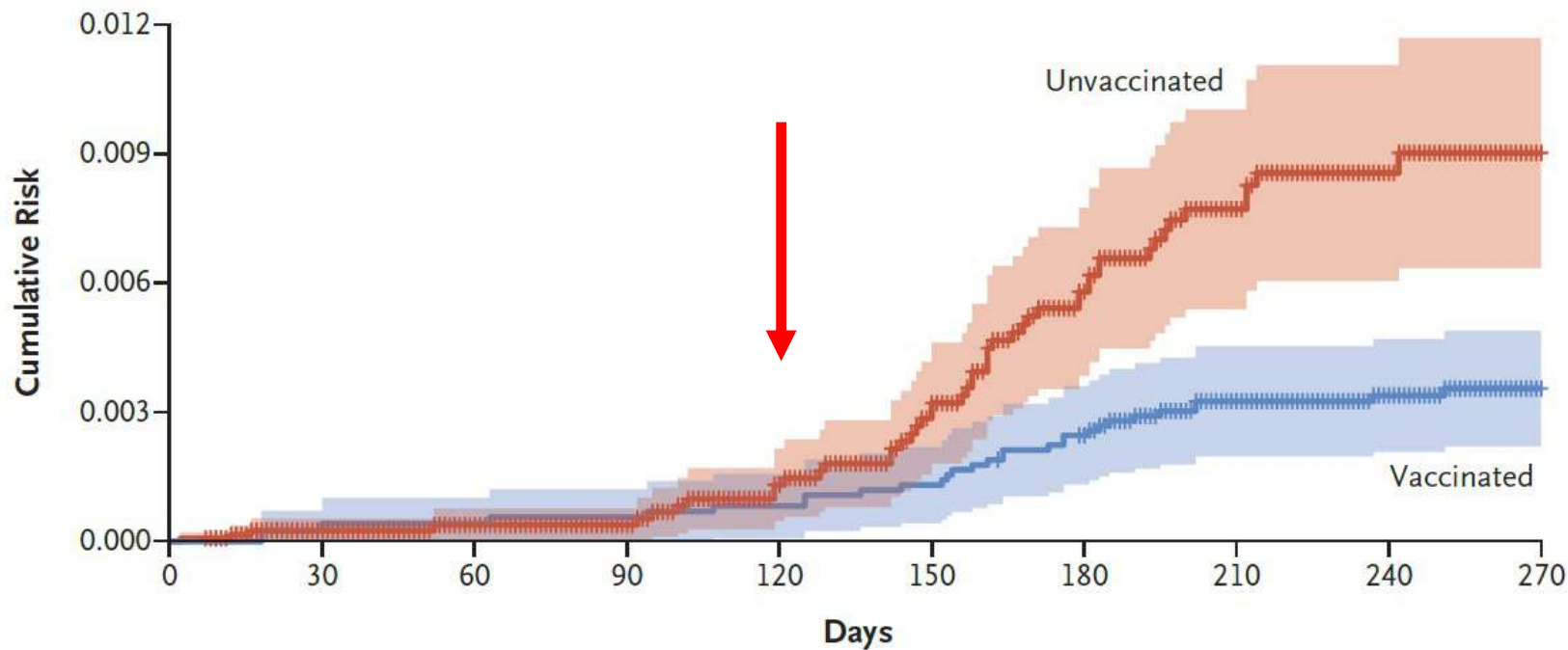
No. at Risk

Unvaccinated	134,849	104,620	95,520	88,252	82,172	75,178	68,564	43,962	24,140	18,146
Vaccinated	18,607	31,145	42,857	46,471	52,218	58,693	64,255	60,263	45,306	36,239

Cumulative No. of Events

Unvaccinated	0	34	49	122	452	916	1,490	1,989	2,113	2,120
Vaccinated	0	1	4	7	24	76	185	292	324	326

B ≥ 65 Yr of Age



No. at Risk

Unvaccinated	14,183	8,599	7,299	6,758	6,177	5,627	5,218	3,733	2,224	1,642
Vaccinated	4,146	5,580	6,955	7,504	8,056	8,552	8,882	8,725	7,015	5,432

**Cumulative No.
of Events**

Unvaccinated	0	3	4	4	10	21	35	44	47	48
Vaccinated	0	2	2	3	5	9	19	26	27	28

ORIGINAL ARTICLE

Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection

V. Hall, S. Foulkes, F. Insalata, P. Kirwan, A. Saei, A. Atti, E. Wellington,

This article was published on February 16, 2022, at NEJM.org.

DOI: 10.1056/NEJMoa2118691

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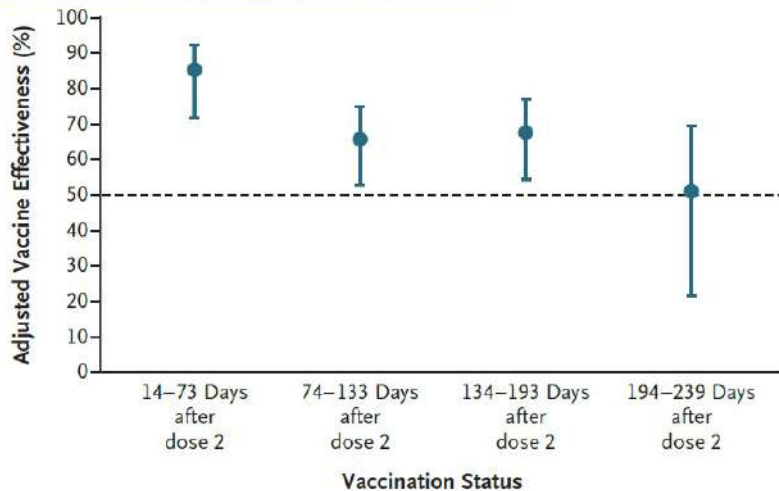
Sağlık çalışanları (PCR, LFD, Antikor ve anket ile takipli), prospektif kohort (SIREN study)

35 768 kişi, %97 iki doz aşı (87 BionTech, 8 Az-Ox), %84 kadın, Medyan yaş 46

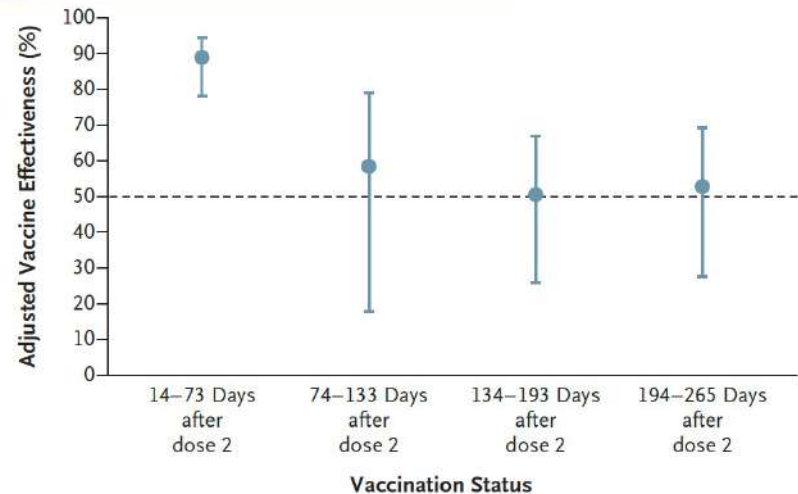
7 Aralık 2020-21 Eylül 2021: 2747 primer, 210 re-infeksiyon

Delta varyantının hakim olduğu 6 aylık dönem

A BNT162b2 Vaccine, Long Interval between Doses

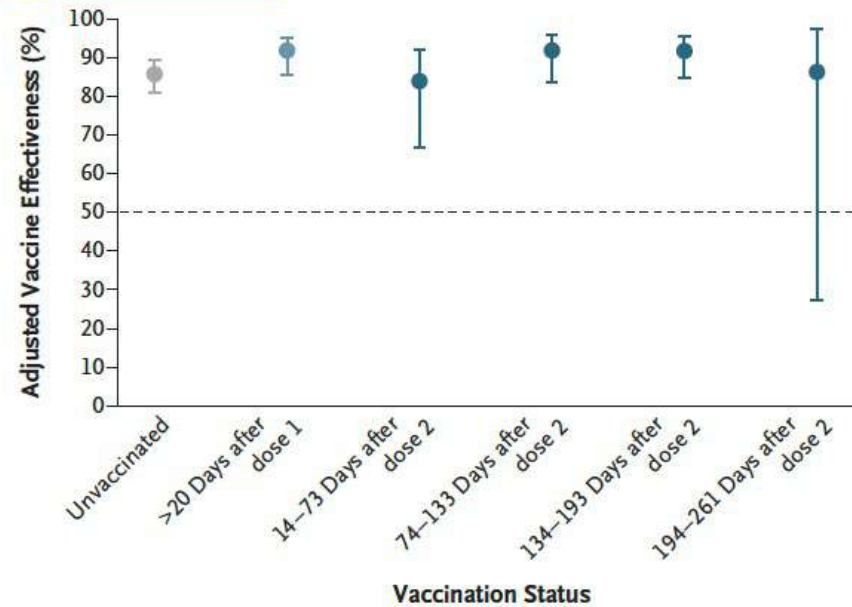


B BNT162b2 Vaccine, Short Interval between Doses

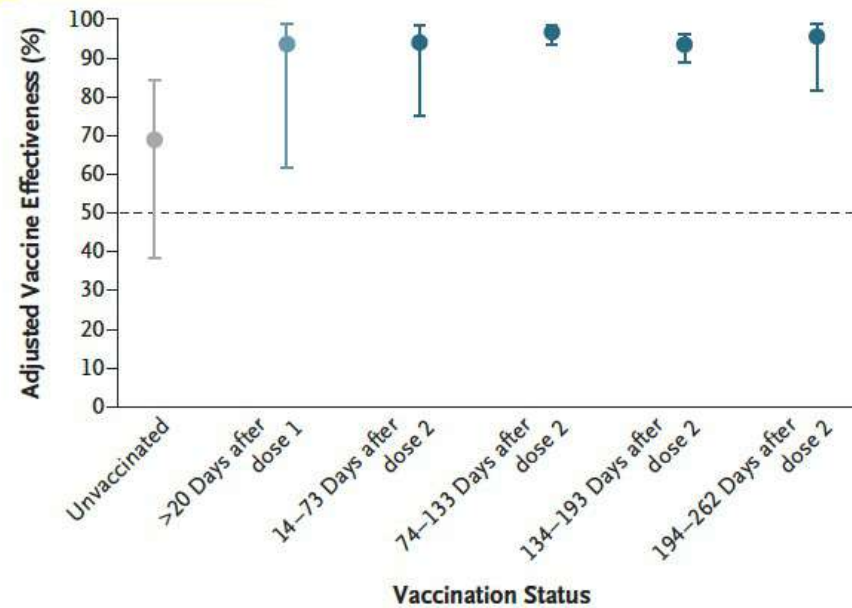


● Unvaccinated ● Vaccinated with 1 dose ● Vaccinated with 2 doses

A Primary Infection ≤ 1 Yr



B Primary Infection >1Yr

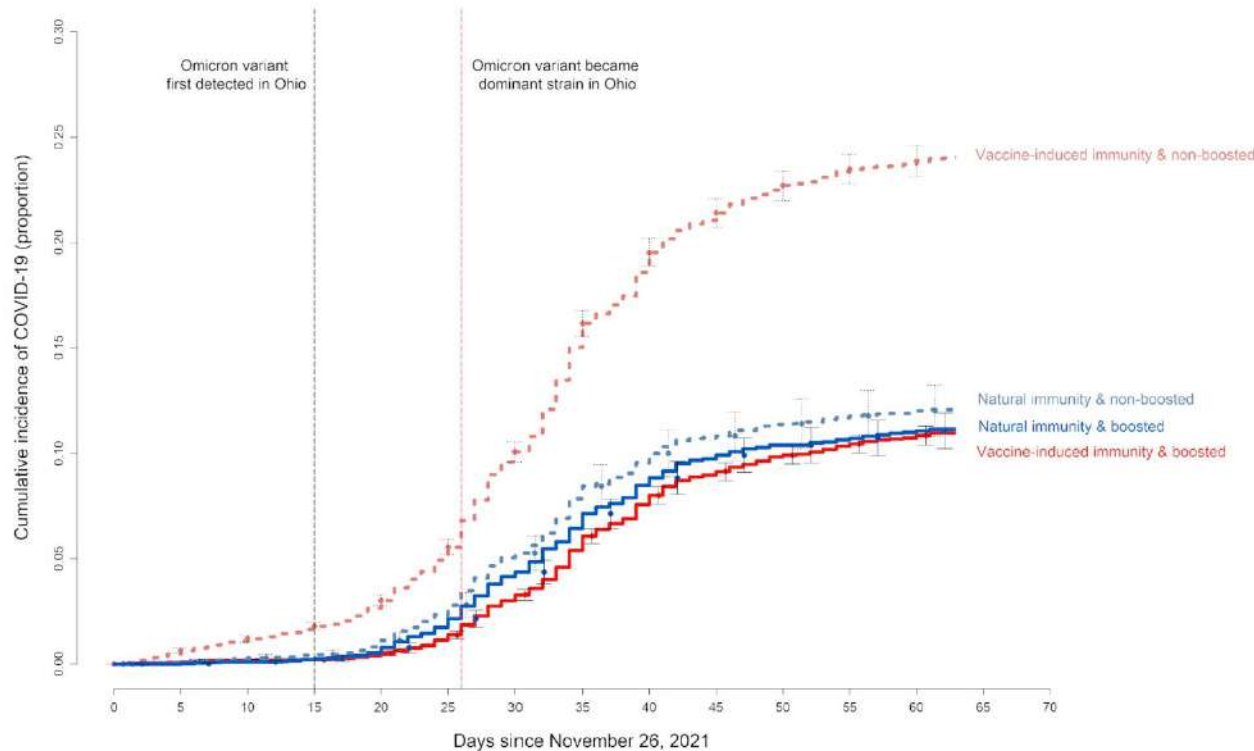


Coronavirus Disease 2019 (COVID-19) Vaccine Boosting in Persons Already Protected by Natural or Vaccine-Induced Immunity

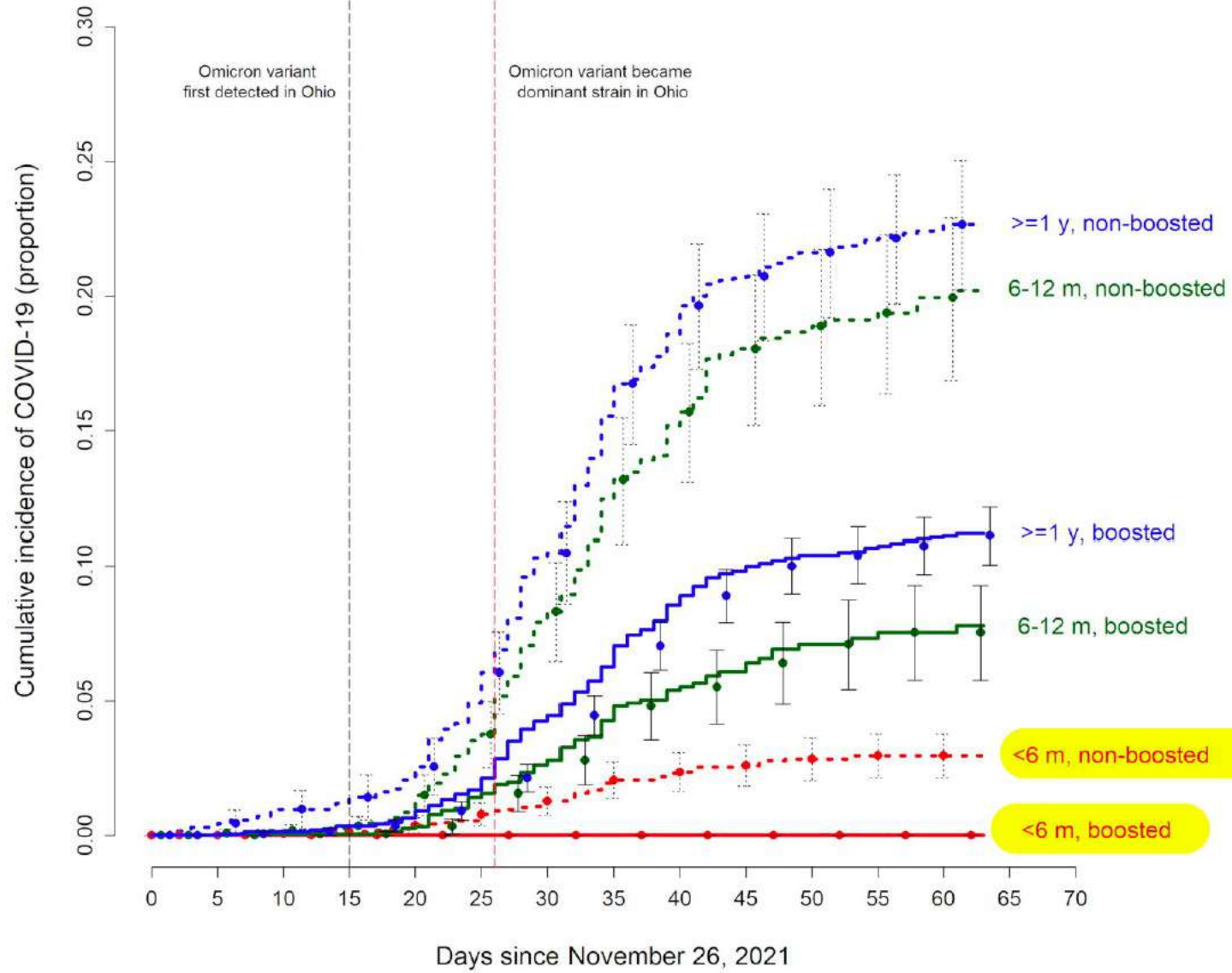
Posted February 13, 2022.

39 766 önceden aşıli veya COVID-19 geçirmiş (8037:%20) «Cleveland Clinic» çalışanı Omikronun yaygın olduğu 2 ay boyunca izlenmiş

Cumulative incidence of COVID-19 among individuals with natural and vaccine-mediated immunity who did and did not receive a vaccine booster

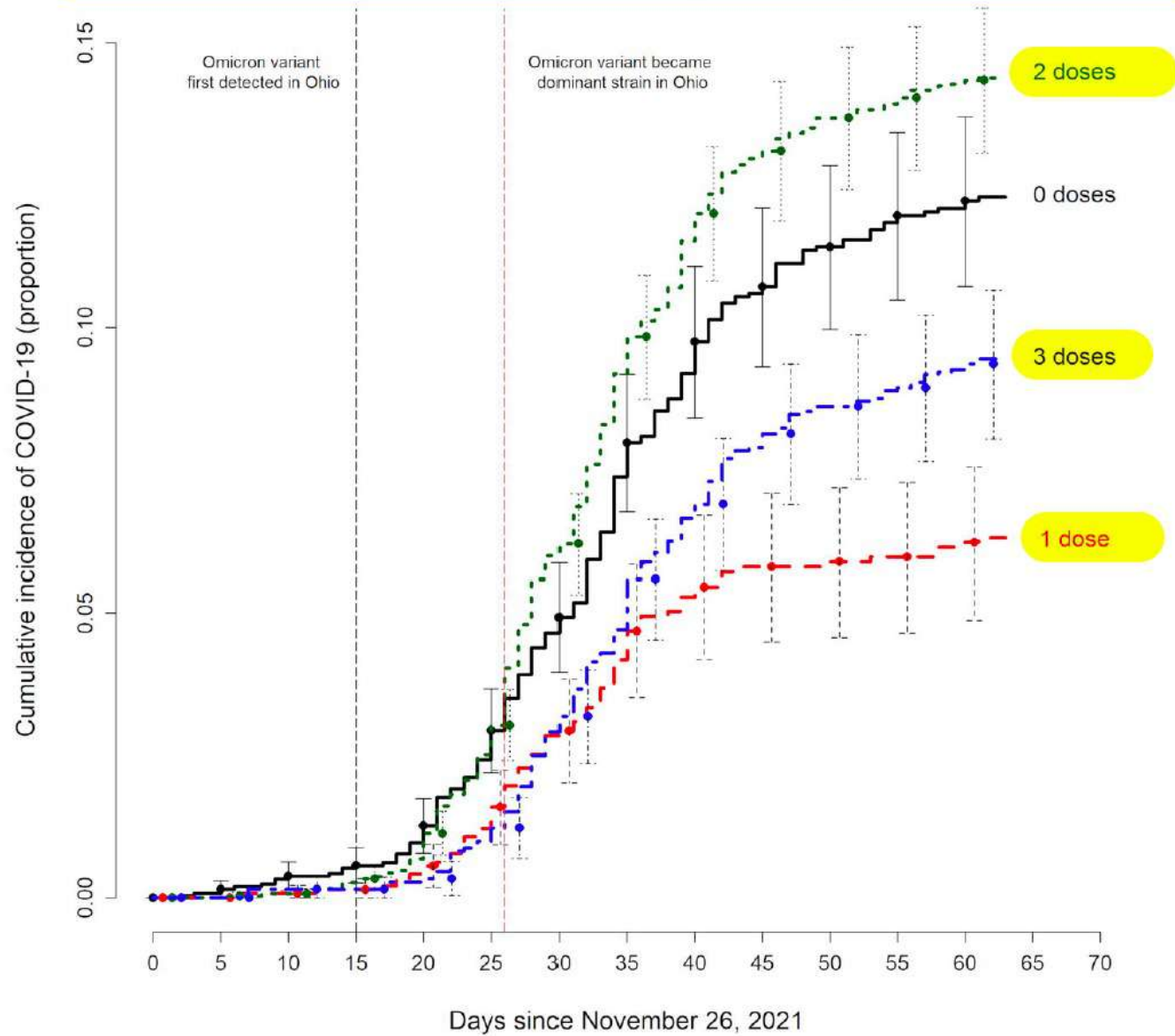


Risk of COVID-19 among individuals with natural immunity stratified by time since prior infection and vaccination

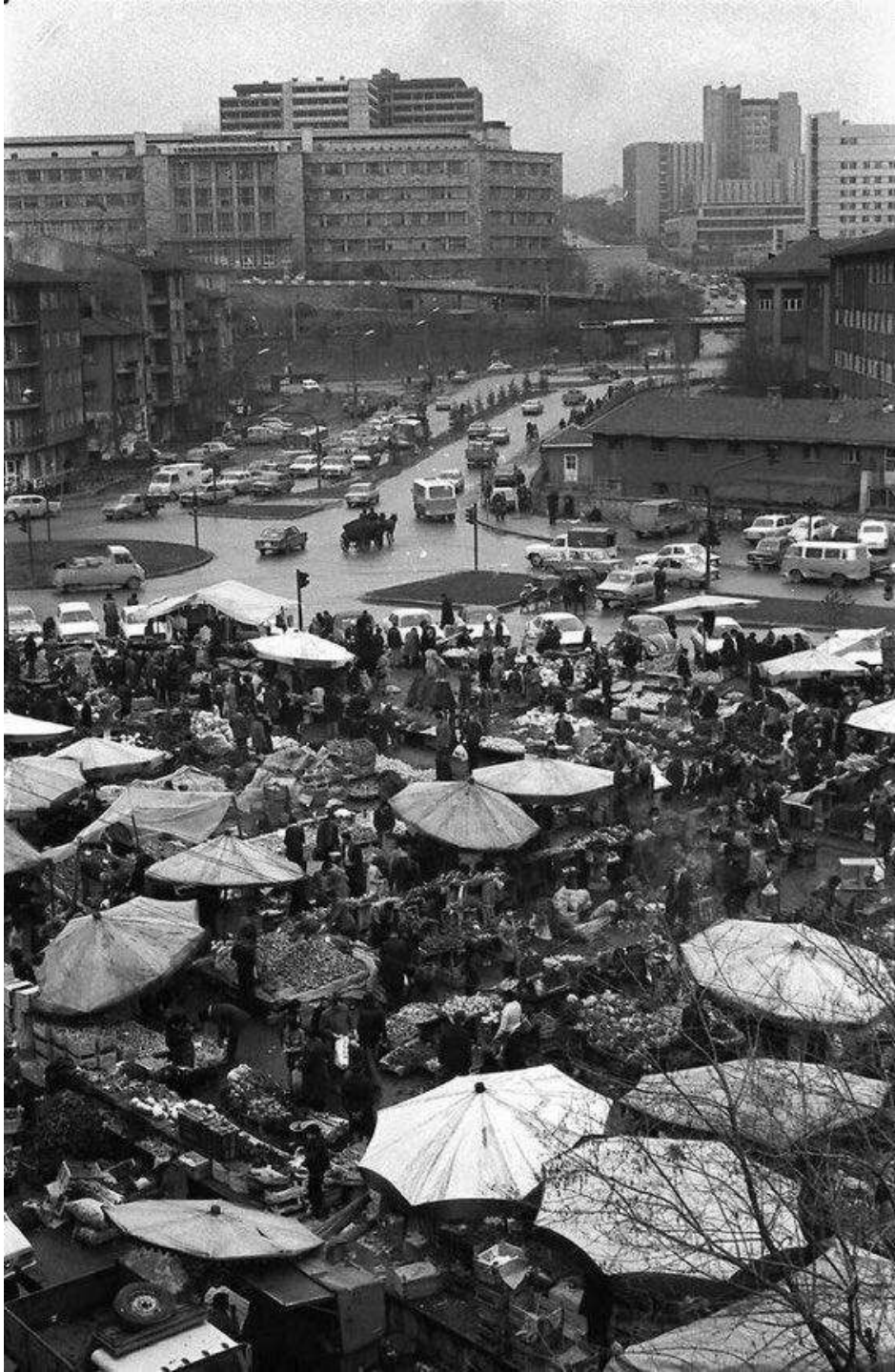


Hastalık geirenler 6 aydan nce aşı yapmanın katkısı ok ok az

Risk of COVID-19 among those with natural immunity, stratified by number of vaccine doses



Hastalık geçirenlere 1'den fazla doz yapmaya gerek yok



teşekkürler