4. US Bureau of Labor Statistics. Home page. Accessed July 29, 2021. https://www.bls.gov/

5. Vasan A, Kenyon CC, Feudtner C, Fiks AG, Venkataramani AS. Association of WIC participation and electronic benefits transfer implementation. *JAMA Pediatr*. 2021;175(6):609-616. doi:10.1001/jamapediatrics.2020.6973

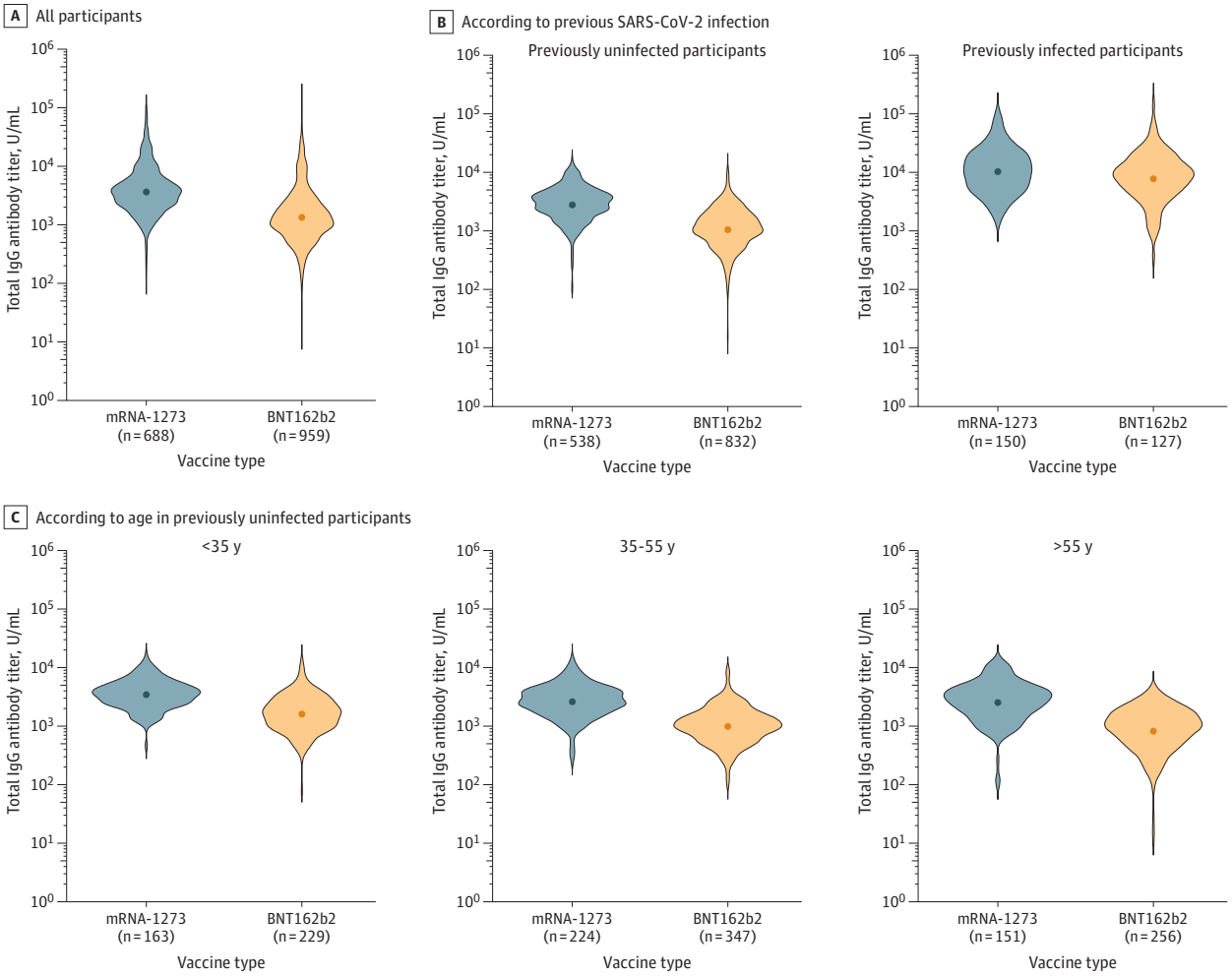
Comparison of SARS-CoV-2 Antibody Response Following Vaccination With BNT162b2 and mRNA-1273

The SARS-CoV-2 messenger RNA (mRNA) vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) have each shown more than 90% efficacy in preventing COVID-19 illness[1,2] but, to our knowledge, humoral immune responses have not been compared directly.

Methods | Health care workers at a tertiary care center (Ziekenhuis Oost-Limburg, Belgium) who were scheduled for vaccination with 2 doses of either mRNA-1273 or BNT162b2 were invited to participate in this prospective cohort. Serologic testing was performed prior to vaccination as well as 6 to 10 weeks after the second dose (between April 27 and May 20, 2021). Total immunoglobulin levels to the receptor-binding domain of the SARS-CoV-2 spike protein were measured with an anti-SARS-CoV-2 S enzyme immunoassay (Elecsys, Roche Diagnostics International Ltd). After vaccination, antibodies against the SARS-CoV-2 nucleocapsid protein were determined. Previous infection was defined as anti-nucleocapsid positivity at any point, anti-spike positivity before vaccination, and/or a history of positive polymerase chain reaction results on nasopharyngeal swab.

Antibody levels were compared after the second dose of each vaccine for the entire cohort; for those previously infected vs uninfected; and by age group (<35, 35-55, and >55 years) among previously uninfected individuals, using the *t* test after $\log_{10}$ transformation. Correlation between

Figure. Humoral Immune Response Following SARS-CoV-2 mRNA Vaccination



Violin plots of circulating SARS-CoV-2 anti–spike protein receptor-binding domain antibodies in serum samples obtained from participants after they received 2 doses of an mRNA vaccine. Inside each violin plot, the geometric mean is depicted as a point. A, Difference between participants vaccinated with mRNA-1273 (Moderna) vs those with BNT162b2 (Pfizer-BioNTech). B, Difference according to previous SARS-CoV-2 infection and the type of mRNA vaccine. C, Difference according to age and the type of mRNA vaccine in previously uninfected participants. All comparisons were significant at $P < .001$ except previously infected participants (panel B), which was significant at $P = .01$.

Table. Multivariable Linear Regression Model of log_{10}-Transformed Antibody Levels After Second Dose of an mRNA COVID-19 Vaccine

	Regression coefficient (95% CI)	*P* value
Vaccine type		
BNT162b2	[Reference]	<.001
mRNA-1273	0.359 (0.326 to 0.392)	
Previous infection with SARS-CoV-2		
Uninfected	[Reference]	
Infected	0.692 (0.649 to 0.736)	<.001
Age, per year (starting at 21 y)	-0.006 (-0.007 to -0.004)	<.001
Sex		
Male	[Reference]	
Female	0.047 (0.005 to 0.089)	.03
Time between vaccination and testing, per day	-0.005 (-0.006 to -0.003)	<.001

age and log_{10}-transformed antibody levels was assessed with Pearson correlation. To adjust for confounding, a multiple linear regression was fitted with inclusion of age, sex, previous infection, and time between vaccination and serologic testing. All tests were 2-sided with statistical significance set at α = .05. Analyses were performed using RStudio (version 1.2.1335). This study was approved by the local institutional review board; participants provided written informed consent.

Results | Of 2499 health care workers who received 2 doses of SARS-CoV-2 mRNA vaccines, 1647 participated in this study. A total of 688 were vaccinated with mRNA-1273 (mean age, 43.2 years; 76.7% women; 21.8% previously infected with SARS-CoV-2), and 959 with BNT162b2 (mean age, 44.7 years; 84.9% women; 13.2% previously infected).

Higher antibody titers were observed in participants vaccinated with 2 doses of mRNA-1273 compared with those vaccinated with BNT162b2 (geometric mean titer [GMT], 3836 U/mL [95% CI, 3586-4104] vs 1444 U/mL [95% CI, 1350-1544]; *P* < .001) (**Figure**, A).

Previously infected participants had higher antibody titers (GMT, 9461 U/mL [95% CI, 8494-10 539]) compared with previously uninfected participants (GMT, 1613 U/mL [95% CI, 1539-1690]) (*P* < .001). In both groups, those vaccinated with mRNA-1273 had higher antibody titers compared with those vaccinated with BNT162b2 (previously uninfected: GMT, 2881 U/mL [95% CI, 2721-3051] vs 1108 U/mL [95% CI, 1049-1170]; *P* < .001; previously infected: GMT, 10 708 U/mL [95% CI, 9311-12 315] vs 8174 U/mL [95% CI, 6923-9649]; *P* = .01). The difference in antibody levels according to previous infection was higher than the difference between the 2 mRNA vaccines (Figure, B, and **Table**).

Antibody levels negatively correlated with age in previously uninfected participants (correlation coefficient, −0.22; *P* < .001), being highest among those younger than 35 years. Across all age categories, previously uninfected participants vaccinated with mRNA-1273 had higher antibody titers compared with those vaccinated with BNT162b2 (*P* < .001 for all comparisons; Figure, C).

The type of mRNA vaccine remained independently associated with the log-transformed antibody titer in a multiple linear regression (*P* < .001; Table).

Discussion | This study demonstrated a significantly higher humoral immunogenicity of the SARS-CoV-2 mRNA-1273 vaccine (Moderna) compared with the BNT162b2 vaccine (Pfizer-BioNTech), in infected as well as uninfected participants, and across age categories. The higher mRNA content in mRNA-1273 compared with BNT162b2 and the longer interval between priming and boosting for mRNA-1273[3] (4 weeks vs 3 weeks for BNT162b2) might explain this difference.

A relationship between neutralization level after SARS-CoV-2 vaccination and protection against COVID-19 has been demonstrated by several studies.[4] As such, the height of the humoral response after vaccination, which correlates with neutralizing antibody titers,[5] might be clinically relevant.

Limitations of this study include the lack of data on cellular immunity and on neutralizing antibodies, as well as the specific focus on health care workers. Whether the observed difference in antibody level translates to a difference in the duration of protection,[4] the protection against variants of concern, and the risk of transmission[6] needs further investigation. Future research should also address the relevance for patients with reduced antibody response after vaccination.

Deborah Steensels, PharmD, PhD
Noella Pierlet, MSc
Joris Penders, MD, PhD
Dieter Mesotten, MD, PhD
Line Heylen, MD, PhD

Author Affiliations: Ziekenhuis Oost-Limburg, Genk, Belgium.

Corresponding Author: Deborah Steensels, PharmD, PhD, Department of Laboratory Medicine, Ziekenhuis Oost-Limburg, Schiepse Bos 6, 3600 Genk, Belgium (Deborah.steensels@zol.be).

Accepted for Publication: August 19, 2021.

Published Online: August 30, 2021. doi:10.1001/jama.2021.15125

Author Contributions: Drs Steensels and Heylen had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Steensels, Penders, Mesotten, Heylen.
Acquisition, analysis, or interpretation of data: Steensels, Pierlet, Penders, Heylen.
Drafting of the manuscript: Steensels, Heylen.
Critical revision of the manuscript for important intellectual content: Pierlet, Penders, Mesotten, Heylen.
Statistical analysis: Steensels, Pierlet, Heylen.
Obtained funding: Steensels, Penders, Mesotten.
Administrative, technical, or material support: Steensels, Penders, Mesotten.
Supervision: Steensels, Penders.

Conflict of Interest Disclosures: None reported.

Funding/Support: Roche Diagnostics International Ltd provided test reagents and Interreg Euregio Meuse-Rhine provided financial support (grant EMR-187 CODAP).

Role of the Funder/Sponsor: Funders were not involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Additional Contributions: We thank Maarten Coemans, MSc, PhD (Leuven Biostatistics Centre, KU Leuven), for his statistical advice. He was not compensated for his contribution.

1. Baden LR, El Sahly HM, Essink B, et al; COVE Study Group. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2021;384(5):403-416. doi:10.1056/NEJMoa2035389

2. Polack FP, Thomas SJ, Kitchin N, et al; C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383(27):2603-2615. doi:10.1056/NEJMoa2034577

3. Voysey M, Costa Clemens SA, Madhi SA, et al; Oxford COVID Vaccine Trial Group. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet*. 2021;397(10277):881-891. doi:10.1016/S0140-6736(21)00432-3

4. 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):1205-1211. doi:10.1038/s41591-021-01377-8

5. Rubio-Acero R, Castelletti N, Fingerle V, et al; KoCo19 study team. In search of the SARS-CoV-2 protection correlate: head-to-head comparison of two quantitative S1 assays in pre-characterized oligo-/asymptomatic patients. *Infect Dis Ther*. 2021;10(3):1505-1518. doi:10.1007/s40121-021-00475-x

6. Levine-Tiefenbrun M, Yelin I, Katz R, et al. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. *Nat Med*. 2021;27(5):790-792. doi:10.1038/s41591-021-01316-7

COMMENT & RESPONSE

Reduced-Dose vs High-Dose Glucocorticoids Added to Rituximab and Remission Induction in ANCA-Associated Vasculitis

To the Editor We have some concerns about the recent study[1] about rituximab and reduced-dose glucocorticoids vs high-dose glucocorticoids in antineutrophil cytoplasm antibody (ANCA)–associated vasculitis. In addition to the limitations of being an open-label, single-country study recruiting only new patients and having a wide noninferiority margin of −0 percentage points, the patients enrolled in this study were older (more likely to have adverse effects with high-dose glucocorticoids), had a higher proportion of myeloperoxidase (MPO) positivity (which is associated with lower chance of relapse), had a higher mean estimated glomerular filtration rate (eGFR), and had no pulse glucocorticoid therapy compared with the studies mentioned by the authors.[2-5] The mean eGFR in the reduced-dose glucocorticoid group was 55 mL/min/1.73 m^2. Therefore, most of these patients had normal to mildly abnormal kidney function, considering their age. Furthermore, because most patients had microscopic polyangiitis/MPO-ANCA positivity, which is less likely to relapse than those with granulomatosis with polyangiitis/proteinase 3 (PR3)–ANCA positivity, they were likely to remain in remission with reduced-dose glucocorticoids. It would be helpful to know if patients with PR3 positivity had the same response rate as MPO-positive patients in the study. Also, we would be interested to learn how the authors chose the treatment regimen, given that the cumulative glucocorticoid dose in the high-dose group was lower than the cumulative dose in the low-dose glucocorticoid group in the PEXIVAS trial.[4] The patient characteristics in the study by Dr Furuta and colleagues[1] were most similar to those in the ADVOCATE trial,[5] but remission rates in ADVOCATE were higher and patients were younger, had lower mean eGFR, and received a higher cumulative glucocorticoid dose. Patients in the RITUXIVAS trial[2] also had a much higher remission rate with standard-dose glucocorticoids, although the patients were sicker (mean eGFR, 20 mL/min/1.73 m^2) and younger, with 60% of patients being PR3 positive.

Patients with mild ANCA-associated vasculitis with good prognostic factors and low risk of relapse may be appropriate for the low-dose glucocorticoid regimen used in this trial,[1] but its use for treatment of patients at high risk of relapse, with greater severity or PR3 positivity, could lead to worse clinical outcomes.

Kunal Chandwar, MD
Puneet Kumar, MD
Urmila Dhakad, MD

Author Affiliations: Department of Clinical Immunology and Rheumatology, King George's Medical University, Lucknow, Uttar Pradesh, India.

Corresponding Author: Kunal Chandwar, MD, Department of Clinical Immunology and Rheumatology, King George's Medical University, Lucknow 226003, India (kunalchandwar@gmail.com).

Conflict of Interest Disclosures: None reported.

1. Furuta S, Nakagomi D, Kobayashi Y, et al; LoVAS Collaborators. Effect of reduced-dose vs high-dose glucocorticoids added to rituximab on remission induction in ANCA-associated vasculitis: a randomized clinical trial. *JAMA*. 2021;325(21):2178-2187. doi:10.1001/jama.2021.6615

2. Jones RB, Tervaert JW, Hauser T, et al; European Vasculitis Study Group. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. *N Engl J Med*. 2010;363(3):211-220. doi:10.1056/NEJMoa0909169

3. Stone JH, Merkel PA, Spiera R, et al; RAVE-ITN Research Group. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. *N Engl J Med*. 2010;363(3):221-232. doi:10.1056/NEJMoa0909905

4. Walsh M, Merkel PA, Peh CA, et al; PEXIVAS Investigators. Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. *N Engl J Med*. 2020;382(7):622-631. doi:10.1056/NEJMoa1803537

5. Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. Avacopan for the treatment of ANCA-associated vasculitis. *N Engl J Med*. 2021;384(7):599-609. doi:10.1056/NEJMoa2023386

To the Editor We would like to point out several issues with the recent trial by Dr Furuta and colleagues.[1] First, the Birmingham Vasculitis Activity Score (BVAS), a validated tool used to assess disease activity in patients with vasculitis, was not high in either glucocorticoid group, indicating that the patients included in this study did not have a high burden of disease. Furthermore, ANCA-associated vasculitis often recurs, and stopping glucocorticoids earlier has been shown to be associated with an increased risk of recurrence.[2] Therefore, reducing disease recurrence is an important consideration in clinical treatment. However, this study[1] did not provide information about whether there was a difference in the rate of recurrence between the reduced-dose and standard high-dose glucocorticoid groups.

Second, while the minimum age of the patients included in this study was 66 years, the typical age of patients with granulomatosis with polyangiitis is 45 to 65 years, and patients with microscopic polyangiitis are generally 55 to 75 years old.[3] Third, it is unclear whether organ involvement was judged by biopsy or clinical symptoms alone. Fourth, the concomitant use of trimethoprim-sulfamethoxazole for *Pneumocystis* pneumonia prophylaxis was recommended in the study. However, in the Results section reporting secondary safety end points, 2 *Pneumocystis* pneumonia cases were reported in the reduced-dose group who had not received prophylactic