Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Post-vaccination SARS-CoV-2 antibody kinetics and protection duration against Omicron in elderly population

Dear Editor,

Coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 is particularly severe in older individuals because of an impaired immune response.[1] The vaccines presently available are less efficacious in older individuals, because of the senescence of their immune systems.[2] A recent letter in Journal of Infection showed the need of a third vaccine dose due to a waning antibody response against new SARS-CoV-2 variants in healthy and immunocompromised individuals.[3] In this study, we analysed the protection against Omicron provided by the immune responses of nursing home residents (NHRs) and a population of healthcare workers (HCWs).

We measured the antibody responses of 106 older adults (> 65 years old) living in 3 French nursing homes and vaccinated with 3 doses of BNT162b, matched with 106 HCWs for sex, past COVID-19 infection and vaccination status. Blood samples were taken 3-6 weeks after their third vaccine dose (12 September 2021- 13 October 2021 for HCWs, 8 November 2021-04 January 2022 for NHRs) before the Omicron epidemic wave erupted in France. The median follow-up was 179 days (IQR: 171-182) for HCWs, and 195 days (IQR: 167-195) for NHRs. Anti-S and anti-N antibodies were measured with an electrochemiluminescent assay (Alinity, Abbott, Sligo, Ireland). Neutralizing antibody titers were assessed by end-point dilution using Vero cells (ATCC, CCL-81^{TM}) and clinical SARS-CoV-2 Omicron BA.1 and BA.2 strains.[5] Infections were detected using a nucleic-acid amplification method (Aptima^{TM}, Hologic, USA)[4] and SARS-CoV-2 RNA was sequenced using single-molecule real-time sequencing (Pacific Biosciences, USA).[6] This study was approved by the French Research Ethics Committee Est-III (COVID BioToul, ID-RCB 2020-A01292-37, ClinicalTrials.gov Identifier: NCT04385108).

The 106 NHRs (81 (76.4%) women, median age: 89 years (range: 56–103)) included 53 (50%) who had been infected before vaccination (positive SARS-CoV-2 RNA or anti-N antibodies). The median age of the 106 paired HCWs was 41 years (range: 21–61). The median BA.1 neutralizing antibody (NAb) titer of the previously-uninfected, vaccinated NHRs was higher (8, IQR: 8-24) than that of the uninfected, vaccinated HCWs (2, IQR: 2-4), $p<0.01$ Wilcoxon signed-rank test). Similarly, the median BA.1 NAb titer in the infected-vaccinated NHRs was higher (16, IQR: 16-32) than that of the matched HCWs (8, IQR: 4-16, $p=0.03$ Wilcoxon). The anti-Omicron BA.2 NAb titers of uninfected NHR (32, IQR: 8-32) and uninfected HCWs (16, IQR:8- 32, $p>0.05$, Wilcoxon signed-rank test) were not significantly different. In contrast, the anti-Omicron BA.2 NAb titers of infected-vaccinated NHRs (32, IQR: 16-64) were significantly higher than those of the infected-vaccinated HCWs (16, IQR: 16-32, $p=0.04$, Wilcoxon signed-rank test). NHRs with no prior SARS-CoV-2 infection had a median binding antibody (BAb) concentration of 1959 BAU/ml (IQR 863-4,364) one month after their third dose of vaccine, not significantly different from that of their matched HCWs (1593 BAU/ml, IQR: 1125–2698 ; $p>0.05$, Wilcoxon signed-rank test, Fig. 1A). The median BAb concentrations of the NHRs who had been infected with SARS-CoV-2 before vaccination were significantly higher (3533 BAU/ml, IQR: 2151–5391) than those of the NHRs who had not been infected (1959 BAU/ml, IQR 863–4364 ; $p=0.03$ Wilcoxon, Fig. 1B). This concentration was also higher than that of infected-vaccinated HCWs (1,931 BAU/ml, IQR: 1202–3558, $p=0.03$, Wilcoxon signed-rank test).

None of the 106 NHR given the third dose of vaccine developed an Omicron BA.1 infection, but 33 (31.1%) were infected with Omicron BA.2 at least 1 month after the booster injection. Their median BA.2 NAb titer one month after the third dose of vaccine was 12 (IQR: 8-32); it was 32 (IQR 8-64) for those who did not become infected after the booster injection. A BA.2 NAb titer below 8 provided 19.2% protection against Omicron BA.2, titers of 16 or 32 gave 85.3% protection and an NAb titer of 64 or more provided 95.6% protection. Similarly, NHRs who were infected with BA.2 SARS-CoV-2 after their third dose of vaccine had median BAb concentration of 1959 BAU/ml (IQR 863–3707); it was 3339 BAU/ml (IQR: 1714–5836 ; $p=0.03$; Wilcoxon rank test) in those who did not subsequently become infected. Most (90%) of the Omicron BA.2 infections occurred in NHRs who had BAb concentrations below 6209 BAU/ml. A BAb concentration below 1000 BAU/ml provided only 25% protection against Omicron BA.2 ; 1000–6000 BAU/ml provided 77.9% protection; while >6000 provided 97.1% protection. Consequently, we set the average protection threshold against Omicron BA.2 at 5000 BAU/ml. The median BA.2 protection time for infected/vaccinated people with initial antibody concentrations > 10,000 BAU/ml was shorter in the NHRs (median 119 days, IQR: 61-223) than in the immunocompetent HCWs (189 days, IQR: 124–405, p <0.01, Wilcoxon signed rank test, Fig. 2 A&C). It was 48 days (IQR: 1-96) for uninfected-vaccinated HCWs and 30 days for uninfected-vaccinated NHRs (IQR: 0-40, p =0.13, Wilcoxon, signed rank test Fig. 2 B&D) whose total antibody concentrations were between 2000 BAU/ml and 10,000 BAU/ml one month after the third injection. There was no protection for the 89.2% of uninfected-vaccinated NHRs whose total antibody concentrations were below 2000 BAU/ml.

The 3-doses antibody responses against Omicron provided less protection than it did against the ancestral strain, although the anti-Omicron responses in NHRs after three doses were as good

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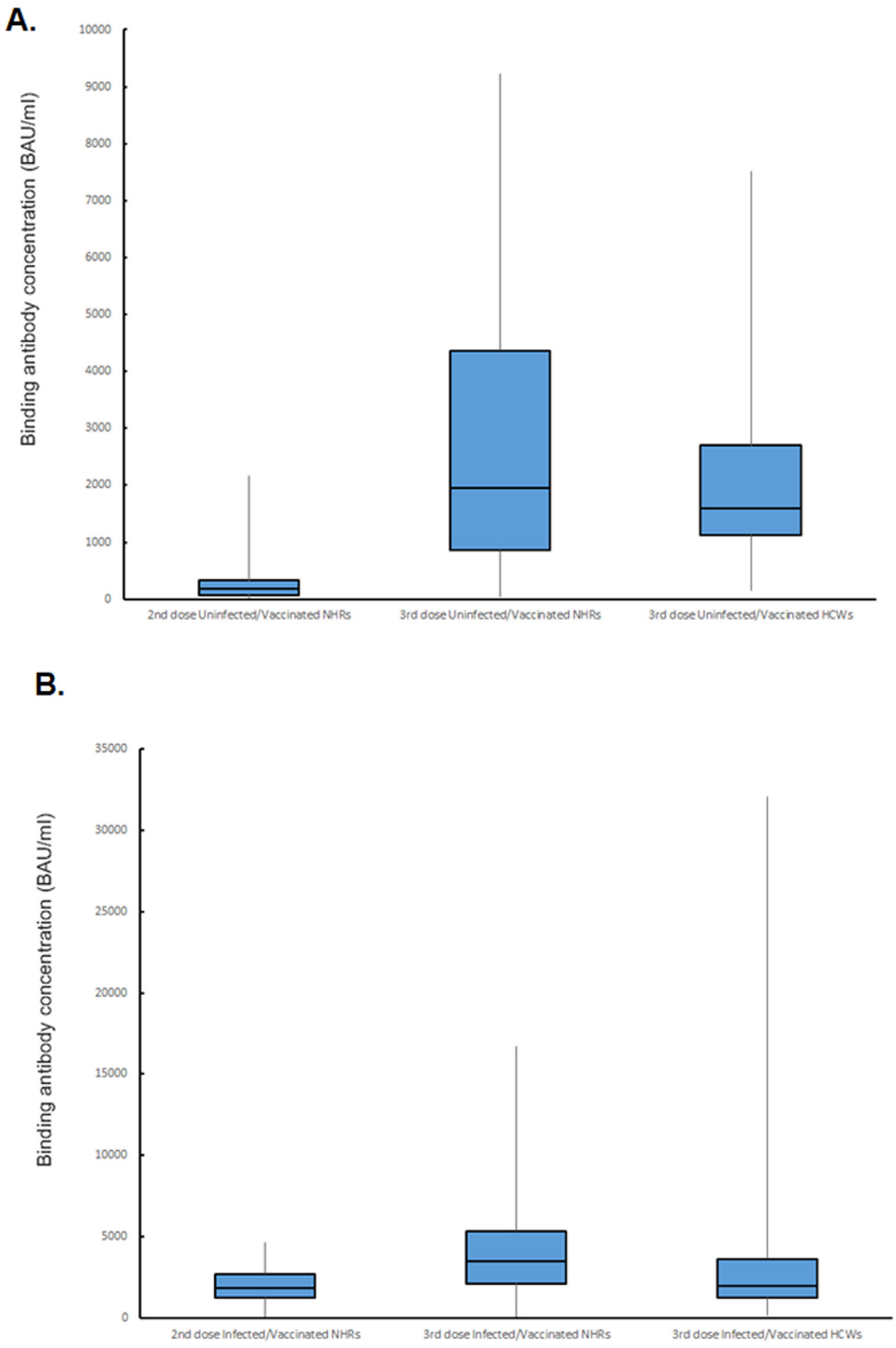

Fig. 1. A. Uninfected-Vaccinated NHRs and HCWs: binding antibody concentrations after 2/3 dose of vaccine. B. Infected-Vaccinated NHRs and HCWs: binding antibody concentrations after 2/3 dose of vaccine.

or better than those of younger adults. None of our NHRs acquired an Omicron BA.1 infection during follow-up, while 31.1% were infected with Omicron BA.2. The anti-BA.2 NAb concentration providing at least 95.6% protection against Omicron BA.2 infection was 64 or higher. This is similar to that needed to protect younger populations against pre-Omicron strains.[7-8] The BAb concentration needed to protect against Omicron BA.2 was also high (about 5000 BAU/ml), the humoral responses of both uninfected-vaccinated HCWs and uninfected-vaccinated NHRs provided insufficient protection. These people could benefit from supplementary doses. On the other hand, the antibody protection decayed faster in NHRs than in HCWs, which may explain why NHRs were protected for a shorter time despite a high initial peak antibody concentration, in agreement with a previous report.[9]

Further studies on vaccination and protective immunity in the elderly should include other markers including T cells responses.

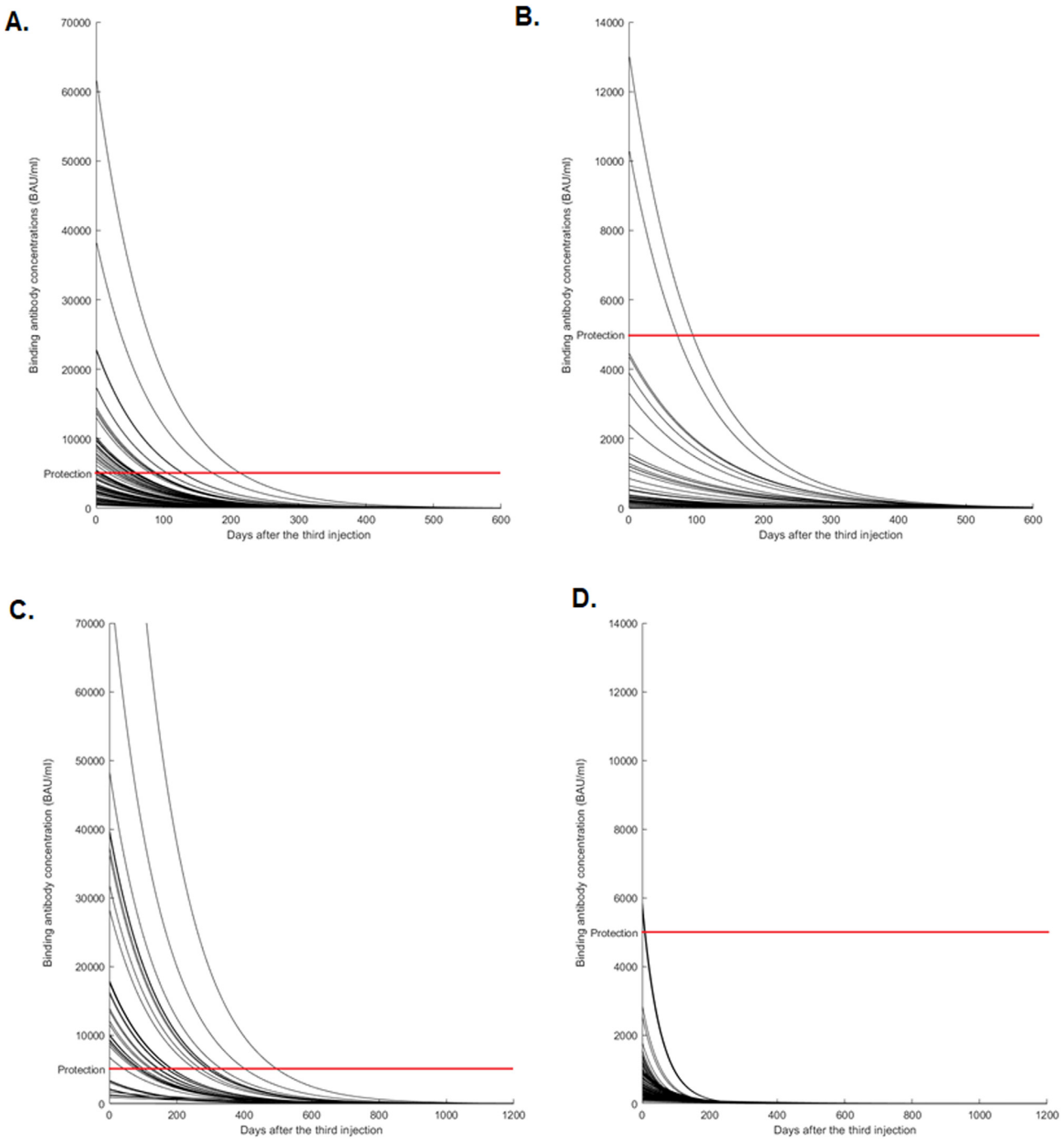

Fig. 2. Binding antibody kinetics after 3 doses of vaccine: A. Infected-vaccinated NHRs B. Uninfected-vaccinated NHRs. C. Infected-vaccinated HCWs. D. Uninfected-vaccinated HCWs.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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References

1. Bartleson JM, Radenkovic D, Covarrubias AJ, Furman D, Winer DA, Verdin E. SARS-CoV-2, COVID-19 and the ageing immune system. *Nat Aging* 2021;**1**(9):769–82. doi:10.1038/s43587-021-00114-7.
2. Collier DA, Ferreira IATM, Kotagiri P, Datir RP, Lim EY, Touizer E, et al. Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2. *Nature* 2021;**596**(7872):417–22. doi:10.1038/s41586-021-03739-1.
3. Faustini S, Shields A, Banham G, Wall N, Al-Taei S, Tanner C, et al. Cross reactivity of spike glycoprotein induced antibody against Delta and Omicron variants before and after third SARS-CoV-2 vaccine dose in healthy and immunocompromised individuals. *J Infect* 2022;**84**(4):579–613. doi:10.1016/j.jinf.2022.01.002.
4. Trémeaux P, Lhomme S, Abravanel F, Raymond S, Mengelle C, Mansuy JM, et al. Evaluation of the Aptima™ transcription-mediated amplification assay (Holog-

ic®) for detecting SARS-CoV-2 in clinical specimens. *J Clin Virol* 2020;**129**:104541. doi:10.1016/j.jcv.2020.104541.
5. Chapuy-Regaud S, Miédougé M, Abravanel F, Da Silva I, Porcheron M, Fillaux J, et al. Evaluation of three quantitative anti-SARS-CoV-2 antibody immunoassays. *Microbiol Spectr* 2021;**9**(3):e0137621. doi:10.1128/spectrum.01376-21.
6. Lhomme S, Latour J, Jeanne N, Trémeaux P, Ranger N, Migueres M, et al. Prediction of SARS-CoV-2 variant lineages using the S1-encoding region sequence obtained by pacbio single-molecule real-time sequencing. *Viruses* 2021;**13**(12):2544. doi:10.3390/v13122544.
7. Dimeglio C, Herin F, Martin-Blondel G, Miedougé M, Izopet J. Antibody titers and protection against a SARS-CoV-2 infection. *J Infect* 2022;**84**(2):248–88. doi:10.1016/j.jinf.2021.09.013.
8. Dimeglio C, Herin F, Da-Silva I, Gernigon C, Porcheron M, Chapuy-Regaud S, et al. Decreased efficiency of neutralizing antibodies from previously infected or vaccinated individuals against the B.1.617.2 (Delta) SARS-CoV-2 variant. *Microbiol Spectr* 2022:e0270621. doi:10.1128/spectrum.02706-21.
9. Dan JM, Mateus J, Kato Y, Hastie KM, Yu ED, Faliti CE, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Science* 2021;**371**(6529) eabf4063. doi:10.1126/science.abf4063.

Chloé Dimeglio*, Pauline Trémeaux
CHU Toulouse, Hôpital Purpan, Virology Laboratory, 31300 Toulouse, France
INSERM UMR1291 – CNRS UMR5051, Toulouse Institute for Infectious and Inflammatory Diseases (INFINITy), 31300 Toulouse, France

Fabrice Herin
Occupational Diseases Department, Toulouse University Hospital, 31000 Toulouse, France
Inserm UMR 1295: Center for research in population health (CERPOP)- Department of Epidemiology and Public Health, Toulouse. University of Toulouse III F-31073, 37, allées Jules Guesde, 31073 Toulouse, France

Isabelle Da-Silva, Marion Porcheron
CHU Toulouse, Hôpital Purpan, Virology Laboratory, 31300 Toulouse, France

Guillaume Martin-Blondel
INSERM UMR1291 – CNRS UMR5051, Toulouse Institute for Infectious and Inflammatory Diseases (INFINITy), 31300 Toulouse, France
Infectious and Tropical Diseases Department, Toulouse University Hospital, 31300 Toulouse, France

Caroline Gernigon
Occupational Diseases Department, Toulouse University Hospital, 31000 Toulouse, France
Inserm UMR 1295: Center for research in population health (CERPOP)- Department of Epidemiology and Public Health, Toulouse. University of Toulouse III F-31073, 37, allées Jules Guesde, 31073 Toulouse, France

Sabine Chapuy-Regaud
CHU Toulouse, Hôpital Purpan, Virology Laboratory, 31300 Toulouse, France

Hélène Villars
Inserm UMR 1295: Center for research in population health (CERPOP)- Department of Epidemiology and Public Health, Toulouse. University of Toulouse III F-31073, 37, allées Jules Guesde, 31073 Toulouse, France
CHU Toulouse (Toulouse University Hospital) Geriatric Department, Hôpital Purpan Pavillon Leriche Place Baylac, 31300 Toulouse, France

Jacques Izopet
CHU Toulouse, Hôpital Purpan, Virology Laboratory, 31300 Toulouse, France
INSERM UMR1291 – CNRS UMR5051, Toulouse Institute for Infectious and Inflammatory Diseases (INFINITy), 31300 Toulouse, France

*Corresponding author at: 330 av de Grande Bretagne, 31052 Toulouse, France.
E-mail address: dimeglio.c@chu-toulouse.fr (C. Dimeglio)