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BRIEF REPORT

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Immunogenicity of the BNT162b2 vaccine in frail or disabled nursing home residents: COVID-A study

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Abstract

Background/Objectives: The safety and immunogenicity of the BNT162b2 coronavirus disease 2019 (COVID-19) vaccine in older adults with different frailty and disability profiles have not been well determined. Our objective was to analyze immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in older adults across frailty and disability profiles.

Design: Multicenter longitudinal cohort study.

Setting and participants: A total of 134 residents aged ≥65 years with different frailty and disability profiles in five long-term care facilities (LTCFs) in Albacete, Spain.

Intervention and measurements: Residents were administered two vaccine doses as per the label, and antibody levels were determined 21.9 days (SD 9.3) after both the first and second dose. Functional variables were assessed using activities of daily living (Barthel Index), and frailty status was determined with the FRAIL instrument. Cognitive status and comorbidity were also evaluated.

Results: Mean age was 82.9 years (range 65–99), and 71.6% were female. The mean antibody titers in residents with and without previous COVID-19 infection were 49,878 AU/ml and 15,274 AU/ml, respectively (mean difference 34,604; 95% confidence interval [CI]: 27,699–41,509). No severe adverse reactions were observed, after either vaccine dose. Those with prevaccination COVID-19 had an increased antibody level after the vaccine ($B = 31{,}337$; 95% CI: 22,725–39,950; $p < 0.001$). Frailty, disability, older age, sex, cognitive impairment, or comorbidities were not associated with different antibody titers.

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Conclusions: The BNT162b2 mRNA COVID-19 vaccine in older adults is safe and produces immunogenicity, independently of the frailty and disability profiles. Older adults in LTCFs should receive a COVID-19 vaccine.

KEYWORDS
BNT162b2 vaccine, COVID-19, disability, frailty, immunogenicity, older adults

INTRODUCTION

Older adults, mainly those living in nursing homes and long-term care facilities (LTCFs), are the most vulnerable population group and are well known to have been disproportionately affected by coronavirus disease 2019 (COVID-19).[1-4] Specifically, this population experiences high COVID-19-related mortality rates with older age, frailty, dementia, and multimorbidity being additional risk factors.[5-7] For these reasons, older adults in LTCFs have been the first group to receive COVID-19 vaccines in many locations.[8]

Vaccines against influenza, pneumococcal infection, and herpes zoster have demonstrated persistence of immunity and efficacy for preventing morbidity and mortality among older adults. However, immunogenicity of traditional vaccines is suboptimal in populations aged 70 and older, likely due to a combination of factors most notably immunosenescence.[9] Although functional status and frailty may predispose to both infection risk and vaccine responsiveness and may be more important than resident age,[10] it has been described that older adults seroconvert after influenza vaccination across frailty strata, indicating that frail individuals may also benefit from this vaccine.[11]

Currently four SARS-CoV-2 vaccines are available, two nucleic acid-based vaccines—BNT162b2 by Pfizer-BioNTech and mRNA-1273 from Moderna—and two adenovirus vector-based vaccines—Ad26.COV2.S from Janssen/Johnson & Johnson and ChAdOx1 nCoV-19 from Oxford-AstraZeneca. There have, however, been a lack of individuals with frailty or disability in these and other randomized clinical trials.[12,13] Recent data from Israel suggest that immunogenicity of BNT162b2 decreases with age, highlighting the importance of monitoring populations not included in clinical trials like very old adults, those in care facilities, with frailty or disability, the most vulnerable to COVID-19.[14]

Here, we report immunogenicity of BNT162b2 in older adults in LTCFs with different frailty and disability profiles, thereby providing real-world observational data in this particularly vulnerable and understudied population.

Key Points

- The BNT162b2 coronavirus disease 2019 (COVID-19) vaccine in older adults is safe and produces immunogenicity, independent of the frailty and disability profile
- Age, sex, comorbidity, and cognitive status do not affect BNT162b2 vaccine immunogenicity
- Only prevaccination COVID-19 status is an independent predictor of immunogenicity

Why Does this Paper Matter?

Older adults develop immunogenicity to the BNT162b2 coronavirus disease 2019 (COVID-19) vaccine. Only prevaccination COVID-19 infection seems to be associated with a higher antibody titer. Our data support the use of BNT162b2 in older adults, irrespective of their level of frailty, disability, age, cognitive impairment, and comorbidity.

METHODS

The COVID-A study is a cohort longitudinal study that included 953 residents from five LTCFs in Albacete. Of these, 297 (31.2%) died in the first three pandemic months. From the remaining 656 (68.8%), we measured antibody levels between days 7 and 43 after the second dose of the BNT162b2 mRNA COVID-19 vaccine (Pfizer, New York, United States, and BioNTech, Mainz, Germany) from 134 consecutive residents of five LTCFs.

Baseline characteristics were not different between the complete 953 samples and the 134 residents included in this study. Inclusion criteria for the COVID-A study were living in one of the five LTCFs in Albacete, Spain, since the beginning of the pandemic, an age of 65 years or older, and permission and availability to participate in the study.[2]

Data regarding sociodemographics, functionality, cognitive status, and clinical variables were collected before the first vaccine dose. The first vaccine dose was administered between December 30, 2020, and January 31, 2021, and second dose between January 20 and February 19, 2021 (mean days 21; SD 0.8). Antibodies were determined between January 28 and March 3, 2021 (mean days from second dose to antibody determination were 21.9; SD 9.3; range 7–42 days). Vaccines were administered on-site at the LTCFs using standard protocols.

Samples were analyzed with the SARS-CoV-2 IgG QUANT (Abbott®) antibody test to detect levels of IgG antibodies that attach to the virus' spike protein on the virus surface in serum or plasma. Data interpretation was negative when titers were below 50 AU/ml and positive when ≥50 AU/ml. Although the upper limit is >40,000 AU/ml, it was possible to use dilution to expand the upper limit to >80,000 AU/ml.

Functional variables assessed were disability in basic activities of daily living measured with the Barthel Index,[15] and frailty status determined with the FRAIL instrument.[16] The Barthel Index was categorized into four categories: no disability (90–100 points), low disability (60–85 points), moderate disability (40–55 points), and severe disability (<40 points). Frailty was considered when the FRAIL instrument score was equal or superior to three positive criteria. Chronic diseases or comorbidities were retrieved from the medical records, and comorbidity was determined with the Charlson Comorbidity Index.[17] High comorbidity was defined as a Charlson Comorbidity Index score of 3 or higher. The cognitive status of the residents was assessed using the Global Deterioration Scale (GDS) from Reisberg.[18] The GDS was categorized into three categories: no dementia (score 1–3), mild-to-moderate dementia (score 4–5), and severe dementia (score 6–7). The diagnosis of COVID-19 infection before vaccination was also retrieved from medical records, based on positive SARS-CoV-2 polymerase chain reaction, positive serology, and/or antigen rapid test.

Data are presented as means ± standard deviation (SD) or number of participants (%). Differences were analyzed with χ^2 tests, Student's *t*-tests, or analysis of variance as indicated. Linear regression models were constructed to analyze the adjusted variables associated with antibody titers in this population. Our research was conducted in accordance with the Helsinki Declaration for human medical research and approved by the local Ethics Review Committee, record 2020/04/039. All participants provided written informed consent before their inclusion in the study.

RESULTS

Table 1 presents the baseline characteristics of the participants. Mean age was 82.9 years (range 65–99) and 71.6% were female. Residents with confirmed prevaccination COVID-19 infection were more frequently frail and with higher comorbidities. The mean antibody titers in residents with and without previous COVID-19 measured 49,878 AU/ml and 15,274 AU/ml, respectively (mean difference 34,604, 95% confidence interval [CI]: 27,699–41,509). Only one resident, with a prior diagnosis of chronic lymphocytic leukemia, did not show evaluable antibody titers (0 AU/ml).

In bivariate analysis, antibody titers correlated significantly with the number of days from the second vaccine dose to the blood sample collection ($r = 0.395$; $p < 0.001$) and between antibody titers and the Charlson Index ($r = 0.205$; $p = 0.018$). IgG titers were 10,852 AU/ml (95% CI: 2167–19,536; $p = 0.015$) higher in those aged 80 years or more (39,304 AU/ml) compared with the younger ones (28,452 AU/ml) and 13,464 AU/ml (95% CI: 3901–23,027; $p = 0.006$) higher in those with a Charlson Index ≥3 (44,661 AU/ml) compared with those with lower comorbidity (31,197 AU/ml) (Figure 1). In contrast, no significant correlation was found between antibody titers and sex, Barthel Index, FRAIL instrument, and GDS ($p > 0.05$).

Multivariate analysis using a linear regression model revealed that only prevaccination COVID-19 was an independent predictor of immunogenicity ($B = 31{,}337$; 95% CI: 22,725–39,950; $p < 0.001$). In this model, by contrast, frailty (FRAIL instrument: $B = 668$; 95% CI: −3553–4774; $p = 0.748$), disability (Barthel Index: $B = 131$; 95% CI: −32 to 294; $p = 0.115$), older age (years old: $B = 299$; 95% CI: −170 to 767; $p = 0.209$), sex (male sex: $B = 4874$; 95% CI: −3553 to 13,300; $p = 0.255$), cognitive impairment (GDS: $B = 1063$; 95% CI: −1075 to 3202; $p = 0.327$), comorbidity (Charlson Index: $B = 676$; 95% CI: −1501 to 3202; $p = 0.540$), or days between vaccination and antibody sampling (days: $B = 249$; 95% CI: −200 to 697; $p = 0.275$) were not associated with different antibody titers. Collinearity was not present among the variables included in the model.

DISCUSSION

No severe adverse reactions or anaphylaxis were observed following either vaccine dose. These data demonstrate

TABLE 1 Baseline characteristics and antibody titers of residents in long-term care facilities studied here

		Prevaccine COVID-19		
	Total sample ($n = 134$)	**Yes ($n = 78$)**	**No ($n = 56$)**	***p***
Age (mean, SD)	82.9 (8.1)	83.6 (7.6)	82.0 (8.8)	0.257
≥80 years (*n*, %)	86 (64.2)	53 (67.9)	33 (58.9)	0.283
Sex (*n*, %)				
Female	96 (71.6)	56 (71.8)	40 (71.4)	0.963
Male	38 (28.4)	22 (28.2)	16 (28.6)	
Barthel Index (mean, SD)	42 (34)	40 (31)	46 (37)	0.302
90–100 (*n*, %)	16 (11.9)	6 (7.7)	10 (17.9)	0.318
60–85 (*n*, %)	31 (23.1)	18 (23.1)	13 (23.2)	
40–55 (*n*, %)	26 (19.4)	17 (21.8)	9 (16.1)	
0–35 (*n*, %)	61 (45.5)	37 (47.4)	24 (42.9)	
FRAIL (mean, SD)	2.3 (1.1)	2.5 (1.1)	2.0 (1.1)	0.012
Frail (*n*, %)	59 (44.0)	42 (53.8)	17 (30.4)	0.007
Disability/Frailty (*n*, %)				
Nonfrail/no severe disability	52 (38.8)	24 (30.8)	28 (50.0)	0.021
Frail/no severe disability	21 (15.7)	17 (21.8)	4 (7.1)	
Severe disability	61 (45.5)	37 (47.4)	24 (42.9)	
GDS (mean, SD)	4.3 (2.4)	4.4 (2.3)	4.1 (2.4)	0.478
1–3 (*n*, %)	49 (36.6)	26 (33.3)	23 (41.1)	0.656
4–5 (*n*, %)	26 (19.4)	16 (20.5)	10 (17.9)	
6–7 (*n*, %)	59 (44.0)	26 (46.2)	23 (41.1)	
Charlson Index (mean, SD)	2.0 (1.7)	2.4 (1.8)	1.5 (1.4)	0.002
≥3 (*n*, %)	59 (44.0)	32 (41.0)	46 (17.9)	0.004
Antibody titers (mean, SD)	35,417 (26,612)	49,878 (21,687)	15,274 (18,557)	<0.001

Abbreviation: GDS, Global Deterioration Scale from Reisberg.

that the BNT162b2 mRNA COVID-19 vaccine is safe in older adults and it generates immunogenicity, irrespective of frailty, disability, cognitive impairment, or old age. The demonstration of immunogenicity after the vaccine in older adults is important, although the prevention of transmission, infection, disease presentation and severity, hospitalization, admission to intensive care units, and mortality are the main outcomes that will need to be assessed in these sorts of future observational studies.[19] We emphasize that these data do not allow us to draw conclusions whether those older adults with immunogenicity after the vaccine will be protected against SARS-CoV-2 infection and COVID-19.

Recruitment of older participants in vaccine trials is challenging despite the high burden of infectious diseases in this population.[20] For this reason, the inclusion of older adults in RCTs has been limited. It is important to proactively enhance the enrolment of older participants in COVID-19 vaccine trials through different strategies like targeted engagement, facilitation programs, and proactive sharing of study results.[19] In the meantime, data from observational real-life studies like ours are relevant to understand the vaccination response of this vulnerable population. A recent study in Israel has described immunogenicity 21 days after first vaccine dose among 514 healthcare workers, adjusted by age, ethnicity, sex, and prior COVID-19 infection. Immunogenicity was similar by ethnicity and sex but decreased with age. Those with prior infection had antibody titers one magnitude order higher than naïve individuals regardless of the presence of detectable IgG antibodies prevaccination.[14] Although we did not compare our sample with young or old participants from the community, antibody titers are high enough to conclude that the vaccine resulted in good immunogenicity.

It has been proposed that immunosenescence of innate and adaptive immunity together with chronic low-grade inflammatory phenotype (CLIP) or inflammaging

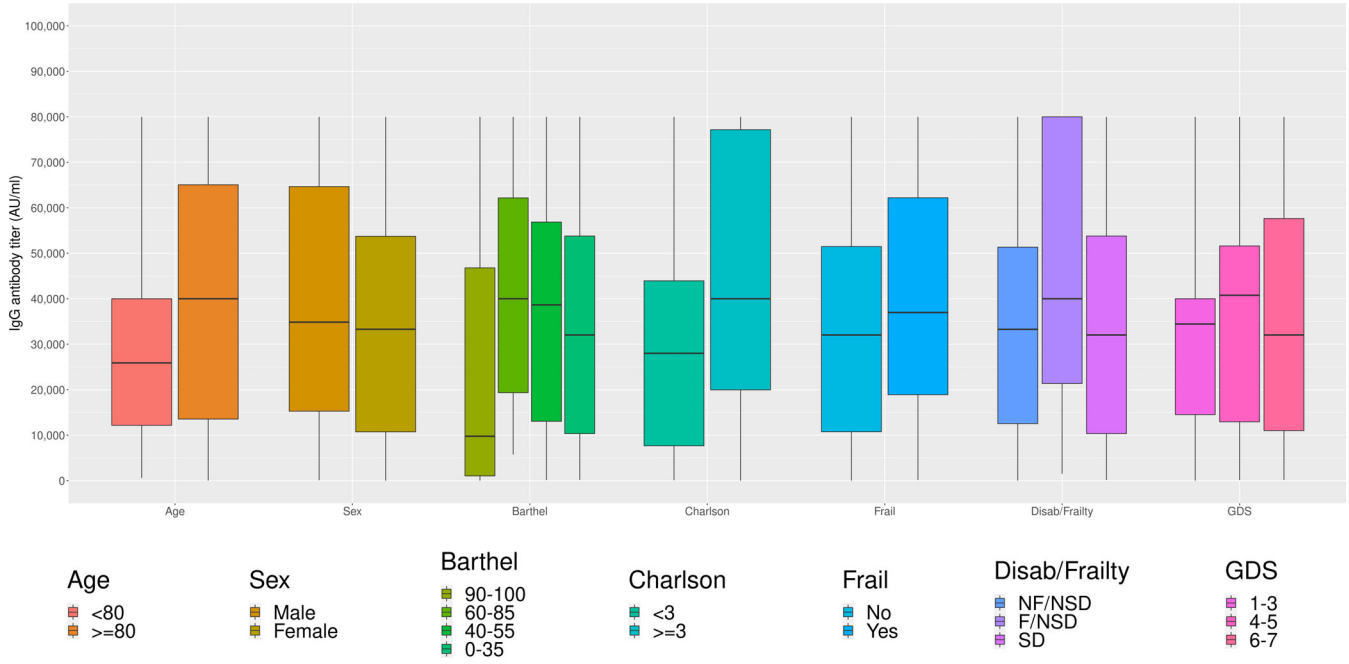

FIGURE 1 SARS-CoV-2 IgG antibody titers depending on older adults' profiles. Disab/Frailty, composite variable of disability in basic activities of daily living and frailty; NF/NSD, nonfrail/no severe disability; F/NSD, frail/no severe disability; SD, severe disability; GDS, Global Deteriorating Scale from Reisberg. *$p < 0.05$; **$p < 0.01$

may be the reasons for poor responses to immunization in older adults.[21] These mechanisms have also been implicated in the pathogenesis of frailty,[22] but the immunogenic response in frail and nonfrail residents was similar in our sample. In acute severe COVID-19 infections, there is impaired cellular immunity, although residents develop positive SARS-CoV-2-specific antibody responses.[23] These findings support the idea that cellular immunity may be more important than humoral immunity in the frailty-associated immunosenescence process, data that require validation in larger studies.[22]

CONCLUSIONS AND IMPLICATIONS

Older adults in LTCFs develop immunogenicity to the BNT162b2 mRNA COVID-19 vaccine with a minimum of toxicity. Only prevaccination COVID-19 was associated with a higher antibody titer. As such, our data support the use of BNT162b2 in geriatric cohorts, irrespective of their level of frailty, disability, age, cognitive impairment, and comorbidity.

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CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest, except. V.M.L. declares no conflict of interest according to the ICMJE Uniform Requirements but discloses the following financial relationship: CEO and shareholder of HepaPredict AB; co-founder and chairman of the board PersoMedix AB; consultancy work for Enginzyme AB. JS declares his conflict at https://www.nature.com/onc/editors, and none are relevant here.

AUTHOR CONTRIBUTIONS

- Sergio Salmerón Ríos: Design of the work, data interpretation, drafting of the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Marta Mas Romero, Elisa Belén Cortés Zamora, María Teresa Tabernero Sahuquillo, Inmaculada García

Nogueras, Juan de Dios Estrella Cazalla, Antonio Murillo Romero: Data acquisition, drafting of the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

- Luis Romero Rizos, Pedro Manuel Sánchez-Jurado, Ginés Sánchez-Nievas, José Joaquín Blas Señalada, Fernando Andrés-Pretel: Data analysis and interpretation, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Volker Martin Lauschke, Justin Stebbing: Data interpretation, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Pedro Abizanda: Design of the work, data analysis and interpretation, drafting of the work, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- All authors had a role in writing the final manuscript and approved the final version.

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There is no sponsor role in the manuscript.

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REFERENCES

1. Comas-Herrera A, Zalakain J, Lemmon E, et al. Mortality associated with COVID-19 in care homes: international evidence. Article in LTCcovid.org, International Long-Term Care Policy Network, CPEC-LSE, 1st February 2021. https://ltccovid.org/2020/04/12/mortality-associated-with-covid-19-outbreaks-in-care-homes-early-international-evidence/.
2. Mas Romero M, Avendaño Céspedes A, Tabernero Sahuquillo MT, et al. COVID-19 outbreak in long-term care facilities from Spain. Many lessons to learn. *PLoS One*. 2020;15:1-15. https://doi.org/10.1371/journal.pone.0241030 eCollection 2020.
3. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc*. 2020;21:915-918. https://doi.org/10.1016/j.jamda.2020.05.045.
4. De La Rica-Escuín M, González-Vaca J, Varela-Pérez R, et al. Frailty and mortality or incident disability in institutionalized older adults: the FINAL study. *Maturitas*. 2014;78:329-334. https://doi.org/10.1016/j.maturitas.2014.05.022.
5. Bielza R, Sanz J, Zambrana F, et al. Clinical characteristics, frailty, and mortality of residents with COVID-19 in nursing homes of a region of Madrid. *J Am Med Dir Assoc*. 2020;22:245-252. https://doi.org/10.1016/j.jamda.2020.12.003.
6. De Smet R, Mellaerts B, Vandewinckele H, et al. Frailty and mortality in hospitalized older adults with COVID-19: retrospective observational study. *J Am Med Dir Assoc*. 2020;21:928-932.doi: 10.1016/j.jamda.2020.06.008.
7. Gutiérrez Rodríguez J, Montero Muñoz J, Jiménez Muela F, Guirola García-Prendes C, Gómez AL. Variables associated with mortality in a selected sample of patients older than 80 years and with some degree of functional dependence hospitalized for COVID-19 in a geriatrics service. *Rev Esp Geriatr Gerontol*. 2020;55:317-325. https://doi.org/10.1016/j.regg.2020.07.002.
8. Gharpure R, Guo A, Bishnoi CK, et al. Early COVID-19 first-dose vaccination coverage among residents and staff members of skilled nursing facilities participating in the pharmacy partnership for long-term care program - United States, December 2020–January 2021. *WR Morb Mortal Wkly Rep*. 2021;70:178-182. https://doi.org/10.15585/mmwr.mm7005e2.
9. Cunningham AL, McIntyre P, Subbarao K, Booy R, Levin M. Vaccines for older adults. *BMJ*. 2021;372:n188. https://doi.org/10.1136/bmj.n188.
10. Talbot HK, Libster R, Edwards KM. Influenza vaccination for older adults. *Hum Vaccin Immunother*. 2012;8:96-101. https://doi.org/10.4161/hv.8.1.18129.
11. Vipin Narang V, Lu Y, Tan C, et al. Influenza vaccine-induced antibody responses are not impaired by frailty in the community-dwelling elderly with natural influenza exposure. *Front Immunol*. 2018;9:2465. https://doi.org/10.3389/fimmu.2018.02465 eCollection 2018.
12. Teo SP. Review of COVID-19 vaccines and its evidence in older adults. *Ann Geriatr Med Res*. 2021. https://doi.org/10.4235/agmr.21.0011. Online ahead of print.
13. Palermo S. Covid-19 pandemic: maximizing future vaccination treatments considering aging and frailty. *Front Med (Lausanne)*. 2020;7:558835. https://doi.org/10.3389/fmed.2020.558835 eCollection 2020.
14. Jabal KA, Ben-Amram H, Beiruti K, et al. Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. *Euro Surveill*. 2021;26:2100096. https://doi.org/10.2807/1560-7917.ES.2021.26.6.2100096.
15. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Md State Med J*. 1965;14:61-65.
16. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging*. 2012;16:601-608. https://doi.org/10.1007/s12603-012-0084-2.

17. Charlson M, Szatrowski T, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47:1245-1251. https://doi.org/10.1016/0895-4356(94)90129-5.
18. Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982;139:1136-1139. https://doi.org/10.1176/ajp.139.9.1136.
19. Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. *Lancet Infect Dis*. 2021;21:e26-e35. https://doi.org/10.1016/S1473-3099(20)30773-8.
20. Allsup SJ, Gosney MA. Difficulties of recruitment for a randomized controlled trial involving influenza vaccination in healthy older people. *Gerontology*. 2002;48:170-173. https://doi.org/10.1159/000052837.
21. Crooke SN, Ovsyannikova IG, Poland GA, Kennedy RB. Immunosenescence and human vaccine immune responses. *Immun Ageing*. 2019;16:25. https://doi.org/10.1186/s12979-019-0164-9.
22. Wilson D, Drew W, Jasper A, et al. Frailty is associated with neutrophil dysfunction which is correctable with phosphoinositol-3-kinase inhibitors. *J Gerontol A Biol Sci Med Sci*. 2020;75:2320-2325. https://doi.org/10.1093/gerona/glaa216.
23. Ni L, Cheng ML, Feng Y, et al. Impaired cellular immunity to SARS-CoV-2 in severe COVID-19 patients. *Front Immunol*. 2021;12:603563. https://doi.org/10.3389/fimmu.2021.603563 eCollection 2021.

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